Joint International Tropical Medicine Meeting 2020

(JITMM Virtual 2020)

"Tropical Disease Control amid the COVID-19 Pandemic"
15-16 December 2020

ABSTRACTS

Tuesday 15 December 2020

Opening Ceremony

8.30-9.00hr

Opening Ceremony by Organizers and Co-organizers

Report

Asst. Prof. Weerapong Phumratanaprapin
Chair, JITMM Virtual 2020 Organizing Committee

Welcome Address

Dr. Opart Karnkawinpong
Director-General, Department of Disease Control, Thailand Ministry of Public Health

Welcome Address

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

Opening Remarks

Prof. Banchong Mahaisavariya
President, Mahidol University

Tuesday 15 December 2020

S1: The 25th Chamlong-Tranakchit Harinasuta Lecture

9.00-9.30hr

Chairperson
Jetsumon Prachumsri

Keynote Speaker

Tedros Adhanom Ghebreyesus
Director General of the World Health Organization

Tuesday 15 December 2020

S2: Chloroquine and hydroxychloroquine for COVID-19 prophylaxis

09.40-11.10hr

Room A

Chairpersons:
1. Kesinee Chotivanich
2. Nicholas Day

Invited speakers:
1. The COPCOV trial- an overview and update
   William Schilling
   Mahidol Oxford Tropical Medicine Research Unit

2. Safety of chloroquine and hydroxychloroquine
   Sir Nicholas White
   Mahidol Oxford Tropical Medicine Research Unit

3. Overview of trials of chloroquine and hydroxychloroquine in COVID-19 (no abstract)
   James Watson
   Mahidol Oxford Tropical Medicine Research Unit

4. Prevention vs Cure: a mechanistic review of chloroquine/ hydroxychloroquine in COVID-19
   Cintia Cruz
   Mahidol Oxford Tropical Medicine Research Unit

Title: The COPCOV trial- an overview and update

Author: William Schilling (Presenter), Mahidol Oxford Tropical Research Unit, Thailand

Background: COPCOV is the largest, and last remaining randomised controlled trial aiming to determine if chloroquine and hydroxychloroquine can prevent COVID-19 in the healthcare setting around the globe. Much has been written and discussed about the potential role of these two old drugs, used in the management of malaria and rheumatological conditions, in the COVID-19 pandemic. 9 months after the pandemic was declared we still do not know if they may be beneficial in the prevention and early treatment of COVID-19, although we do know they are not life-saving in late-stage treatment. Exaggerated concerns about safety driven by low quality evidence, in some cases fabricated, have damaged the long-held excellent reputation of safety of these drugs. Politicisation, overgeneralization, polarised opinion and negative media coverage have all made it very difficult to continue the trials needed to assess risks and benefits objectively and inform policies and practices, and many continue to be recommended and given these drugs around the world. In this talk, an overview of the COPCOV trial is given and the scientific background discussed, as well as the subsequent events which have shaped the trial's course. Finally, in light of roll out of vaccines, there is reflection on the rationale and on-going importance of the trial to answer one of the most prominent questions of the COVID-19 pandemic.

Title: Safety of chloroquine and hydroxychloroquine

Author: Sir Nicholas J White (Presenter), Mahidol Oxford Tropical Research Unit, Thailand, Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

Background: The 4-aminoquinolines chloroquine and hydroxychloroquine have both been proposed as potential treatments of COVID-19. These drugs are among the most widely used drugs ever, and in terms of human exposure, may be the drugs to which humans have been most exposed. There has been renewed interest in their toxicity profiles. In general, they are safe and well tolerated, but are dangerous in overdose and cause toxicity to the eyes and muscles (including the heart) with long term high dose usage. Their potential for acute cardiotoxicity (notably the risk of torsade de pointes) reflected by ECG QT prolongation has been much debated. Overall the results of trials in COV-19 are very reassuring. This presentation will review the evidence for toxicity, focusing on cardiotoxicity.

Title: Prevention vs Cure: a mechanistic review of of chloroquine/ hydroxychloroquine in COVID-19

Author: Cintia Cruz (Presenter), Mahidol Oxford Tropical Research Unit, Thailand

Background: The pandemic coronavirus disease-19 (COVID-19) counts more than 34.000.000 cases across the globe and caused 1.000.000 deaths. There is currently no treatment nor vaccine approved for this condition, and a number of different drugs for prophylaxis or treatment against COVID-19 are being studied and/or used off-label in different countries. Among those investigational drugs, Chloroquine (CQ) and hydroxychloroquine (HCQ), used for malaria and rheumatic diseases respectively have gained broad interest. But unlike no other drugs, have been subject of huge controversy mainly driven by media and politics. Our aim is to present the pharmacodynamic reasoning and discussing evidence behind the hypothesis that CQ/HCQ work in COVID-19 pre-exposure prophylaxis even if they don´t show any benefit in treatment nor post exposition prevention.

Study Design & Methods: We´ll present- The pharmacodinamics of chloroquine and hydroxychloroquine in viral infections. - Data on efficacy: Anti covid-19 in vitro and in vivo pre-clinical activity, as well as other potential mechanisms of antiviral activity.
Results: Lack of efficacy in treatment and post exposure indications and its potential explanation will be discussed.

Conclusions: The question of whether these drugs work in pre-exposure prophylaxis for covid-19 remains unanswered though, as do definitive answers as to whether they work in post-exposure prophylaxis or early treatment. In vitro evidence, knowledge of the pharmacokinetic properties of the drug and the pathophysiology of disease all support the earlier use of these drugs and support pre-exposure prophylaxis to be their most likely successful application against COVID-19, even if they are proven not to work used in other scenarios. There is a consensus, promoted by the World Health Organisation, that large and definitive randomised controlled trials are needed to provide the much-needed evidence in this global emergency. However, many obstacles have appeared for clinical research in general, and for these drugs in particular.We advocate for the clinical equipoise that still exists for the hypothesis that CQ and HCQ can be useful in the pre-exposure prophylaxis of COVID-19.

Tuesday 15 December 2020

S3: Malaria parasite epidemiology and population dynamics during elimination

9.40-11.10hrs

Room B

Chairperson: Liwang Cui

Invited speakers:

1. Estimates of *Plasmodium falciparum* population demography in the context of multidrug resistance
   Shannon Takala-Harrison
   University of Maryland School of Medicine, United States

2. Population genomic insights into the impact of malaria control on *Plasmodium falciparum* transmission dynamics and sources of resurgence
   Alyssa Barry
   Deakin University, Australia

3. Population dynamics and structure of *Plasmodium vivax* in the Greater Mekong sub-region during elimination
   Liwang Cui
   University of South Florida, United Sates

4. Multilevel effects of targeted mass drug administration for elimination of *P. falciparum malaria* on the Thailand-Myanmar border
   Daniel Parker
   University of California, Irvine, United States

Title: Estimates of *Plasmodium falciparum* population demography in the context of multidrug resistance

Author: Shannon Takala-Harrison (Presenter), University of Maryland School of Medicine, United States

Background: The emergence of multidrug-resistant *P. falciparum* has prompted efforts to eliminate malaria from the Greater Mekong Subregion. Estimates of identity-by-descent (IBD) are being used to understand the genetic relatedness and effective population size of parasite populations in relation to human movement, targeted interventions, and the geographic properties of a region. Such estimates may allow strategic allocation of resources and evaluation of progress toward elimination. In this work, we used IBD estimates and migration surfaces to understand *P. falciparum* population structure, migration, and effective population size, and how these estimates are impacted by selective sweeps.

Study Design & Methods: Genome-wide SNPs were called from 1,722 clinical isolates from 54 districts in the GMS and Bangladesh, as well as from whole genome sequencing data generated from 276 clinical isolates collected at a single study site in northern Cambodia over five years. IBD segments were inferred between pairs of isolates using Beagle 4.1. IBD estimates and migration surfaces were examined to understand parasite migration and fine-scale population structure based on the regional data set. IBDne was used to estimate effective population size (Ne) in the local data set, both including and excluding genomic regions with IBD peaks or known drug resistance genes.

Results: Pairwise IBD sharing revealed parasite population structure at a district level. Migration surfaces indicated potential migration barriers corresponding to malaria-free urban centers, geographical features, and some political borders. In Cambodia, IBD sharing within and between districts increased in more recent time frames. Based on the local dataset, 2.0% ± 0.6% of pairs shared IBD segments. IBD segments were distributed genome wide, and IBD peaks did not include known drug resistance genes. After removing IBD segments associated with known drug resistance genes or IBD peaks, estimates of Ne increased up to 2-fold in the last 8-10 generations; however, the overall pattern of Ne over the past 100 generations remained similar.

Conclusions: Estimates of IBD sharing and migration surfaces were able to identify regional parasite migration patterns and population structure in intermediate time frames. However, the high level of IBD sharing among parasites collected in more recent time frames, driven in part by selection for drug resistance, may present challenges for application of IBD-based metrics to understand parasite population demography in this setting.

Title: Population genomic insights into the impact of malaria control on *Plasmodium falciparum* transmission dynamics and sources of resurgence

Author: Alyssa Barry (Presenter), Deakin University, Australia

Background: Genomic epidemiology has emerged as an important component of the toolbox to guide malaria control and elimination. Parasite genotyping using marker panels that capture the diversity and relatedness amongst parasite genomes within the local area are critical to provide accurate insights into transmission dynamics and gene flow. Whilst microsatellite markers provide indications that declining prevalence increases focal inbreeding, they fail to capture significant changes in relatedness patterns or changes in population structure. SNP barcodes comprised of more than 100 biallelic SNPs are more reliable to measure Identity by Descent (IBD) patterns and this analysis captures relatedness patterns within and between populations with greater resolution than traditional population-level metrics.

Study Design & Methods: SNP barcodes and IBD approaches were used to monitor *Plasmodium falciparum* populations in Papua New Guinea over a period of declining transmission from 2005 to 2014 and resurgence in 2016.

Results: We have shown limited changes in overall parasite diversity but an increase in pairwise IBD. Successful control leads to multiple bottlenecks resulting in distinct IBD clusters found focally within villages in a background of diverse genotypes. As malaria once again resurges, lineages from these focal clusters expand and spread between villages and provinces, and distinct clusters recombine to generate new recombinant lineages.

Conclusions: Monitoring parasite population genomics during control reveals impacts on the underlying parasite population and highlights the importance of ongoing sustained control together with genomic surveillance to prevent hard-won gains against malaria being reversed.

Title: Population dynamics and structure of *Plasmodium vivax* in the Greater Mekong sub-region during elimination

Author: Liwang Cui (Presenter), University of South Florida, United Sates

Background: As countries within the Greater Mekong Sub-region (GMS) of Southeast Asia have committed to eliminating malaria by 2030, *Plasmodium vivax* has become the predominant malaria parasite in many endemic regions. To gain a better understanding of transmission dynamics, we want to understand how the scaled-up control interventions affect the parasite population structure and dynamics.

Study Design & Methods: We investigated the changes in parasite populations along two international borders over 3 and 10 years using microsatellite markers. We further used population genomics to study parasite population structure and differentiation in the GMS.

Results: Genetic diversity in the parasite populations remained high, but there were substantial decreases in polyclonal infections in the border populations studied over the years, with corresponding decreases in the multiplicity of infection. Consistent with the shrinking map of malaria transmission in the GMS over time, there were also increases in multilocus linkage disequilibrium, suggesting more fragmented and increasingly inbred parasite populations. Using genome-wide SNPs, we compared 21 *P. vivax* genomes from the China-Myanmar border with over 200 samples from the rest of the GMS. We found that the China-Myanmar border parasites displayed a higher proportion of monoclonal infections, and 52% shared over 90% of their genomes in identity-by-descent segments with at least one other sample from the same place, suggesting a preferential expansion of certain parasite strains in this region, likely resulting from the *P. vivax* outbreaks occurring during this study period. We found substantial population differentiation between the eastern and western GMS, whereas the eastern GMS parasite populations (from Cambodia and Vietnam) were largely undifferentiated. Such a genetic differentiation pattern of the *P. vivax* populations from the GMS parasite was largely explainable through geographic distance.

Conclusions: A better understanding of the control efforts on parasite population changes will guide more targeted control efforts to eliminate malaria in the GMS.

Title: Multilevel effects of targeted mass drug administration for elimination of *P. falciparum* malaria on the Thailand-Myanmar border

Author: Daniel Parker (Presenter), University of California, Irvine, United States

Background: The burden of malaria has decreased in much of the Greater Mekong Subregion. All nations of the GMS have committed to eliminating malaria by the year 2030. One major obstacle to achieving elimination is asymptomatic infections, which are likely infectious and are unlikely to be detected and treated by conventional means. A proposed solution to this problem is targeted mass drug administration (MDA), whereby communities with identified reservoirs are asked to take antimalarials regardless of the absence or presence of symptoms. MDA is strongly dependent on community buy-in, requiring a sufficient proportion of the population to participate in order to achieve the desired effect. Here is present detailed, empirical, spatio-temporal data on the effects of MDA on malaria incidence in target villages along the Thailand-Myanmar border.

Study Design & Methods: Epidemiological and demographic data were collected as part of a pilot study in four villages in Kayin State, Myanmar on the safety and effectiveness of MDA to eliminate *P. falciparum* malaria. All households in the villages were georeferenced and all individuals in the study were linked to their respective households via a demographic surveillance system. Exploratory spatial analyses were used to look at the dynamics of incident malaria cases post-MDA. A multi-level regression was used to test for individual and neighborhood level effects of MDA with regard to incidence malaria.

Results: Regardless of individual participation, villagers from neighborhoods with the highest levels of MDA adherence had 90% decreased odds of having a *P. falciparum* case post-MDA. High mosquito biting rates, living in a house with someone else who had malaria, and previously having a malaria infection were also predictive of having an incident *P. falciparum* case post-MDA.

Conclusions: Clusters of non-adherence to MDA can frustrate elimination efforts.

Tuesday 15 December 2020

S4: Neurobehavioral impact of tropical diseases

09.40-11.10hr

Room C

Chairperson: Matthew Reed

Invited speakers:

1. Neurocognitive impact of Zika Virus infection in adult rhesus macaque
   Denise Hsu
   Armed Forces Research Institute of Medical Sciences, Thailand

2. Mental distress and neuroimmune activation in acute infection predicts treatment response and long-term HIV disease outcomes
   Robert Paul
   UMSL, United States

Title: Neurocognitive impact of Zika Virus infection in adult rhesus macaques

Author: Denise Hsu (Presenter), Armed Forces Research Institute of Medical Sciences, Thailand

Co-authors: Stefan Fernandez, Sandhya Vasan, Lishomwa Ndhlovu, Rawiwan Imerbsin, Luis Lugo, Alexandra Schuetz, Robert Paul, Kayvon Modjarrad, Kesara Chumpolkulwong, Michael Corley , Dutsadee Inthawong, Taweewun Hunsawong

Background: Zika Virus (ZIKV) infection affects many regions of the world. Infection during pregnancy is associated with microcephaly, developmental and neurologic impairments. The impact of ZIKV on neurocognition in adult infection is unknown.

Study Design & Methods: Adult rhesus macaques (4 male and 4 female) aged 5-8 years were trained to perform neurocognitive assessment using the Cambridge Neuropsychological Test Automated Battery (CANTAB) administered via a touch screen. CANTAB assessments occurred before and after subcutaneous ZIKV inoculation at 1 million plaque forming unit.

Results: All animals had detectable ZIKV in plasma at day 1 post-inoculation (PI) that peaked at day 2 PI (median 5.9, IQR 5.6-6.2 log10 GE/mL). In all animals, ZIKV became undetectable in plasma by day 14 PI but persisted in lymphoid tissues. ZIKV was not detected in cerebral spinal fluid (CSF) supernatant at any assessment period. Low levels of ZIKV were detected in the meninges and brain of 2 animals. ZIKV infection was also associated with a transient elevation in soluble and cellular markers of immune activation in the peripheral blood and CSF. Transient reduction in reaction speed and accuracy on CANTAB testing was identified in a subset of animals.

Conclusions: Zika virus infection was associated with transient plasma viremia, immune activation in the peripheral blood and CSF as well as neurocognitive impairment in a subset of animals.

Title: Mental distress and neuroimmune activation in acute infection predicts treatment response and long-term HIV disease outcomes

Author: Robert Paul (Presenter), UMSL, United States

Background: Approximately 40% of people living with HIV (PLWH) do not achieve a favorable clinical phenotype after sustained use of suppressive ART. This heterogeneity cannot be fully explained by individual differences in treatment compliance. Prior studies focused on developing models to explain heterogeneous treatment outcomes after ART have utilized analytic methods that are generally insensitive to interactions and nonlinear patterns in complex clinical data.

Study Design & Methods: Baseline and 96-week follow-up data from 433 participants enrolled in RV254/SEARCH 010 were included in the analysis. Individuals were classified according to favorable/unfavorable phenotypes based on previously established criteria (i.e., AIDS-defining illness or grade 4 AEs, CD4<500 cells/mm3, CD4/CD8 ratio<1.0, viral load> 20 copies). Gradient-boosted multivariate regression (GBM) was implemented to identify the features Model performance was defined by the average Area Under the Curve (AUC). Additionally, multi-variate group-based trajectory analyses were conducted to identify distinct subgroups from baseline to week 96. Inferential models examined baseline variables that differed by subgroup.

Results: The linear GBM predicted phenotype designation at Week 96 with an average accuracy of 72. CD4 and CD8 T cells were dominant features in the classifier, with additional contributions from monocyte counts, neurocognitive performance, later Fiebig stage, and participant age. The 2-way interaction model improved classification to 79%. This model more clearly identified CD4/CD8 T cell ratio inversion as the primary contributor to poor treatment outcomes with additional contributions from interactions involving treatment regimen, immune suppression, Fiebig stage, viral load, plasma neopterin, neurocognitive performance and mental distress. Group-based trajectory analyses identified four distinct CD4/CD8 ratio subgroups. Mental distress at baseline differentiated individual membership in the CD4/CD8 ratio subgroups.

Conclusions: Interactions between viral, immune, and host features efore ART predict treatment phenotype designation years after treatment onset. Mental distress, particularly when the viral reservoirs are seeded, creates a tipping point for the induction of immune mechanisms that lead to chronic inversion of CD4/CD8 T cell ratio, and in turn, increased risk for clinical complications in PLWH defined as virally suppressed.

Tuesday 15 December 2020

S5: New targets for detection and intervention in melioidosis

09.40-11.10hr

Room D

Chairpersons**:**

1. Narisara Chantratita
2. Paul Brett

Invited speakers**:**

1. Innate-like lymphocytes in melioidosis
   Shelton Wright
   University of Washington, United States

2. Blood transcriptomics to characterize key biological pathways and identify biomarkers for predicting mortality in melioidosis
   Thatcha Yimthin
   Mahidol University, Thailand

3. Tetraspanins are involved in *Burkholderia pseudomallei*-induced cell-to-cell fusion of phagocytic and non-phagocytic cells
   Tanes Sangsri
   Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Thailand

4. Seroprevalence of *Burkholderia pseudomallei* in low-incidence melioidosis areas of Thailand and Myanmar
   Janjira Thaipadungpanit
   Department of Clinical Tropical Medicine and Mahidol-Oxford Tropical Medicine Research Unit, Faculty, Thailand

Title: Innate-like lymphocytes in melioidosis

Author: Shelton Wright (Present), University of Washington, United States

Background: Innate-like lymphocytes are highly conserved T cell subsets which can be activated within hours of infection and do not require antigen-presentation. The role of gamma-delta T cells in severe pneumonia such as that caused by the tropical pathogen *Burkholderia pseudomallei* is unknown. We hypothesized that gamma-delta T cells in clinical melioidosis and animal models of pulmonary infection serve a critical role in the initial inflammatory response.

Study Design & Methods: We investigated the role of gamma-delta T cells by employing human samples as well as mouse models of infection. Whole blood samples were obtained from Thai patients with melioidosis and cell populations were identified by flow cytometry. Additionally, mice infected with aerosolized *Burkholderia thailandensis* were subsequently analyzed for pulmonary T cell populations and the functional role of gamma-delta T cells.

Results: Thai adults with melioidosis have evidence of a peripheral gamma-delta T cell response that may be associated with survival. Furthermore, gamma-delta T cells also appear to be activated in the lungs of *B. thailandensis*-infected mice and may play a role in bacterial clearance and immune response regulation.

Conclusions: gamma-delta T cells are activated in both clinical melioidosis and animal models of pulmonary melioidosis. Further studies will seek to elucidate the functional mechanisms related to gamma-delta T cell activation.

Title: Blood transcriptomics to characterize key biological pathways and identify biomarkers for predicting mortality in melioidosis

Author: Thatcha Yimthin (Presenter), Mahidol University, Thailand

Co-authors: Chumpol Morakot, Clare Eckold, Ekkachai Thiansukhon, Ganjana Lertmemongkolchai, Jacqueline Margaret Cliff, Ji-Sook Lee, Kittisak Tanwisaid, Megan Andrada, Narisara Chantratita, Narongchai Sangsa, Nicholas Day, Noppol Buasi, Peeraya Ekchariyawat, Rungnapa Phunpang, Somchai Chuananont, Sunee Chayangsu, T. Eoin West, Taniya Kaewarpai, Wasun Chantratita, Wirayut Silakun

Background: Melioidosis is a tropical infectious disease caused by the Gram-negative bacillus, *Burkholderia pseudomallei* that is often lethal in many endemic areas. The objective of this study was to characterize the transcriptome in melioidosis patients and identify genes associated with outcome.

Study Design & Methods: RNA-seq was performed on whole blood RNA in a discovery set of 29 melioidosis patients and 3 healthy controls using Ion AmpliSeq Transcriptome. Transcriptomic profiles of patients who did not survive to 28 days were compared with patients who survived and healthy controls. RT-qPCR of 28 differentially expressed genes was performed in a validation set of 60 melioidosis patients and 20 healthy controls.

Results: In RNA-seq analysis, 65 genes were significantly up-regulated and 218 were down-regulated in non-survivors compared to survivors. Up-regulated genes were involved in myeloid leukocyte activation, Toll-like receptor cascades and reactive oxygen species metabolic processes. Down-regulated genes were hematopoietic cell lineage, adaptive immune system and lymphocyte activation pathways. RT-qPCR in the validation set of patients confirmed differential expression of a subset of genes. IL1R2, GAS7, S100A9, IRAK3, and NFKBIA were significantly higher in non-survivors compared with survivors ($P < 0.005$) and healthy controls ($P < 0.0001$). The AUCs of these genes for mortality discrimination ranged from 0.80-0.88. In survivors, expression of IL1R2, S100A9 and IRAK3 genes decreased significantly over 28 days ($P < 0.05$).

Conclusions: Whole blood transcriptomics characterizes the host response in melioidosis. Expression levels of specific genes are potential biomarkers to predict outcomes. These findings augment our understanding of this often severe infection.

Title: Tetraspanins are involved in *Burkholderia pseudomallei*-induced cell-to-cell fusion of phagocytic and non-phagocytic cells

Author: Tanes Sangsri (Presenter), Department of Microbiology and Immunology, Faculty of Tropical Medicine, Mahidol University, Thailand

Co-authors: Alisa Tubsuwan, Lynda J. Partridge, Narisara Chantratita, Natnaree Saiprom, Peter Monk

Background: Tetraspanins are four-span transmembrane proteins of host cells that facilitate infections by many pathogens. *Burkholderia pseudomallei* is an intracellular bacterium and the causative agent of melioidosis, a severe disease in tropical regions. This study investigated the role of tetraspanins in B.pseudomallei infection.

Study Design & Methods: We used flow cytometry to determine tetraspanins CD9, CD63, and CD81 expression on A549 and J774A.1 cells. Their roles in *B. pseudomallei* infection were investigated in vitro using monoclonal antibodies (MAbs) and recombinant large extracellular loop (EC2) proteins to pretreat cells before infection. Knockout of CD9 and CD81 in cells was performed using CRISPR Cas9 to confirm the role of tetraspanins.

Results: Pretreatment of A549 cells with MAb against CD9 and CD9-EC2 significantly enhanced *B. pseudomallei* internalization, but MAb against CD81 and CD81-EC2 inhibited MNGC formation. Reduction of MNGC formation was consistently observed in J774.A1 cells pretreated with MAbs specific to CD9 and CD81 and with CD9-EC2 and CD81-EC2. Data from knockout experiments confirmed that CD9 enhanced bacterial internalization and that CD81 inhibited MNGC formation.

Conclusions: Our data indicate that tetraspanins are host cellular factors that mediated internalization and membrane fusion during *B. pseudomallei* infection. Tetraspanins may be the potential therapeutic targets for melioidosis.

Title: Seroprevalence of *Burkholderia pseudomallei* in low-incidence melioidosis areas of Thailand and Myanmar

Author: Janjira Thaipadungpanit (Presenter), Department of Clinical Tropical Medicine and Mahidol-Oxford Tropical Medicine Research Unit, Faculty, Thailand

Co-authors: Thomas Althaus, Supawat Chatchen, Wanitda Watthanaworawit, Paul J Brett, Nicholas Day, Yoel Lubell, Narisara Chantratita

Background: Melioidosis is an important disease with over 160,000 estimated cases annually worldwide. In Thailand, the other regions have lower numbers of culture-confirmed melioidosis cases comparing with Northeast because of unawareness of disease, asymptomatic cases, or unable to access reliable diagnosis tools. This study aims to investigate the melioidosis burden in the areas having low reported case numbers in Thailand and Myanmar.

Study Design & Methods: All 1,320 patient sera and 150 healthy sera from four regions in Thailand and Myanmar were screened for melioidosis using the anti-Hcp1 IgG ELISA, with 1.16 optical density (OD) as the positive result cut-off. The anti-Hcp OD was categorized into levels to estimate the bacterial exposures by age and region groups.

Results: In this study, Chiang Rai (Northern Thailand) have the highest number of positive results for the Hcp1-ELISA following by Ratchaburi (central Thailand). In Chiang Rai sites, the proportion of positive Hcp1 ELISA was higher in child patients comparing with adult patients. The proportions Hcp1 ELISA levels and positive results decline by ages of patients. There was no positive Hcp1-ELISA result in the serum collections from Maesot (Western Thailand) and Rangoon (Lower Myanmar).

Conclusions: This study demonstrated the higher seroprevalence of melioidosis in febrile child cases than adult cases in the low endemic area. Further investigation and surveillance on melioidosis among children in northern Thailand are essential.

Tuesday 15 December 2020

S6: New normal of occupational setting in the era of COVID-19 (Thai/Eng Session)

09.40-11.10hr

Room E

Chairperson: Chuleekorn Tanathitikorn

Invited speakers:

1. Risk assessment for prevention and control of COVID-19 in factory and workplace (no abstract)
   Rungprakai Wirichai
   Division of Occupational and Environmental Diseases (DOED), Ministry of Public Health, Thailand

2. A cluster of Coronavirus Disease 2019 (COVID-19) among healthcare workers related to a COVID-19 death at a private hospital, Bangkok, 2020 (no abstract)
   Patcharaporn Dejburum
   Ministry of Public Health, Thailand

3. Thailand National Safety and Health Administration (SHA) for COVID-19 prevention (no abstract)
   Danai Teewunda
   Department of Health, Ministry of Public Health, Thailand

4. Clean air technology to prevent air-borne and droplet COVID-19 infection (no abstract)
   Anuphap Laor, Kriengsak Suriyapor, and Manus Rattanasuwan
   Ministry of Public Health, Thailand

5. Migrant workers and COVID-19 response in Thailand (no abstract)
   Aree Moungsookjareoun
   WHO Country Office for Thailand

Tuesday 15 December 2020

Poster session 1: COVID-19, Travel Medicine, others

11.20-12.20hr

Room A

1. Effect of geospatial related physical ambiance and socioecological factors on COVID-19
   Kyaw Soe Htun
   Defence Services Medical Academy, Myanmar

2. The readiness of COVID-19 response in Myanmar: community-based surveillance system of ethnic health organizations through innovative approaches
   Merry Moo
   Health Information System Working Group, Myanmar

3. Modelling the impact of intervention strategies on first wave and prediction the second wave of COVID-19 in Thailand
   Wiriya Mahikul
   Faculty of Medicine and Public Health, HRH Princess Chulabhorn College of Medical Science, Thailand

4. Knowledge, attitude, and practices toward coronavirus disease 2019 among international travelers
   Suttiporn Prapaso
   Faculty of Tropical Medicine, Mahidol University, Thailand

5. Production of diagnostic monoclonal antibodies useful for COVID-19 nucleocapsid protein detection
   Jeong-Heon Lee
   Department of Microbiology, Ajou University School of Medicine, South Korea

6. Chimeric antigen receptor T cell, an alternative treatment for hepatitis C virus infection
   Monrat Chulanetra
   Mahidol University, Thailand

7. *Atractylodes lancea* (Thunb.) D.C. inhibited cholangiocarcinoma cell growth and proliferation through down-regulation of ERK signaling cascade
   Pongsakorn Martviset
   Faculty of Medicine, Thammasat University, Thailand

8. Antitumor effects of fucoidan via apoptotic induction on cholangiocarcinoma
   Pathanin Chantree
   Faculty of Medicine, Thammasat University, Thailand

9. Travel profile and purpose of people getting yellow fever vaccine at travel clinic
   Sirirak Thanasakulprasert
   Faculty of Tropical Medicine, Mahidol University, Thailand

10. Multiple various anatomical site of hookworm-related cutaneous larva migrans- A case report
    Ploi Lakanavisid
    Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

Title: Effect of geospatial related physical ambiance and socioecological factors on COVID-19

Author: Kyaw Soe Htun (Presenter), Defence Services Medical Academy, Myanmar
Co-author: Ko Ko Win

Background: The COVID-19 is caused by novel corona virus that has spread to almost all over the world with high momentum within in a very short time and killed hundreds of thousands of people and has officially been categorized as a pandemic by World Health Organization. The spread of many Emerging Infectious Diseases has been reported to be predisposed by socio-ecological factors, including socio-economic and climate factors. The inter-connection between the transmission rate of COVID-19 and above factors are yet to understood properly to support better strategies for predicting, preventing and coping with many challenges.

Study Design & Methods: This cross-sectional analytical study was conducted on data gathering from WHO source on selected sixty countries (Asia pacific 55 countries and five countries of highest incidence of infection). In this study, countries of lack of data and incomplete information were excluded in this study. This study was conducted from December 2019 to May 2020. The subjects had been properly used the secondary data and information from WHO webpage officially to analyze for evaluation of correction between the selected variables of each country. Ethical approval was obtained from Institutional Review Board of Defence Services Medical Research Centre (DSMRC, IRB) for the use of secondary data from official webpages.

Results: The incidence rate, cumulative mortality rate and daily cumulative index were significantly associated with socio-ecological factors. It was indicated that some geospatial data (temperature, UV index and humidity) associated in reduced rate of COVID-19 risk but air pollution significantly associated with increased risk. Some of them (moisture, wind speed and rainfall) did not affect on spread of infection.

Conclusions: The highest population migration and entry of passenger in some countries posed significant risk vastly on spread of infection. Current study is an exploratory review in nature to inspire further conduct of a comprehensive investigations for impact of physical ambience and also aims for standing research network to study in local and regional countries.

Title: The readiness of COVID – 19 response in Myanmar: community-based surveillance system of ethnic health organizations through innovative approaches

Author: Merry Moo (Presenter), Health Information System Working Group, Myanmar
Co-authors: Saw Nay Htoo, Pue Pue Mhote, Aung Than Oo, Mee Eh Htoo, Paw Khu, Kyaw Thura Tun

Background: Reliable and essential health information sources for policy formulation, proper interventions, and resource allocation to address priority health challenges remain one of the top challenges for both Myanmar government and Ethic Health Organizations (EHOs). The EHOs provide Primary Health Care (PHC) services to the vulnerable population in eastern Myanmar for decades and founded Health Information System Working Group (HISWG) to improve the availability and quality of essential health data generating system. During the COVID-19 pandemic, innovations in all aspects of health information technologies are essential.

Study Design & Methods: EHOs have been preparing the community-based surveillance system to meet the WHO's surveillance strategy for COVID-19 in collaboration with implementation partners through utilizing information technology. The response guideline was developed for ethnic health facilities and community level to trace cases including suspected and asymptomatic cases through identifying symptoms and travel history. A mobile application was developed and the user trainings for health workers were conducted. A real-time web-based case-monitoring system is established and performed.

Results: The web-based COVID-19 surveillance system has been established in 79 clinics and 538 villages in 4 townships of Karen State, eastern Myanmar, and 772 of health workers and village health volunteers are equipped with case surveillance materials and mobile application to respond suspected cases within their communities.

Conclusions: It indicates that EHOs' COVID-19 surveillance mechanism addresses the essential surveillance strategies for COVID-19 human infection recommended by WHO, and well-established within their catchment areas even though COVID-19 is a new emergence pandemic. However, there are many limitations to its containment.

Title: Modelling the impact of intervention strategies on first wave and prediction the second wave of COVID-19 in Thailand

Author: Wiriya Mahikul (Presnter), Faculty of Medicine and Public Health, HRH Princess Chulabhorn College of Medical Science, Chulabhorn, Thailand
Co-authors: Palang Chotsiri, Wirichada Pan-ngum

Background: Coronavirus diseases 2019 (COVID-19) has been quickly spreading out worldwide. This study aims to assess and predict the incidence of COVID-19 in Thailand including the preparation and evaluation of intervention strategies.

Study Design & Methods: A mathematical modelling approach was assisted in the estimation and prediction of the disease transmission dynamic using the reported incidence, recovery, and case-fatality provided by the Center for COVID-19 Situation Administration, Thailand. An SEIR (i.e. a susceptible, exposed, infected, recovered model) was implemented and model parameters were estimated using the Bayesian approach.

Results: The developed model predicted that the highest number of COVID-19 daily incidence was approximately 156 cases (95% credible intervals, 106–272 cases), at the end of March. After Thailand declared the Emergency decree the number of new cases and case-fatality decreased. Regrading the model predictions, the incidence reached zero in the end of June if the on-going interventions were strictly and widely implemented, including social distancing, work from home, hand washing, mask wearing, screening, isolation, and state quarantine. These stringent recommendations reduced the effective reproductive number (Rt) to 0.75 per day (95% CI: 0.54-0.96) during April and May. Sensitivity analysis showed that the contact rate and the mean number of infectious migrants per day were the most influencing parameters affecting number of new cases in the country.

Conclusions: The evaluation by modelling has shown that the intervention strategies in Thailand have been highly effective in mitigating disease propagation. Continuing with these strict disease prevention behaviours could minimise the risk of second wave of COVID-19 outbreak in Thailand.

Title: Knowledge, attitude, and practices toward coronavirus disease 2019 among international travelers

Author: Suttiporn Prapaso (Presenter), Mahidol University, Thailand
Co-authors: Viravarn Luvira, Sant Muangnoicharoen, Watcharapong Piyaphanee, Punnee Pitisuttithum, Wiwat Chancharoenthana, Archin Songthap, Saranath Lawpoolsri Niyom

Background: International travel is one of the factors contributing to COVID-19 spreading. This study aims to determine knowledge, attitude, and practices (KAP) toward COVID-19 among Thai and foreign travelers including expatriates living in Thailand during the pandemic.

Study Design & Methods: Self-administered questionnaires were collected at Travel Clinic, Hospital for Tropical Diseases and in public areas of Bangkok, Thailand between May and August 2020.

Results: This preliminary results consist of 318 participants (77% Thai). The majority of non-Thai participants were expatriates (71.2%). The mean age was 36 ±9.5 years and 41.8% were male. It was reported by 77% of participants that COVID-19 pandemic greatly affected travel plan and 71% had to cancel or postpone their trip. Major sources of COVID-19 knowledge of participants were social media, television/radio, and organizational websites. Overall, the mean knowledge and attitude score were 69.5 ±13.8% and 71.1 ±6.3%, respectively. Most participants (80%) agreed that traveling abroad should be discouraged during the outbreak. For practices, 90% of participants reported the basic preventive measures against COVID-19 such as always wearing masks and frequent hand washing. Half of participants avoided public areas or public transportation. Regular update knowledge and recommendation was reported in 75% of participants.

Conclusions: Most participants had good KAP towards COVID-19 which might be attributed from the global concern and multiple accessible knowledge sources. However, the results might not represent all international travelers due to the small sample size and the effect of international travel restriction in many countries including Thailand.

Title: Production of diagnostic monoclonal antibodies useful for covid-19 nucleocapsid protein detedtion

Author: Jeong-Heon Lee (Presenter), Department of Microbiology, Ajou University School of Medicine, Korea
Co-authors: A-Young Park, Hae-Jin Sohn, A-Jeong Ham, Ho-Joon Shin

Background: COVID-19 causing pandemic infection in the world is diagnosed by PCR for amplifying virus genes at the beginning of hospitalization. And, although the test for IgM and IgG antibodies formation in blood is being practiced, it is necessary to develop diagnostic monoclonal antibodies for antigen detection, as which commercialize the rapid on-site diagnostic kit.

Study Design & Methods: The nucleocapsid protein (NP) gene of corona virus was constructed into an pExp5 NT-TOPO vector and expressed in *E. coli* and insect cells, recombinant NP (rNP) were purified with Ni-NTA column. After immunizing mice with the rNP, hybridomas were obtained by the cell-fusion technique. To obtain monoclones producing the monoclonal antibody, the limiting dilution technique was performed. Selected monoclones were injected into mice to obtain ascite fluid, and then monoclonal antibodies were purified by Protein-A column. To observe the antigen-sensitivity, monoclonal antibodies were reacted with various rNP antigens and evaluated by ELISA.

Results: Obtained rNP (about 50 kD m/w) was immunized to mice, and antibody formation was confirmed. After cell fusion, monoclonal antibodies of 2C8, 2A5, 2E3, 2D10, 2G12, 2C4, 3F2, 3G10, 3E11, and 3B1 were produced. As a result of antigen-antibody reaction with four kinds of rNP antigens (our rNPs, R and S company rNPs), the ELISA OD value was 1.205 ~ 3.806 (PBS, 0.152; healthy serum, 0.182; immune serum, 3.259), which were confirmed with Western blot analysis.

Conclusions: These highly reactive diagnostic monoclonal antibodies may be useful for the development of a rapid kit of COVID-19 antigen diagnosis.

Title: Chimeric antigen receptor T cell, an alternative treatment for hepatitis C virus infection

Author: Monrat Chulanetra (Presenter), Center of Research Excellent on Therapeutic proteins and Antibody Engineering, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
Co-authors: Kittirat Glab-ampai, Wanpen Chaicumpa

Background: T cell exhaustion is a hallmark of chronic infection, including the HCV. Losing T cell function result in failure to get rid of the HCV infection and control viremia. Despite the availability of direct-acting antiviral drugs for the treatment of HCV infection, resistances to these regimens have been reported. Chimeric antigen receptor (CAR) T cells, which can recovery T cell function could be an alternative treatment for HCV infection.

Study Design & Methods: To identified HCV proteins produced on the surface of prolonged HCV infected Huh7 cells, mouse polyclonal antibodies were generated by immunization of mice with purified recombinant HCV proteins. The HCV proteins which are expressed on the surface of infected cells were detected by IFA assay. Phage bio-panning with chronic HCV infected cells was performed and test the binding ability to the infected cells. A single-chain antibody fragment sequence of the binding clone was used for CAR construction. The CAR construct was introduced to Jurkat cells using lentiviral vector and test the function by co-culturing with the prolonged HCV infected cells

Results: From the IFA result, NS3 and NS5A are the HCV proteins expressed on the surface of the prolonged-HCV-infected Huh7 cells. The bio-panning result and binding test obtained 7 clones that bind to the HCV infected cells, which 3 of them are sibling clones. The CAR construct introduced to Jurkat cell lines has around 2% surface expression. The CAR-transduced-Jurkat cells were able to produce interferon-ɣ after co-culturing with the prolonged-HCV infected cells.

Conclusions: Chimeric antigen receptor T cells that target prolonged-HCV infected cells were constructed and the CAR T cells were able to perform T cell function. However, the ability of the CAR on primary T cells should be further investigated.

Title: *Atractylodes lancea* (Thunb.) D.C. inhibited cholangiocarcinoma cell growth and proliferation through down-regulation of ERK signaling cascade

Author: Pongsakorn Martviset (Presenter), Faculty of Medicine, Thammasat University, Thailand
Co-authors: Luxsana Panrit, Kesara Na-Bangchang

Background: Cholangiocarcinoma (CCA), originated from cholangiocytes in the biliary ducts, is one of the most progressive metastatic cancer. Anti-CCA activity of the ethanolic extract of *Atractylodes lancea* (Thunb) DC. rhizome (AL), as well as the isolated active compounds, have been well documented in various in vitro and in vivo models. Nevertheless, the exact targets of action remain unclear. ERK (extracellular signal-regulated kinase) is a cytosolic protein that is involved in several cell signaling cascades and thereby triggering cell proliferation through phosphorylation and activation of the downstream molecules.

Study Design & Methods: The study aimed to investigate the inhibitory effects of AL on the ERK signaling molecules (ERK, p-ERK, Myc, cyclin D, cyclin E, and eIF4B) and the growth and proliferation of CCA cells by MTT assay, cell proliferation assay, and Western analysis.

Results: The potency of cytotoxic activity of AL (by MTT assay) was about three times higher than the standard drug 5-fluorouracil. The IC50 (concentration that inhibits cell growth by 50%) of AL in the three CCA cell lines CL-6, HuCCT-1 and Huh28 were 26.58, 36.83 and 32.69 mg/ml, respectively. The cells were treated with AL at the IC50 for 0, 12, 24, 48, and 72 hours in the presence of ERK inhibitors. Protein expression was determined by Western blot analysis. Results suggested the lack of significant inhibitory effect of AL on ERK but the p-ERK expression at 48 and 72 hours of exposure in all cell types. Myc and cyclin E were slightly down-regulated, while cyclin D was significantly down-regulated at 72 hours of exposure in all cell types with different potencies. The expression of eIF4B was markedly inhibited in HuCCT-1 but slightly inhibited in CL-6 and Huh28 cells.

Conclusions: In conclusion, the ERK signaling cascade and downstream molecule is a potential target of action of AL in CCA.

Title: Antitumor effects of fucoidan via apoptotic induction on cholangiocarcinoma

Author: Pathanin Chantree (Presenter), Division of Anatomy, Department of Preclinical science, Faculty of Medicine, Thammasat University, Thailand
Co-authors: Pongsakorn Martviset, Kesara Na-Bangchang

Background: Cholangiocarcinioma (CCA) is the malignancy of epithelial cells of the biliary tract. Many studies suggested that fucoidan has anticancer potential. The objective of the present study was to determine the cytotoxic effects and mechanism of cell death induced by fucoidan extracted from Fucus vesiculosus on CCA cell line (CL-6) in comparison with human embryonic fibroblast cell line (OUMS).

Study Design & Methods: CL-6 and OUMS cells were treated with 0, 100, 200, and 300 μg/mL of ucoidan. Cell viability was measured using MTT assay. Apoptosis was measured with a flow cytometry-based assay. Chromatin condensation and nuclear fragmentation were determined using Hoechst 33342 staining. Mitochondrial membrane potential (ΔΨm) was determined using the JC-1 kit. The apoptotic and anti-apoptotic markers study were done by western blot analysis.

Results: The viable cell number of treated CL-6 cells was decreased whereas OUMS was not affected. Annexin V/PI staining revealed that fucoidan could induce apoptosis in CL-6 cells. Western blot analysis suggested the up-regulation of apoptotic markers including cleaved caspase-3, cleaved PARP, and Bax, but down-regulation of anti-apoptotic markers, Bcl-2. Fucoidan could disturb ΔΨm and induce chromatin condensation with nuclear fragmentation.
Conclusions: Fucoidan has potential in antitumor effect against CL-6 cells manifested by the induction of apoptosis.

Title: Travel profile and purpose of people getting yellow fever vaccine at travel clinic

Author: Sirirak Thanasakulprasert (Presenter), MCTM student, Thailand
Co-authors: Watcharapong Piyaphanee, Udomsak Silachamroon, Wirongrong Chierakul, Kittiyod Poovorawan, Thundon Ngamprasertchai, Sopon Iamsirithaworn, Visal Moolasart

Background: Yellow fever vaccine is mandatory vaccine according to IHR 2005 and these countries were in tropical areas. Many Thais visited travel these areas with different travel profiles. Knowing the travel profile and purposes could benefit in planning for individual travelers.

Study Design & Methods: Cross-sectional study among 379 Thais visited travel clinics between Dec 2018 – Jul 2019 using tructured questionnaire.

Results: Among the participants work was the main purpose of work (227, 59.9%), followed by travel (131, 34.6%), study (2.1%), Military/humanitarian (2.1%) and visiting friends and relatives (VFRs; 1.3%). Most of these people traveled to South Africa (13.2%). Among these yellow fever vaccines about 60 participants (15.6%) got underlying disease(s) which hypertension/dyslipidemia were the most common underlying disease(s). About 29.8% stayed at destination country at least 30 days (majority purpose for work <20.6%>). Median duration of stay was 14 days (IQR 42). Influenza vaccine was the most common co-administered vaccine (19.8%).

Conclusions: This study found many Thais traveled to yellow fever belt for work and trend to stayed at these countries for more than 7 days. Besides yellow fever which they got vaccinated other risk of illness should be discussed. Knowing of these people travel profile improved understanding of the specific risks or needs, which possible strengthen the better match viewpoint on discussion, education, and prevention.

Title: Souvenirs from the beach: uncommon presentation of hookworm-related cutaneous larva migrans

Author: Ploi Lakanavisid (Presenter), Faculty of Medicine, Burapha University, Thailand
Co-author: Wasin Matsee

Background: Hookworm-related cutaneous larva migrans (HrCLM) is a common dermatological problem among travelers. We present a case report of a returning traveler from Cambodia with multiple lesions of cutaneous larva migrans in different anatomical sites.

Study Design & Methods: A 43-year-old male, traveler from New Zealand, presented at Hospital for Tropical Diseases in Thailand with multiple intensely pruritic eruptions for 2 weeks. The rash started 6 days after he lay down on Kep beach in Cambodia. He spent one day reading books on the sand beach with only a pair of shorts, without using beach blanket.Physical examination revealed multiple serpiginous erythematous raised tracks (Figure A) over his anterior chest, abdomen, and both thighs; total of 9 lesions, various in length (1.5-8 cm) (Figure B-C), which are clinically diagnostic of Hookworm-related cutaneous larva migrans.The complete blood count showed eosinophilia (11%) with absolute eosinophil count 1,001/µL.

Results: He was treated with a 3-day course of oral albendazole (400mg/day). After 1 week, his lesions were much improved (Figure D). His eosinophil count decreased to normal level (3.9%) with absolute eosinophil count 323/µL.
Figure A: https://drive.google.com/open?id=15MKdoFNknHM_hrYj7HcZdrGfr0W2qUhi
Figure B: https://drive.google.com/open?id=18Jay8C9ValCJvoQCgdzH_AP0iy5uz0bz
Figure C: https://drive.google.com/open?id=1DUjdhh5ie1sUcCp25dH0B9I3iq3my837
Figure D: https://drive.google.com/open?id=1h4W_gBTxTyAGc9-BoVQsPg4rnbcnljEX

Conclusions: Hookworm-related cutaneous larva migrans is a common dermatological problem among travelers. It's caused by cat/dog hookworms. Human can be infected via contact with filariform larvae through skin penetration, frequently found on beaches in tropical/subtropical areas. Although 1-3 lesions are more common, multiple lesions in different anatomical sites can be presented. For prevention, travelers should avoid directly contact with sand or soil by wearing clothes, shoes or using beach blanket.

Tuesday 15 December 2020

Free paper I: Malaria

11.20-12.20hr

Room B

Chairpersons:

1. Wang Nguitragool
2. Wanlapa Roobsoong

Speakers

3. Further evidence needed to change treatment policy for safe and effective radical cure of *P. vivax malaria*
   Varunika Ruwanpura
   Menzies School of Health Research, Australia

4. Dose optimization of tafenoquine for malaria prophylaxis and elimination
   Michael Gregory
   Naval Medical Research Unit TWO, United States

5. A randomized controlled trial of the triple artemisinin combination therapy artemether-lumefantrine plus amodiaquine versus artemether-lumefantrine for multidrug-resistant *Plasmodium falciparum* malaria
   Thomas Peto
   MORU, Thailand

6. Elucidating changes in host signaling in and around Plasmodium-infected hepatocytes *in-vivo*
   Elizabeth Glennon
   Seattle Children's Research Institute, United States

7. Interactive web-based platform for malaria surveillance and environmental analysis
   Florian Girond
   Institut de Recherche pour le Développement / Institut Pasteur du Cambodge, Cambodia

8. Risk factors of metabolic acidosis and kidney injury in children with severe malaria: a secondary analysis of a randomised trial
   Grace Mzumara
   Malawi-Liverpool Wellcome Trust, Malawi

9. Factors associated with targeted mass drug administration long-term impact on *P. falciparum* incidence and prevalence in a malaria elimination setting of Eastern Myanmar
   Jordi Landier
   Aix Marseille Univ, INSERM, IRD, SESSTIM, Marseille, France

10. Selecting an optimal dosing regimen for a novel antimalarial combination therapy: OZ439-DSM265
    Saber Dini
    Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, University, Australia

11. Bayesian within-host modelling of red blood cell dynamics and primaquine-induced haemolysis in glucose-6-phosphate dehydrogenase
    Parinaz Mehdipour
    Melbourne School of Population and Global Health, Australia

Title: Further evidence needed to change treatment policy for safe and effective radical cure of *P. vivax* malaria

Author: Varunika Ruwanpura (Presenter), Menzies School of Health Research, Australia
Co-authors: Caroline A Lynch, Emily Gerth-Guyette, Kamala Thriemer, Koen P Grietens, Lek Dysoley, Mebratom Haile, Minerva Theodora, Ric Price, Spike Nowak

Background: New treatment options and diagnostic tools are now available to tackle vivax malaria. Yet countries are hesitant to invest in new options without further evidence on key country-specific aspects to support new policy introduction. At the 2019 Asia Pacific Malaria Elimination Network's Vivax Working Group meeting in Kathmandu, Nepal, participants took part in a round table discussion to identify further evidence required.

Study Design & Methods: At this discussion, National Malaria Control Program (NMCP) representatives and research partners were allocated to different roundtables to capture their diverse perspectives effectively. Further research needed highlighted by these two groups was listed as nine questions and discussed at a follow up workshop. NMCP participants were asked to rank these questions in order of priority. Follow-up interviews were also held with select NMCP representatives post-conference to verify identified evidence gaps.

Results: Overall results highlight a call by NMCPs for country-level evidence regarding the accuracy of G6PD diagnostic tests, operational feasibility of radical cure options within health systems and cost-effectiveness analysis of new tools. Research partners highlighted the need for further evidence regarding drug tolerability and safety, patient adherence, and feasibility and health system capacity.

Conclusions: Safe and effective roll out of radical cure has regularly been identified by countries as a major challenge to accelerating malaria elimination in vivax endemic countries. New treatment options and tools make 2030 regional elimination goals a stronger possibility. Evidence gaps identified in this paper need to be prioritised and addressed in tandem with WHO's upcoming treatment guideline recommendations to make this a possibility.

Title: Dose optimization of tafenoquine for malaria prophylaxis and elimination

Author: Michael Gregory (Presenter), Naval Medical Research Unit TWO, United States
Co-authors: Joel Tarning, Nicholas Martin, GD Shanks, Julie Simpson, TT Nguyen, HH Quang, Michael D. Edstein, HH Song, Mark M. Fukuda, Marvin Sklar

Background: Malaria control efforts in Southeast Asia focus on preventing the spread of drug resistance and treatment with the use of artemisinin combination therapies (ACT). However, current prophylactic agents such as doxycycline and atovaquone/proguanil are cumbersome with the need for daily use, and high ACT treatment failures rates are of immense concern in this region. Tafenoquine was FDA approved in 2018 for prophylaxis against all *Plasmodium* species. The approved prophylaxis dose is 200 mg weekly, but with a blood elimination half-life of 15 days, tafenoquine potentially could be used as a monthly regimen for both prophylaxis and malaria elimination. We provide our plans to test the safety and tolerability of tafenoquine given monthly to healthy volunteers.

Study Design & Methods: The study design is an open-label, single-arm, dose escalating study to determine the safety, tolerability and pharmacokinetics of tafenoquine in 200 healthy Vietnamese volunteers administered weekly 200 mg tafenoquine maintenance doses and then consecutively two monthly 600 mg tafenoquine doses followed by two monthly 800 mg tafenoquine doses.

Results: The logistics surrounding this study are currently being organized, and therefore, we present herein the study design and rationale.

Conclusions: If a monthly tafenoquine regimen is proven to be as safe and well tolerated as the approved weekly 200 mg regimen it offers the attraction of using tafenoquine monthly for travelers and military personnel, as well as part of a seasonal malaria chemoprophylaxis oriented approach with an ACT for lengthy blood stage suppression for malaria elimination.

Title: A randomized controlled trial of the triple artemisinin combination therapy artemether-lumefantrine plus amodiaquine versus artemether-lumefantrine for multidrug-resistant *Plasmodium falciparum* malaria

Author: Thomas Peto (Presenter), MORU, Thailand

Co-authors: Rupam Tripura, Nghia Ho Dang Trung, James Callery, Dysoley Lek, Chea Nguon, Mavuto Mukaka, Olivo Miotto, Mehul Dhorda, Rob van der Pluijm, Joel Tarning, Mallika Imwong, Nicholas Day, Lorenz von Seidlein, Tran Tinh Hien, Nicholas White, Arjen Dondorp

Background: Artemisinin-and partner drug-resistant *Plasmodium falciparum* has spread in Southeast Asia limiting antimalarial treatment options. In Cambodia and Vietnam the triple artemisinin-based combination therapy (TACT) artemether-lumefantrine plus amodiaquine is unevaluated, and the ACT artemether-lumefantrine has not previously been deployed.

Study Design & Methods: An open label randomised controlled trial in 3 sites: west Cambodia, north-east Cambodia, and Vietnam, recruited patients aged between 2-65 years with a history of fever within 24 hours or temperature >37.5oC, and microscopy-confirmed uncomplicated *P. falciparum* mono-infection or mixed with non-falciparum species. Patients were randomly allocated 1:1 by sealed envelope to treatment with either artemether-lumefantrine, or artemether-lumefantrine plus amodiaquine. Clinical staff provided study drugs orally with fatty food, twice daily, over 3 days. Staff performing laboratory investigations and non-site investigators were masked to treatment allocation. The primary outcome was an intention-to-treat analysis of PCR-corrected 42-day adequate clinical and parasitological response (ACPR), and of ACPR stratified by site. The trial is complete and registered on ClinicalTrials.gov, NCT03355664.

Results: Between 18 March 2018, and 30 January 2020, 451 patients were screened and 312 patients were enrolled. The PCR-corrected Kaplan Meier estimate of efficacy of artemether-lumefantrine was 94.5% (95%CI 89.3-97.2) vs artemether-lumefantrine plus amodiaquine 96.6% (95%CI 92.1-98.6), hazard ratio 0.6 (0.2-1.9). Artemether-lumefantrine plus amodiaquine was well tolerated and safe, but the addition of amodiaquine did moderately increase the proportion of patients with mild adverse events. This is consistent with a previous clinical trial and with the known properties of amodiaquine itself.

Conclusions: Artemether-lumefantrine and the triple therapy artemether-lumefantrine plus amodiaquine were safe and efficacious for the treatment of uncomplicated malaria in both Vietnam and Cambodia.

Title: Elucidating changes in host signaling in and around *Plasmodium*-infected hepatocytes *in vivo*

Author: Elizabeth Glennon (Presenter), Seattle Children's Research Institute, United States
Co-authors: Roobsong Wanlapa, Jetsumon Prachumsri, Noah Sather, Alexis Kaushansky

Background: Upon transmission to the human host, Plasmodium sporozoites travel to the liver, where they infect a single hepatocyte. Current evidence suggests hepatocytes are significantly altered upon Plasmodium infection and that infection in the liver significantly impacts the subsequent immune response. However, low infection rates within the liver, particularly in the case of the dormant hypnozoite form, have made proteomic studies of infected hepatocytes challenging.

Study Design & Methods: We applied digital spatial profiling (DSP) to characterize host signaling within *Plasmodium yoelii*-infected mouse livers. DSP uses antibodies linked to a barcoded oligonucleotide with a photocleavable linker to measure levels of 50-100 host total and phosphorylated proteins within defined regions of fixed tissue. We measured changes in protein levels within infected hepatocytes and in bystander cells.

Results: We were able to reliably detect protein levels in single *P. yoelii*-infected hepatocytes, facilitating the evaluation of variation among individual infected cells within the same host. Moreover, we identified alterations in host signaling within uninfected cells that neighbor infected hepatocytes, suggestive of signal propagation and immune cell infiltration that may alter the early response to infection. Finally, we have begun to apply DSP to a humanized mouse model of *P. vivax* infection.

Conclusions: Identifying signaling that propagates from infected cells may provide insight into how *Plasmodium* creates a favorable microenvironment within the liver and how liver-stage infection influences subsequent immunity. By identifying changes in phosphosignaling within and around infected cells, we hope to gain insight into the cellular niche that promotes liver stage parasite development and hypnozoite dormancy.

Title: Interactive Web-based platform for Malaria surveillance and environmental analysis

Author: Florian Girond (Presenter), Institut de Recherche pour le Développement / Institut Pasteur du Cambodge, Cambodia
Co-authors: Jade R Rae, Jordi Landier, Jean Gaudart, Morgan Mangeas, Vincent Herbreteau, François Nosten

Background: The overall objective of the Malaria Elimination Task Force (METF) started in 2014 in Karen/Kayin state, Myanmar is to reduce the prevalence of clinical and subclinical *P. falciparum* infections relying on early diagnostic and treatment at community-based Malaria Posts (MPs) and targeted mass drug administration in high prevalence villages. Interpreting significant changes hidden in routine tables of weekly data requires innovative surveillance systems involving the intertwining of new technologies, such as satellite observation of environmental conditions and use of geographical information systems and interactive web analytical tools.

Study Design & Methods: Since 2014, 1,205 MPs have been progressively established at village level reporting weekly incident malaria cases. Investigate local-scale environmental and meteorological variables linked to malaria transmission retrospectively and prospectively requires a dedicated environmental surveillance system. An automated system has been developed to produce over the 1205 MPs weekly i) Sentinel-2 vegetation and water indices time series within a buffer of 500 meters over each MP, ii) and CHIRPS rainfall time series data within a buffer of 2000m over each MP.

Results: A technology web interactive platform has been developed using R software to allow epidemiologists to identify and focus on specific data points. Among the 1205 MPs, 78 of them, located in Area 1, still exhibit a seasonality pattern in their time series, a prerequisite for environmental time series analysis. Seasonal Auto Regressive Integrated Moving Average with exogenous factors (SARIMAx) are automatically processed on the fly at individual or clustered MPs with real-time graphical feedback and model accuracy indicators.

Conclusions: The web environmental malaria surveillance system is an added value for malaria elimination in the Karen/Kayin state to interpret signals in malaria surveillance data along with environmental dynamics. Such a system might also be reinforced by automated spatial clustering method and integration of transmission-reducing interventions. This approach is a step toward the implementation of a malaria early warning system. Thus a system entirely based on free and open-source data and technology, should also benefit other initiatives aimed at improving surveillance data analysis.

Title: Risk factors of metabolic acidosis and kidney injury in children with severe malaria: a secondary analysis of a randomised trial

Author: Grace Mzumara (Presenter), Malawi-Liverpool Wellcome Trust, Malawi
Co-authors: Stije Leopold, Kevin Marsh, Eric Ohuma, Mavuto Mukaka, Arjen Dondorp

Background: Severe metabolic acidosis (SMA) and acute kidney injury (AKI) are major causes of mortality in children with severe malaria but they are often underdiagnosed in low resource settings.

Study Design & Methods: We conducted a retrospective analysis of the Artesunate Versus Quinine in the Treatment of Severe Malaria in African Children trial (AQUAMAT) to identify admission features of SMA and AKI in 5425 children (1- 4years) from nine African Countries. We performed univariable and multivariable logistic regression analyses with relevant candidate predictors for SMA and AKI respectively.

Results: The factors associated with SMA (Base excess < - 8mmol/l) were deep breathing (OR: 5.41, CI: 4.26 – 6.89), hypoglycaemia (OR: 5.22, CI: 3.80 – 7.18), AKI (OR: 3.99, CI: 3.30 – 4.81), coma (OR: 1.79 CI: 1.36 – 2.35), respiratory distress (OR: 1.49, CI: 1.21 – 1.83), prostration (OR: 1.64 CI: 1.30 – 2.03) and severe anaemia (OR: 1.40, CI: 1.11 – 1.77). Factors associated with AKI (Blood Urea Nitrogen > 20mg/dl) were; increasing age (OR: 1.20, CI: 1.15 – 1.25), coma (2.47, CI: 1.78 – 3.42), prostration (OR: 1.52 CI: 1.14 – 2.02), decompensated shock (OR: 1.74, CI: 1.15 – 2.63), black water fever (CI: 1.81. CI: 1.22 – 2.69), jaundice (OR: 3.31 CI: 2.01 – 5.47), SMA (OR: 4.02 CI:3.30 – 4.89), mild anaemia (OR: 1.36, CI: 1.05 – 1.76), severe anaemia (OR: 1.48, CI: 1.11 – 1.96), hypoglycaemia (OR: 2.02, CI: 1.58 – 2.59), hypernatremia (OR: 5.74, CI: 2.69 – 12.26) and hyperkalaemia (OR: 5.31. CI: 4.15 – 6.80).

Conclusions: Early diagnosis and treatment of AKI and SMA in children with severe malaria can be aided by reliable indicators of these complications.

Title: Factors associated with targeted mass drug administration long-term impact on *P. falciparum* incidence and prevalence in a malaria elimination setting of Eastern Myanmar

Author: Jordi Landier (Presenter), Aix Marseille Univ, INSERM, IRD, SESSTIM, Marseille, France
Co-authors: Florian Girond, Madeline Cannon, Aung Myint Thu, Suphak Nosten, Saw Win Tun, Khin Maung Lwin, Jade Rae, May Myo Thwin, Ladda Kajeechiwa, Gilles Delmas, Francois Nosten, Vincent Herbreteau, Jacher Wiladphaingern, Jean Gaudart

Background: *Plasmodium falciparum* (PF) elimination requires new interventions to overcome increasing antimalarial and insecticide resistances. Mass drug administration (MDA) targets asymptomatic PF carriage to decrease transmission. Immediately after MDA, population participation largely explains impact. Beyond 3 months, studies reported contrasted durations of MDA effect. We analysed factors associated with the sustained impact of MDA on PF incidence and prevalence in Eastern Myanmar.

Study Design & Methods: Villages received a 3-month MDA intervention with DHA-piperaquine. Ultrasensitive qPCR malaria prevalence was measured before and 1 year after MDA. Malaria posts (MP) provided community-based access to early diagnosis and treatment and reported weekly malaria cases. Weekly PF case counts recorded post-MDA in each village were analysed in a generalized linear mixed model with a village-level random effect and adjusting for seasonality. Main covariates were participation to MDA, population mobility, PF incidence in neighbouring villages, functionality of MP, village environment.

Results: The analysis included 70 villages receiving MDA between May 2013 and July 2017 corresponding to >15000 weekly reports. PF prevalence decreased by 93% in median (from 19.1% (interquartile range (IQR)=10.8-27.3 pre-MDA to 1.6% (IQR=0-5.1) post-MDA). Post-MDA follow-up lasted 4.2 years in median (range=2.6-6.6 years) with a median of 16 clinical PF cases recorded (range=0-171).In a multivariate model, PF incidence showed an increase during the first year post intervention, before decreasing regularly afterwards. Incidence was higher in villages reporting >1 stock-out of rapid tests or treatments during the previous month (incidence rate ratio (IRR)=1.51 ; 95% confidence interval (95%CI)=1.26-1.82). Incidence also increased in villages where PF incidence rose during the previous month in neighbouring villages within a 5-km radius (IRR=1.17(1.13-1.121) for each increase by 1 case/1,000/week). Villages located away from specific landscape features had lower incidence compared to villages located nearby (IRR(95%CI)=0.87(0.81-0.93) per 1km away from high altitude broadleaved forests ; respectively 0.92(0.87-0.97) per 1km away from low altitude agricultural forest areas). Adding 1 round of MDA or MSAT (in 11 villages) was associated with a strong decrease (IRR=0.36 (0.25-0.51)).

Conclusions: Occurrence of stock-outs was strongly associated to post-MDA incidence. This suggests a critical role of MP for the management of post-MDA incident PF episodes. Furthermore, persisting incidence in nearby villages was also associated with post-MDA incidence. MDA intervention planning requires adequate dimensioning of the campaign to cover hotspots extending beyond a single village. The use of MP-based surveillance data could help decision-making. Finally, persistent PF incidence near specific landscapes requires investigation. Intensified interventions (with supplementary vector control or mass interventions) could be required in response to specific environmental contexts.

Title: Selecting an optimal dosing regimen for a novel antimalarial combination therapy: OZ439-DSM265

Author: Saber Dini (Presenter), Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, University, Australia
Co-authors: Julie Simpson, Nathalie Gobeau, Mohammed Cherkaoui, Anne Kümmel, James McCarthy, David Price, Sophie Zaloumis

Background: The efficacy of artemisinin-based combination therapies (ACTs), currently the first-line antimalarial treatments, is declining due to the emergence of resistance of malaria parasites to these drugs. This has led drug development initiatives to search for new antimalarial compounds and explore novel combination therapies to replace the failing ACTs. We have developed a biologically informed within-host model, validated against data from volunteer infection studies, to guide critical drug development decisions.

Study Design & Methods: A within-host model, linking the concentrations of OZ439 and DSM265 to their combined killing action, was developed, which accounts for the differential killing of these compounds against stages of the parasite's lifecycle. Interaction between the drugs was accommodated in the model using different empirical approaches. Data collected from 13 malaria-infected volunteers treated with OZ439-DSM265 were used to estimate the model parameters in a hierarchical Bayesian framework. Posterior-predictive simulations of the model were used to determine the dosing regimen required to cure at least 90% patients.

Results: The results showed that OZ439-DSM265 can effectively reduce parasite burden, despite the estimated antagonistic interaction between the drugs. The importance of incorporating parasite age-specificity of killing action of the compounds in the model was demonstrated. Model predictions found that 600mg of OZ439 and 400mg of DSM265 provide a day 42 cure rate of 90%, where the drug exposure profiles for these doses overlap reducing the likelihood of resistance selection by the parasites.

Conclusions: The dosing regimens for OZ439-DSM265 determined from our data-informed in silico model suggest this compound can be a suitable candidate to replace failing ACTs. The determination of optimal dosing regimens for OZ439-DSM265 within our simulation framework informs the drug development process of this compound and ensures efficient allocation of logistical and financial resources for future phase 2 and 3 clinical trials.

Title: Bayesian within-host modelling of red blood cell dynamics and primaquine-induced haemolysis in glucose-6-phosphate dehydrogenase

Author: Parinaz Mehdipour (Presenter), Melbourne School of Population and Global Health, Australia
Co-authors: Sophie Zaloumis, Julie Simpson, James Watson, Robert Commons, Saber Dini

Background: Almost half of the malaria cases in Asia and South America are due to *Plasmodium vivax*. Primaquine is the only widely available drug that targets dormant *P. vivax* parasites in the liver, thereby preventing relapsing vivax malaria, however, primaquine can cause haemolysis in glucose-6-phosphate dehydrogenase (G6PD) deficient individuals. We developed a compartmental within-host model for red blood cell (RBC) dynamics to explore the safety of primaquine regimens for vivax malaria patients with G6PD deficiency.

Study Design & Methods: The model captured deviations from the normal process of RBC production and destruction by modifying three main parameters, RBC lifespan, release time of reticulocytes into the circulation and production rate of RBC. The compartmental within-host RBC model was fitted to longitudinal haemoglobin and reticulocyte measurements from 75 G6PD deficient patients using a Bayesian hierarchical framework.

Results: Posterior predictive simulations demonstrated that a stepwise increase in daily administered primaquine dose would be relatively safe for G6PD deficient individuals. Compared to patients treated with regimen (a) (lower initial dose of 5mg/kg with dosing every 5 days up to 30 days) those treated with regimen (b) (high initial dose of 7.5mg/kg followed by dosing every 5 days up to 20 days) had a lower haemoglobin nadir at day 7, but a greater haemoglobin recovery and higher haemoglobin concentration at day 30.

Conclusions: The results suggest an alternative ascending primaquine dosing regimen to the current dosing scheme of 0.75 mg/kg weekly for a total of 8 weeks will reduce the risk of primaquine-induced anaemia in G6PD deficient individuals with vivax malaria.

Tuesday 15 December 2020

Lunch session: Translational genomics: finding the needle in the haystack with digital PCR (Sponsored by QIAGEN)

11.20-12.20hr

Room C
Speaker: Karolina Setyowati

Senior Sales Application Specialist, APEC, QIAGEN

Tuesday 15 December 2020

Poster session 2 (Zoonosis)

11.20-12.20hr

Room D

1. Ectoparasites and their associated pathogens in Cambodia
   Daliya Nop
   US Naval Medical Research Unit 2, Cambodia

2. *In vitro* effects of multi-purpose disinfecting solutions towards survivability of acanthamoeba genotype t4 in Malaysia
   Rosnani Hanim Mohd Hussain
   Universiti Teknologi MARA (UiTM), Malaysia

3. New insights into the *in-silico* prediction and molecular docking of *Giardia intestinalis* protease resistance to nitro imidazole
   Dashwa Langbang
   Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), India

4. Molecular cloning of thioredoxin gene from pathogenic *Naegleria fowleri* trophozoite after transcriptomic analysis with RNA-sequencing
   Hae-Jin Sohn
   Department of Microbiology, Ajou University School of Medicine, South Korea

5. Antimicrobial susceptibility profiles of *Salmonella enterica* from slaughtered swine and pork products in Metro Manila, Philippines
   Jonah Feliza Mora
   University of the Philippines Diliman, Philippines

6. Molecular characterization of filarial species causing extralymphatic filariasis in Thailand
   Patsharaporn Sarasombath
   Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

7. Study of canine filariasis in Chanthaburi and Narathiwart, Thailand using microfluidic device combined with real-time PCR
   Achinya Phuakrod
   Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

8. Genomic insights into the antibiotic resistance and virulence of human and swine related *Enterococcus faecalis*
   Shiang Chiet Tan
   University of Malaya, Malaysia

Title: Ectoparasites and their associated pathogens in Cambodia

Author: Daliya Nop (Presenter), U.S. Naval Medical Resarch Unit TWO, Cambodia
Co-authors: Daliya Nop, Didot Budi Prasetyo, Phanit Pang, Satharath Prom, Vireak Heang, Vandeth Sin, Nin Noch, Dany Chheang

Background: Ectoparasite-borne diseases are distributed globally. The greatest burden of these diseases occur in tropical and subtropical countries where they can overwhelmingly affect the poorest populations. In Cambodia, the information about vector diversity and epidemiology of ectoparasite-borne diseases remains limited and underestimated. The aim of this study was to define ectoparasites diversity and their associated pathogens in Cambodia.

Study Design & Methods: In collaboration with Department of Health, Ministry of National Defense and Forestry Administration Cambodia, entomological surveys were conducted in Kampong speu, Battambang, Preah Vihear, and Pursat provinces. Ectoparasites were collected from peridomestic animals and from the environment using dragging and flagging methods. Collected ectoparasites were morphologically identified, then pooled by species, host, and location for molecular screening of ectoparasite-borne diseases.

Results: From a total 490 pools (N=4661 individual) of ectoparasites tested, Rickettsia spp. were detected in 225/258 pools of fleas, 6/210 ticks, and 1/21 louse. Bartonella spp. were detected in 10/227 fleas. None of samples tested were positive for Anaplasmataceae, Coxiella spp., and Yersinia pestis.

Conclusions: The detection of Rickettsia and Bartonella in ectoparasites collected from peridomestic animals suggests a potential public health risk in these regions. These data should be used to update policies and vector control strategies.

Title: *In vitro* effects of multi-purpose disinfecting solutions towards survivability of acanthamoeba genotype t4 in Malaysia

Author: Rosnani Hanim Mohd Hussain (Presenter), Universiti Teknologi MARA (UiTM), Malaysia
Co-authors: Wan Nur Afiqah Wan Kamaruddin, Mohd Kamel Abdul Ghani, Naveed Ahmed Khan, Ruqaiyyah Siddiqui, Tengku Shahrul Anuar Tengku Ahmad Basri

Background: In the past decade, there has been an increased incidence of Acanthamoeba keratitis, particularly in contact lens users. The use of ineffective contact lens disinfecting solution is one of the most important risk factors for this infection. Thus, this study was conducted to evaluate the in vitro effects of multi-purpose disinfecting solutions (MPDS) against Acanthamoeba T4 trophozoites and cysts.

Study Design & Methods: Samples from contact lens paraphernalia and environmental were propagated for monoxenic culture and adjusted in final concentration of 1 x 105 cells/ml. Amoebicidal and cysticidal assays were performed by incubating trophozoites and cysts with OPTI-FREE® Express®, ReNu® Fresh™, Complete® Multi-Purpose Solution and Unica® Sensitive, as per manufacturer's minimum recommended disinfectant time (MMRDT) and up to 12 h at 30ºC.Trypan blue hemocytometer-based microscopic counts measured amoebicidal and cysticidal effects while the viability of Acanthamoeba trophozoites and cysts was confirmed by re-inoculating them onto 1.5% non-nutrient agar plates.

Results: None of the MPDS showed amoebicidal and cysticidal effects during the MMRDT. However, OPTI-FREE® Express® demonstrated a significant difference in average cell reduction for both stages within 6 h of exposure. When subjected to 12 h exposure, both OPTI-FREE® Express® and ReNu® Fresh™ showed significant reduction in the number of trophozoite and cyst cells. All MPDS were largely ineffective, with 100% survival of all isolates at MMRDT. In contrast, OPTI-FREE® Express® had shown a better amoebicidal effect towards environmental isolates after 12 h of exposure.

Conclusions: The commercially available MPDS used in this testing provided minimal effectiveness against the protozoa regardless of contact time.

Title: New insights into the *in-silico* prediction and molecular docking of giardia intestinalis protease resistance to nitroimidazole

Author: Dashwa Langbang (Presenter), Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), India
Co-authors: Rahul Dhodapkar, Subhash Chandra Parija

Background: *Giardia intestinalis* is a flagella protozoan residing in the human intestine causing diarrhea. Usually, metronidazole and nitroimidazole were used for the treatment of giardiasis worldwide. Pyruvate Ferredoxin oxidoreductase protease enzyme may play a role inactivation of these drugs that may lead to resistance. Therefore, the present study was carried out to predict the structure and characterize them structurally as well as functionally by using appropriate in-silico methods.

Study Design & Methods: The proteins sequences of wild type and mutant strains were retrieved from the NCBI and aligned using ClustalW. While 3D structure of ligand was derived from PubChem. Homology modeling of these target proteins was performed by Modeller9v19. The model was loop refined and was validated using RMSD. Molecular simulation of proteins was performed by GROMAC 5. The possible binding sites of proteins were searched using Computed Atlas of Surface Topography of proteins (CASTp) server and the accurate molecular docking of the ligand with proteins was performed using the docking tool AutoDock.

Results: The wild complex maintained an approximate 4H-bonds, while the mutant complex could hardly maintain a single H-bond by the end of the simulation, suggesting that 4-nitroimidazole is highly stable in the wild complex. Since the compound occupies this binding site by making stable H-bond with key interacting residues, the function of the mutant may be altered that may lead to resistance.

Conclusions: The present study increases our understanding of nitroimidazole-resistance mechanisms and this study would be useful for the design derivatives of nitroimidazole that inhibits protein function more efficiently.

Title: Molercular cloning of thioredoxin gene from pathogenic *Naegleria fowleri* trophozoite after transcriptomic analysis with NA-sequencing

Author: Hae-Jin Sohn (Presenter), Department of Microbiology, Ajou University School of Medicine, Korea
Co-authors: A-Jeong Ham, Ho-Joon Shin, Jeong-Heon Lee, A-Young Park, Jong-Hyun Kim, Suk-Yul Jung

Background: Free-living *Naegleria fowleri* founds in freshwater and soil worldwide. *N. fowleri* causing the fatal primary amoebic meningoencephalitis (PAM) is known as "Brain Eating Amoeba". Recently, PAM has been increased in connection with watersports and the wrong water supply facilities. Regarding the search for pathogen-related gene, the transcriptomic analysis between pathogenic N. fowleri and nonpathogenic N. gruberi is useful.

Study Design & Methods: Differentially expressed transcriptome profiles of pathogenic N. fowleri and nonpathogenic N. gruberi trophozoite were analyzed by de novo assembly RNA-sequencing. One of them, thioredoxin upregulated in N. fowleri, was constructed into the cloning vector. The nf-thioredoxin gene was fully sequenced from pathogenic N. fowleri. The nf-thioredoxin gene was amplified from an nf-thioredoxin cloned vector. pEXP5-NT TOPO vector, transformed into BL21(DE3) *E. coli*. The recombinant Nf-thioredoxin was purified with His-tag Ni-NTA column. And intracellular localization was observed by Nf- thioredoxin immune sera.

Results: The assembly procedure resulted in mean full length of 63,997 nucleotides in total 28,110 transcript contigs and 36.54 % of C+G contents. Transcriptome database indicated that upregulated 26,332 genes in pathogenic N. fowleri showed 2 folds expression in comparison with nonpathogenic N. gruberi. The nf-thioredoxin gene is composed of 766 bp (encodes 255 amino acid) and produced 28 kDa recombinant protein (rNf-thioredoxin). The intracellular localization of the Nf-thioredoxin found on amoeba cytoplasm.

Conclusions: Finally, this Nf-thioredoxin may provide new insights into the pathogenic-related genes in *N. fowleri* survival and infectivity.

Title: Antimicrobial Susceptibility Profiles of Salmonella enterica from Slaughtered Swine and Pork Products in Metro Manila, Philippines

Author: Jonah Feliza Mora (Presenter), University of the Philippines Diliman, Philippines
Co-authors: Alyzza Marie Calayag, Windell Rivera

Background: Salmonella enterica is one of the four key global causes of foodborne diseases. Its most common reservoirs include poultry, horses, cattle, and swine, among others. Pork is one of the most consumed livestock commodities globally and is likewise the most common source of Salmonella infections. Due to the crude use of antimicrobials in livestock, antimicrobial resistant S. enterica have been increasingly observed to be isolated from swine samples.

Study Design & Methods: In this study, we aimed to profile the antimicrobial susceptibility of 1,167 S. enterica isolated from tonsils and jejuna from freshly slaughtered swine and pork products sampled from abattoirs and wet markets across the four districts in Metro Manila, Philippines. Antimicrobial susceptibility testing (AST) was done using VITEK®2 ID/AST instrument (bioMérieux, France).

Results: AST revealed the highest non-susceptibility rates in penicillins (ampicillin), fluoroquinolones (ciprofloxacin), and folate pathway inhibitors (trimethoprim/sulfamethoxazole). Out of the 1,167 isolates, 151 (12.9%) were extended spectrum beta lactamase (ESBL)-producers and 370 (31.7%) were multidrug-resistant (MDR).

Conclusions: Non-susceptibility of the isolates to medically important and priority antimicrobials and the occurrence of a high MDR percentage suggest that antimicrobial use in farms must be strictly regulated and monitored. This study can be used to investigate the clustering of AMR strains in specific districts and municipalities in Metro Manila and trace these back to where they occur in the pork food chain.

Title: Molecular characterization of filarial species causing extralymphatic filariasis in Thailand

Author: Patsharaporn T. Sarasombath (Presenter), Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
Co-authors: Panitta Sitthinamsuwan, Kosol Roongruanchai, Monrat Chulanetra, Sirichit Wongkamchai

Background: Filarial worms are nematode parasites in the Filarioidea superfamily cause the disease called filariasis. Transmission of filarial worms occurs through blood-feeding of the Diptera insects including mosquitoes and black files. Extralymphatic filariasis is an uncommon that can be caused by several lymphatic filarial species, including zoonotic filaria of animal origins. Infection of the animal filariae in human referred to as zoonotic filariasis may be asymptomatic or induce little to severe host immune response especially when the worms die in tissues. The most common site of zoonotic filarial nematodes recovered in human is in subcutaneous tissue.

Study Design & Methods: Five cases of extralymphatic filariasis were presented at the Faculty of Medicine Siriraj Hospital from 2015-2020. We identified the causative species of 5 extralymphatic filariasis cases by histological staining and confirmed by molecular diagnosis of the partial mitochondrial 12S ribosomal RNA (12 mt rRNA) and internal transcribed spacer 1 (ITS1).

Results: Three of five cases were caused by *Brugia pahangi*, a lymphatic filaria of cats and dogs. One case was caused by *Brugia malayi*, a lymphatic filaria of human. The last case was caused by *Dirofilaria repens*, a subcutaneous filaria of cats and dogs.

Conclusions: All five extralymphatic filariasis cases in Thailand occurred in the filariasis non-endemic areas. It is possible that the infections in these 5 cases were zoonotic in nature. This raised concern regarding the zoonotic transmission of filariasis from natural animal reservoirs in Thailand.

Title: Study of canine filariasis in Chanthaburi and Narathiwart, Thailand using microfluidic device combined with real-time PCR

Author: Achinya Phuakrod (Presenter), Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
Co-authors: Sirichit Wongkamchai, Bungon Sermsart, Monrat Junlanate, Darawan Wanachiwanawin, Kati Zealai, Witsaroot Sripumkhai, Sumas Loymek

Background: Filarial species that parasitize dogs are of worldwide zoonotic and veterinary significance. Due to the increasing zoonotic filarial infection from animals to humans, surveillance of filarial infection in dogs is important. The present study aims to determine the prevalence of canine filarial species of veterinary and public health importance in Narathiwat and Chanthaburi provinces which is an endemic and non-endemic area of lymphatic filariasis respectively.

Study Design & Methods: Blood was taken from a total of 551 dogs including 273 dogs and 278 dogs from Narathiwat and Chanthaburi province respectively. Microfilariae were detected and species were identified from the blood samples using a combination of novel semi-automated microfluidic device and high resolution melting real time PCR (HRM real time PCR).

Results: A total of 62 from 273 dogs (22.7%) from Narathiwat province as well as a total of 45 from 278 dogs (16.2%) from Chanthaburi province were positive for microfilariae respectively. The predominant species of canine filaria identified from Narathiwat was *Dirofilaria immitis* while *Brugia pahangi* was the most common species of canine filaria identified from Chanthaburi province.

Conclusions: High rates of filarial infections found in the present study strongly implicate dogs as potential reservoirs for zoonotic filarial parasites. Knowledge of occurrence and impact of zoonotic parasites in dog populations is crucial to prevent the infection in animals and people, and to control the risk of spreading of the filariae. Furthermore, the microfluidic device assisted by HRM real time PCR facilitates rapid, higher-throughput detection and identification of infection with filariae in blood samples, and could be used to diagnose lymphatic filariasis in humans.

Title: Genomic insights into the antibiotic resistance and virulence of human and swine related *Enterococcus faecalis*

Author: Shiang Chiet Tan (Presenter), University of Malaya, Malaysia
Co-authors: Cindy Shuan Ju Teh, Kwai Lin Thong

Background: *Enterococcus faecalis* is an opportunistic pathogen commonly found in the gut of humans and animals. Owing to the massive use of antibiotics in swine industry, the emergence of multidrug-resistant (MDR) *Enterococcus faecalis* has gained significant attention as strains of animal origin has been reported as potential threat for public health.

Study Design & Methods: Two *Enterococcus faecalis* strains EF218 (farmer) and EF250 (swine) previously isolated from the same farm were recovered for this study. Whole-genome sequencing was performed using Illumina Miseq platform. Virulence Factors of Pathogenic Bacteria Database and Comprehensive Antibiotic Resistance Database were used to identify the virulence and antibiotic determinants of the strains. The genomes were aligned with reference strains V583 for comparative genome analysis.

Results: The genome size for EF218 and EF250 were 2.86 Mb and 2.83Mb with 37.4% and 37.5 GC content, respectively. Six major antibiotic determinants were found in EF218, which included antibiotic target modifying enzyme, antibiotic inactivation enzyme, and resistance genes for lincosamide, macrolide, streptogramin and aminoglycoside resistances. In addition, EF250 also carried three additional resistance determinants which are the antibiotic target replacement protein, trimethoprim and chloramphenicol resistance genes. Virulence genes ace, asaI, ebpA, ebpB and efaA were present in both strains. However, gelE encoding for gelatinase was only present in EF218. Comparative genomic analysis showed that the strains that colonize different hosts were genetically similar.

Conclusions: Both strains in this study exhibit similar resistance and virulence traits. As strains with high similar resistance pattern and virulence profiles from animal and humans had also been reported elsewhere, a deeper understanding on *Enterococcus faecalis* from animal origin as a potential human hazard is vital to evaluate their risk in relation to public health.

Tuesday 15 December 2020

Lunch session: Recent knowledge of antibody and antibody enhancement
Sponsore by MiCAN Technologies Inc.

11.20-12.20hr

Room E

Speakers:

1. Expression of nucleic acid-encoded human monoclonal antibody against dengue virus by electroporation *in vivo* (no abstract)
   Surachet Benjathummarak
   Mahidol University, Thailand

2. Vaccine development and antibody dependent enhancement of SARS-CoV-2 (no abstract)
   Tatsuo Shioda
   Osaka University, Japan

3. Introduction of cMylc cell for SARS-CoV-2 research (no abstract)
   Jun Shimizu
   MiCAN Technologies Inc., Japan

Tuesday 15 December 2020

S7: The research and control for COVID-19 in Taiwan (Sponsored by National Yang Ming University)

12.30-14.00hr

Room A

Chairperson: Steve Hsu-Sung Kuo

Invited speakers:

1. COVID-19 in Taiwan: democracy, technology and civil society
   Wen-Chen Chang
   National Chiao Tung University School of Law, Taiwan, R.O.C.

2. Strategies for COVID-19 control in Taiwan
   Kuang-Yao Yang
   School of Medicine, National Yang-Ming University, Taiwan, R.O.C.

3. Mask or non-mask? Robust face detection with/without facial masks
   Hong-Han Shuai
   National Chiao Tung University, Taiwan, R.O.C.

4. COVID-19 vaccine development in Taiwan, a case study
   Chia En Lien
   National Yang Ming University, Taiwan, R.O.C

Title: COVID-19 in Taiwan: democracy, technology and civil society

Author: Wen-Chen Chang (Presenter), National Chiao Tung University School of Law, Taiwan

Background: Taiwan has demonstrated to the world its strength and success in combating the spread of COVID-19 despite decades of exclusion from the World Health Organization and close economic ties with China. The Strength was particularly build on the recent experiences in the SARS outbreak of 2003, resulting in a comprehensive legal regime, better-equipped medical professionals and public awareness for such serious communicable diseases.

Study Design & Methods: This research paper examines Taiwan's legal and regulatory responses with COVID-19. The focus of analyses are placed upon legal and social enforcement mechanisms that have been relied upon in implementing those legal and regulatory measures including mandatory testing, quarantine, strict control and distribution of medical supplies such as face masks, travel bans, and social distancing among others.

Results: As this research paper demonstrates, the dynamics and collaborations between an accountable government, a robust civil society, and a strong capacity in the medical system, and the high-tech sector are the keys to Taiwan's success in combating COVID-19.

Conclusions: The experience of Taiwan shows that, to mitigate tensions between resolving public health crisis and ensuring individual freedoms and rule of law, what are necessary are not always well specified laws, but a legal framework under which democratic processes can function to respond promptly and ensure accountability.

Title: Strategies for COVID-19 control in Taiwan

Author: Kuang-Yao Yang (Presenter), School of Medicine, National Yang-Ming University, Taiwan, R.O.C.

Background: Coronavirus disease 19 (COVID-19) is a global health threat and causes significant medical, economic, social and political implications since Jan. 2020. Several strategies for combating COVID-19 have been adopted across countries, but confirmed cases are still rising in the world. From its 2003 SARS experience, Taiwan's government established a public health response mechanism for enabling rapid actions for this crisis. The strategies for COVID-19 control in Taiwan included big data analytics, new technology, and proactive testing. Based on early recognizing and managing the crisis, effective communications and politics, Taiwan Central Epidemic Command Center (CECC) has controlled COVID-19 transmission efficiently. Taiwan is an example of how responding adequately to a crisis and protecting the welfares of citizens.

Title: Mask or Non-Mask? Robust face detection with/without facial masks

Author: Hong-Han Shuai (Presenter), National Chiao Tung University, Taiwan
Co-authors: Wen-Huang Cheng, Chun-Wei Yang

Background: According to the suggestions from WHO, masks should be used as part of a comprehensive strategy of measures to suppress transmission and provide protection against COVID-19. In order to force the crowd to wear face masks in public, existing approaches usually hire surveillance staffs to monitor the entries. However, it is dangerous and labor-intensive for the surveillance staffs to monitor the crowds. Therefore, with the advance of deep learning, we propose the first system that can automatically detect if a person in a picture is wearing a face mask or not.

Study Design & Methods: Face mask detection can be defined as the task of 1) detecting whether a person wearing a mask or not and 2) locating the position of the face, which can be regarded as a special case of object detection. However, different from general object detection, it is challenging to detection a person wearing a mask or not since 1) wearing masks or not is only partially different, 2) there are different colors/styles of masks, and 3) occlusions are similar to face masks. Therefore, in order to solve these challenges, we propose a novel CNN-based model with a newly-designed loss. Moreover, to facilitate a real-time application, the trained model is compressed to reduce the model size and computation.

Results: Experimental results show that the proposed approach can achieve real-time monitoring (greater than 30FPS) while the F1 score is higher than 98% on the real dataset.

Conclusions: In this work, we demonstrate how AI can facilitate the strategy of measures to suppress transmission and provide protection against COVID-19 by detecting if a person in a picture is wearing a face mask or not. In the future, we plan to investigate the possibility of integrating the social distance function into the detection model.

Title: COVID-19 vaccine development in Taiwan, a case study

Author: Chia En Lien (Presenter), National Yang Ming University, Taiwan, R.O.C.

Background: With over 30 million people infected and nearly one million deaths, the COVID-19 pandemic has the world scrambling for the development of vaccines and treatments. Medigen Vaccine Biologics Corp. (MVC) is based in Taiwan and is devoted to developing and manufacturing high quality cell-based vaccines.

Study Design & Methods: MVC has licensed technology of stabilized prefusion spike protein S-2P from the US NIH as the vaccine antigen. In search for suitable adjuvants to minimize immunopathology, MVC has partnered with Dynavax to deliver Th1-biased CpG 1018 adjuvant in addition to the conventional aluminum hydroxide.

Results: In multiple studies, mice immunized with S-2P in combination with CpG 1018 and aluminum hydroxide induced high levels of spike protein specific-IgG and neutralization antibodies when assayed with pseudovirus and wild type SARS-CoV-2. The formulation was also able to induce cross-reaction against the dominant strain in Europe and the Americas, D614G. Dose-ranging study in rats found no vaccine-related serious adverse effects in single or two dose administration of S-2P with CpG 1018 and alum. MVC currently uses stable CHO cells for antigen production and with the capacity of our CMO, MVC expects to expand production to 400 million doses by end of 2021. Phase I clinical trial IND conditional approval has been granted and recruitment of subjects will commence shortly. MVC plans to initiate phase II clinical trial in Q4 2020.

Conclusions: MVC is actively establishing and maintaining regional and global partnerships including regulatory authorities and vaccine manufacturers to facilitate the fast-track development and approval of the vaccine.

Tuesday 15 December 2020

S8: Advances in malaria diagnostics

12.30-14.00hr

Room B

Chairpersons:

1. Norman Waters
2. Mariusz Wojnarski

Invited speakers:

1. The emerging threat of mutant parasites causing malaria rapid diagnostic test failures
   Qin Cheng
   ADFMIDI, Australia

2. Hemozoin-based diagnostics for point-of-care early malaria detection in resource limited settings
   David Bell
   Hemex Health, United States

3. Advances in antigen detection, new ways of thinking about malaria diagnostics performance
   Gonzalo Domingo
   PATH, United States

4. Clinical evaluation of the BioFire global fever panel: a multiplex diagnostic for malaria, chikungunya, dengue, and leptospirosis
   Brian W. Jones
   BioFire Defense, United States

Title: The emerging threat of mutant parasites causing malaria rapid diagnostic test failures
Author: Qin Cheng (Presenter), ADFMIDI, Australia

Background: Malaria rapid diagnostic tests (RDTs) are deployed in almost all malaria endemic countries providing rapid malaria diagnosis for case management. The majority of these RDTs rely on the detection of *P. falciparum* histidine-rich protein 2 (HRP2) for diagnosing *P. falciparum* malaria. Mutant parasites lacking HRP2, first reported in Peru, are undetectable by the mainstay HRP2-detecting RDTs causing false negative results. These mutant parasites have now been reported in many countries worldwide posing a major threat to malaria diagnosis and case management globally. It is important to determine the prevalence and distribution of these mutant parasites so that alternative diagnostic tools can be recommended to guide case management in affected areas.

Study Design & Methods: In collaborations with country MOHs and field teams we have conducted molecular surveillance to detect mutant parasites lacking HRP2 in Peru, Eritrea, Uganda, Sudan, South Sudan and Nigeria.

Results: We demonstrated that mutant parasites lacking HRP2 are a major cause of RDT failures. Our findings also show that prevalence of mutant parasites is highly heterogeneous between and within countries and that mutant parasites appear to have emerged de novo and are selected for by the use of HRP2-detecting RDTs.

Conclusions: Mutant parasites lacking HRP2 are a major cause of RDT failures. Continuous surveillance is required to detect and report the presence, prevalence and distribution of mutant parasites lacking HRP2 to inform diagnosis and case management policies. It is also important to develop and evaluate alternative diagnostic tests.

Title: Hemozoin-based diagnostics for point-of-care early malaria detection in resource limited settings

Author: David Bell (Presenter), Hemex Health, United States
Co-authors: Patti White, Kingkan Pidtana, Worachet Kuntawunginn, Tyler Witte, Lycchea Huot, Priyaleela Thota, Dysoley Lek, Thay Kheang Heng, Sohei Hom, Somethy Sok, Mariusz Wojnarski, Norman Waters, Kittijarankon Phontham

Background: While malaria rapid diagnostic tests based on lateral flow assay technology have revolutionized management of malaria and acute fever, they remain inadequately sensitive to non-*falciparum* malaria. Approved malaria diagnostics face an increasing challenge as *P. falciparum* parasites with mutations deleting expression of HRP2 become more widespread. Haemozoin, a biproduct of malaria parasite digestion of hemoglobin, has long been considered as a promising and highly specific target for a new diagnostic approach to move beyond these limitations. However, success in developing a field-ready assay that matches the simplicity and robustness of RDT-based diagnosis has remained elusive.

Study Design & Methods: AFRIMS in partnership with Hemex Health Gazelle Diagnostic will evaluate new haemozoin-based assay aimed at remote and low-resourced health facilities. This in-vitro assay utilizes the magnetic properties of haemozoin, detecting change in light passing through a column as the haemozoin crystals rotate within a changing magnetic field.

Results: The assay, recently commercialized in several countries, provides a similar limit of detection as routine RDTs for falciparum and considerably lower LOD (higher sensitivity) for *P. vivax* infection, as demonstrated in recent testing in Cambodia and elsewhere.

Conclusions: The rapidity of the assay (1.5 minutes to result) opens the potential for very rapid screening of febrile individuals in border or community screening situations. The reliance on haemozoin for detection removes the limitations of lateral flow RDTs on gene deletions in the detection of HRP2. Recent results will be presented, together with a discussion of the potential applications of this field-stable, ultra-rapid approach to diagnosis.

Title: Advances in antigen detection, new ways of thinking about malaria diagnostics performance

Author: Gonzalo Domingo (Presenter), PATH, United States

Background: Malaria rapid diagnostic tests (RDTs) have become an essential tool for malaria case management and surveillance. In contrast to microscopy, which detects malaria parasites, RDTs detect protein antigens expressed by the parasites. The two most commonly used antigens–histidine-rich protein 2 (HRP2) and lactate dehydrogenase (LDH)–display very different dynamics during a malaria infection and therefore impact how RDTs perform, especially when compared against the PCR, the gold standard for diagnosis of malaria infection. In recent years, highly sensitive quantitative assays for these antigens have been developed and applied towards better understanding the performance of RDTs in different epidemiological settings

Study Design & Methods: Data from one such commercially available assay: the Q-Plex™ Human Malaria Array (Quansys Biosciences, USA) are analyzed to (i) investigate the performance of RDTs within clinical evaluation studies and (ii) predict the performance of RDTs based on analyticalperformance characteristics of the RDT. Additionally, use of these quantitative antigen detection platforms for surveillance is explored.

Results: Assessing the RDT performance against a reference antigen assay can resolve true false-positives arising from specificity issues versus false positives arising from antigen persistence beyond parasite clearance. In combination with a database of quantitative antigen data from clinical specimens, the Q-Plex Human Malaria Array allows in-silico comparative assessment of different RDTs, especially in context of emerging needs such as HRP2 deletions. The same database suggests applications of this tool for surveillance and infection classification.

Conclusions: Highly sensitive quantitative antigen assays are valuable tools to evaluate RDTs, for surveillance and other applications beyond.

Title: Clinical evaluation of the BioFire Global Fever Panel: a multiplex diagnostic for malaria, chikungunya, dengue, and leptospirosis

Author: Brian Jones (Presenter), BioFire Defense, United States
Co-authors: Ashley Wiltsie, Cynthia Andjelic, Cynthia Phillips, David Rabiger, Haley Halberg, Madeline Veloz, Marissa Burton, Mark Gurling, Natalie Batty, Olivia Jackson, Pascal Belgique

Background: Identifying the causal agent of Acute Febrile Illness is often slow and difficult. The FilmArray Global Fever (GF) Panel, developed by BioFire Defense in collaboration with the U.S. Department of Defense and NIAID, uses an automated, multiplex-nested PCR system to evaluate whole blood samples for multiple pathogens simultaneously in under an hour.

Study Design & Methods: BioFire Defense conducted a prospective clinical study to evaluate the GF Panel when used to test blood collected from recently febrile subjects. Eleven locations around the world tested 1,867 specimens. Comparator testing consisted of in-house developed PCR assays followed by bidirectional sequencing.

Results: The rate of positive detections was 35% (652/1867), with *Plasmodium spp.* accounting for the majority of positives (53.4%, 348/652) and dengue virus the second most (40.5%, 264/652). Other detected pathogens include Leptospira, West Nile virus, Zika virus, Leishmania, Crimean-Congo hemorrhagic fever virus, and chikungunya virus. Twenty-eight (28) specimens had more than one detected pathogen. When compared to in-house PCR assays, positive percent agreement ranged between 92.7-100%, and negative percent agreement ranged between 99.3-100%. However, when the GF Panel result was compared to site-specific malaria testing, the PPA ranged between 94.7-100% and the NPA ranged between 43.3-100%.

Conclusions: The GF Panel is apparently more sensitive than microscopy, producing "discrepancies" for this comparison. The wide range in NPA between sites could be due to variation in microscopy technique; the GF Panel eliminates such variation because it is fully automated. The results show that the GF Panel could aid in rapid and actionable diagnosis caused by multiple, sometimes co-occurring, pathogens.

Tuesday 15 December 2020

S9: **Re-emergence of chikungunya virus**

12.30-14.00 hr

Room C

Chairperson: Pornsawan Leaungwutiwong

Invited speakers:

1. Host factors involved in chikungunya virus replication
   Yusuke Maeda
   Research Institute for Microbial Diseases, Osaka University

2. A novel sub-lineage of chikungunya virus East/Central/South African genotype Indian Ocean lineage caused sequential outbreaks in Bangladesh and Thailand
   Juthamas Phadungsombat
   Mahidol Osaka Center for Infectious Diseases (MOCID)

3. Improved rapid diagnosis test kits of chikungunya virus infection
   Emi Nakayama
   Research Institute for Microbial Diseases, Osaka University

4. Clinical management of chikungunya virus infection (no abstract)
   Wirongrong Chierakul
   Faculty of Tropical Medicine, Mahidol University

Title: Host factors involved in chikungunya virus replication

Author: Yusuke Maeda (Presenter), Research Institute for Microbial Diseases, Osaka University, Japan

Background: A mutation recently occurred in chikungunya virus (CHIKV) allowed the virus to be transmitted by *A. albopictus*, a common mosquito in Japan, and is considered to be associated with recent outbreak of chikungunya fever. Thus, the clinical importance of CHIKV is increasing. The purpose of this study is to reveal the host factors involved in CHIKV genome replication and to lead to drug development.

Study Design & Methods: Many host factors are required with CHIKV four non-structural proteins, nsP1, P2, P3 and P4, for replication of CHIKV genome. To reveal these host factors, APEX2, an engineered peroxidase, was fused with nsP1 and nsP3 and expressed in HEK293 and U251 cells together with other non-structural proteins. APEX2 biotinylated host proteins in close proximately to nsP1 and nsP3 by adding biotin-phenol and hydrogen peroxide. Biotinylated proteins were purified by streptavidin-magnet beads and analyzed by mass-spectrometry. Host proteins identified by mass-spectrometry were examined whether the proteins were functionally related with CHIKV replication using knockdown and knockout systems.

Results: *In vivo* proximity biotin-labeling method using APEX2 fused to nsP1 and nsP3 identified more than a hundred proteins closely located to CHIKV replicase in common to both HEK293 and U251 cells. Notably, among them, many proteins were components/regulators of stress granules and actin/microtubules systems. Some of these host proteins were confirmed to positively function in replication by knockdown and knockout systems.

Conclusions: *In vivo* proximity labeling method is one of superior methods to identify components of complex, even if the protein-protein interaction is transient or labile. By analyzing the proteins identified here in detail would lead to comprehension of how replication system of CHIKV works and discovery of host proteins as drug targets.

Title: A novel sub-lineage of chikungunya virus East/Central/South African genotype Indian Ocean lineage caused sequential outbreaks in Bangladesh and Thailand

Author: Juthamas Phadungsombat (Presenter), Mahidol-Osaka Center for Infectious Diseases, Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Hisham Imad, Mizanur Rahman, Emi E. Nakayama, Sajikapon Kludkleeb, Thitiya Ponam, Rummana Rahim, Abu Hasan, Kanaporn Poltep, Atsushi Yamanaka, Wasin Matsee, Watcharapong Piyaphanee, Weerapong Phumratanaprapin, Tatsuo Shioda

Background: In recent decades, chikungunya virus (CHIKV) has become geographically widespread. In 2004, the CHIKV East/Central/South African (ECSA) genotype moved from Africa to Indian ocean islands and India followed by a large epidemic in Southeast Asia. In 2013, the CHIKV Asian genotype drove an outbreak in the Americas. Since 2016, CHIKV has re-emerged in the Indian subcontinent and Southeast Asia.

Study Design & Methods: Thirty-four of positive CHIKV sera were obtained from Bangladesh in 2017 and Thailand in 2019 and were determined for the whole genome by NGS. To investigate evolutionary relationships and genetic diversity of CHIKVs, the complete coding regions of the obtained sequences were combined with the public sequences from GenBank covering the geography and time spanning from the 1950s to the latest outbreak and used for phylogenetic analysis.

Results: Phylogenetic trees revealed that the recent CHIKVs were of Indian Ocean Lineage (IOL) of genotype ECSA, similar to the previous outbreak. However, these CHIKVs were all clustered into a new distinct sub-lineage apart from the past IOL CHIKVs, and they lacked E1-A226V, which enhances CHIKV replication in *Aedes albopictus*. Instead, all the re-emerged CHIKVs possessed mutations of E1-K211E and E2-V264A. Molecular clock analysis suggested that the new sub-lineage CHIKV was introduced to Bangladesh around late 2015 and Thailand in early 2017.

Conclusions: This novel sub-lineages of ECSA IOL CHIKV carrying E1-K211E and E2-V264A have expanded from the northern Indian subcontinent to Thailand through Bangladesh. It is important to see whether this new sub-lineage of ECSA-IOL CHIKV could expand into other regions of the world.

Title: Improved rapid diagnosis test kits of chikungunya virus infection

Author: Emi Nakayama (Presenter), Research Institute for Microbial Diseases, Osaka University, Japan
Co-authors: Aekkachai Tuekprakhon, Juthamas Phadungsombat, Keita Suzuki, Pornsawan Leaungwutiwong, Tatsuo Shioda

Background: Chikungunya virus (CHIKV) consists of three genotypes: East/Central/South African (ECSA), West African (WA), and Asian. Previously, a rapid immunochromatographic (IC) test detecting CHIKV E1-antigen showed high sensitivity for ECSA-genotype viruses. Subsequently, however, this kit showed poor performance against the Asian-genotype virus that is spreading in the American continents. We found that the reactivity of one monoclonal antibody (MAb) used in the IC kit is affected by a single amino acid substitution in E1. Therefore, we developed new MAbs that exhibited specific recognition of all three genotypes of CHIKV.

Study Design & Methods: Using the newly generated MAbs, we developed a novel version of the IC kit. To evaluate the sensitivity, specificity, and cross-reactivity of the new version of the IC kit, we first used cultured CHIKV and E1-pseudotyped lentiviral vectors. We then used clinical specimens obtained in Aruba in 2015 and in Bangladesh in 2017 for further evaluation of kit sensitivity and specificity. Another alphavirus, sindbis virus (SINV), was used to test kit cross-reactivity.

Results: We developed a new IC kit with improved sensitivity to Asian-genotype CHIKV using a combination of 5 MAbs. The new version of the kit detected Asian genotype CHIKV at titers as low as 10^4 plaque-forming units per mL, a concentration that was below the limit of detection of the old version. The new kit exhibited sensitivity to the ECSA genotype that was comparable to the old version, yielding 92% sensitivity and 100% specificity in the testing of patient sera obtained in the 2017 outbreak in Bangladesh.

Conclusions: Our new CHIKV antigen-detecting kit demonstrated high levels of sensitivity and lacked cross-reactivity against SINV. These results suggested that our new version of CHIKV E1-antigen detection kit is ready to be tested in areas endemic for the Asian and ECSA genotypes of CHIKV.

Tuesday 15 December 2020

S10: Future trends in vaccine for melioidosis

12.30-14.00hr

Room D

Chairpersons:

1. Ganjana Lertmemongkolchai
2. Narisara Chantratita

Invited speakers:

1. Melioidosis subunit vaccines: recent developments and future directions
   Paul Brett
   University of Nevada, Reno School of Medicine, United States

2. Identification and characterization of novel melioidosis vaccine candidates
   Mary Burtnick
   University of Nevada, Reno School of Medicine, United States

3. Hemolysin co-regulated protein 1 (Hcp 1) variant is associated with decreased virulence and low antigenicity in *Burkholderia pseudomallei*
   Sarunporn Tandhavanant
   Faculty of Tropical Medicine, Mahidol University, Thailand

4. Human immune responses to vaccine candidate antigens in a melioidosis-endemic area in Thailand
   Sineenart Sengyee
   Faculty of Tropical Medicine, Mahidol University, Thailand

Title: Melioidosis subunit vaccines: recent developments and future directions

Author: Paul Brett (Presenter), University of Nevada, Reno School of Medicine, United States

Background: *Burkholderia pseudomallei*, the etiologic agent of melioidosis, is a CDC Tier 1 select agent that causes severe disease in both humans and animals. Diagnosis and treatment of melioidosis can be challenging and in the absence of optimal chemotherapeutic intervention, acute disease is frequently fatal. Melioidosis is an emerging infectious disease for which no licensed vaccine currently exists. Due to the potential misuse of *B. pseudomallei* as a biothreat agent, as well as its impact on public/animal health in endemic regions, there is significant interest in developing vaccines for immunization against diseases caused by this bacterial pathogen.

Study Design & Methods: Several studies have demonstrated that *B. pseudomallei* expresses a number of structurally conserved protective antigens. Included amongst these are multiple surface exposed polysaccharides and a variety of cell-associated/secreted proteins. Based on this information, these antigens have become important components of the multivalent subunit vaccine candidates that we are developing in our laboratory. We propose that an efficacious vaccine for immunization against melioidosis can be developed by combining polysaccharide-based conjugates with specific *B. pseudomallei* protein(s) to produce a single, antigenically-defined formulation.

Results: Using murine models of acute melioidosis, our current research is focused on evaluating the protective capacity of these vaccine preparations with the goal of identifying suitable candidates for advancement into Phase I clinical trials.

Conclusions: Collectively, it is anticipated that our studies will provide valuable insights towards the rational design of a safe, affordable and effective vaccine to combat melioidosis.

Title: Identification and characterization of novel melioidosis vaccine candidates

Author: Mary Burtnick (Presenter), University of Nevada, Reno School of Medicine, United States

Background: *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, a Type VI secretion system (T6SS-1), a deubitiquitinase (TssM), an actin motility protein (BimA) and the VirAG two-component regulatory system.

Study Design & Methods: Previous work in our laboratory and others has demonstrated that expression of these virulence factors is tightly regulated and only occurs following contact of *B. pseudomallei* with or internalization into host cells. Additionally, we have identified in vitro growth conditions that activate the expression of these intracellular virulence factors.

Results: When *B. pseudomallei* was grown in minimal media devoid of iron, we detected the expression of T6SS-1 genes as well as bimA and tssM suggesting that these media conditions mimicked the intracellular environment. Extending upon these studies, we recently used a novel cell-surface labeling technique in combination with proteomics-based approaches to identify over 100 additional *B. pseudomallei* proteins that are up-regulated under iron deplete conditions.

Conclusions: Studies are currenly underway to assess the potential use of these newly identified antigens as novel melioidosis vaccine candidates.

Title: Hemolysin co-regulated protein 1 (Hcp1) variant is associated with decreased virulence and low antigenicity in *Burkholderia pseudomallei*

Author: Sarunporn Tandhavanant (Presenter), Mahidol University, Thailand
Co-authors: Rungnapa Phunpang, Peeraya Ekchariyawat, Claire Chewapreecha, Natnaree Saiprom, Thatcha Yimthin, Sineenart Sengyee, Rathanin Seng, Adul Dulsuk, Ganjana Lertmemongkolchai, T. Eoin West, Narisara Chantratita

Background: Hemolysin co-regulated protein 1 (Hcp1) is a virulence factor of *Burkholderia pseudomallei*. hcp1, located within T6SS-1, plays an essential role in the *B. pseudomallei* intercellular spread. Hcp1 is a potential diagnostic target and vaccine candidate. We hypothesized that *B. pseudomallei* population may have variation in hcp1 and affect their virulence and antigenicity.

Study Design & Methods: Whole genome sequencing (WGS) analysis was used to examine the variation of hcp1 in 699 clinical isolates in Thailand. To assess the Hcp1 specific antibodies, we performed ELISA using two recombinant Hcp1 proteins from wild-type strain K96243 (WT) and variant strain DR90076A as target antigens. 33 plasma samples from melioidosis patients infected with WT (N=19) and variant (N=14) strains were used. To determine pathogenicity, we compared multinucleated giant cell (MNGC) formation efficiency in a human lung epithelial cell line after 10-h infection.

Results: By mapping WGS data against K96243 reference genome, we observed two Hcp1 types consisting of WT (N=684, 97.9%) and variant (N=14, 2.0%) in clinical isolates. 87% nucleotides and 81% amino acids of variant Hcp1 were identical to WT. The median levels of IgG against WT-Hcp1 from patients infected with WT strains was significantly higher than patients infected with variant strains. In contrast, low IgG levels against variant-Hcp1 was detected from both patient groups. MNGC formation analysis demonstrated that the variants induced less MNGC than the WT strains.

Conclusions: We have identified hcp1 variants in clinical *B. pseudomallei* isolates. Our data suggest that Hcp1 variation may influence the pathogenicity and immunogenicity of *B. pseudomallei.*

Title: Human immune responses to vaccine candidate antigens in an melioidosis-endemic area in Thailand

Author: Sineenart Sengyee (Presenter), Mahidol University, Thailand
Co-authors: Atchara Yarasai, Boonthanom Moonmueangsan, Chumpol Morakot, Mary N Burtnick, Narisara Chantratita, Paul J Brett

Background: Melioidosis is a serious infectious disease with a diverse clinical manifestation. Meliodosis is caused by Gram-negative *Burkholderia pseudomallei*. The mortality and morbidity of melioidosis is high in the South East Asia and no licensed vaccines currently exist. Understanding of immune response during *B. pseudomallei* infection is critical for vaccine development for melioidosis. This study aimed to evaluate human cellular and humoral immune responses against four vaccine candidate antigens of *B. pseudomallei*.

Study Design & Methods: We determined peripheral blood mononuclear cell (PBMC) and IgG antibody responses against Hcp1, AhpC, TssM, LolC antigens and positive controls, phytohaemagglutinin (PHA) and Cytomegalo-, Influenza, and Parainfluenza viruses (CPI) peptide pool, in 91 acute melioidosis patients and 100 healthy donors from Northeast of Thailand by IFN-γ ELISpot and ELISA.

Results: Hcp1 and TssM induced significantly higher IFN-γ responses in acute melioidosis patients compared with healthy donors. Survival from melioidosis was significantly associated with cellular immune responses to all antigens. T cell responses of melioidosis patients against CPI peptide pool were low during acute illness and restored at day 28. We observed high IgG levels against Hcp1, AhpC and TssM in acute melioidosis patients at day 0 but there was no significant difference in antibody responses against these three antigens between survivors and non-survivors.

Conclusions: This study provided insights into understanding the cellular and humoral immune responses against vaccine candidate antigens of *B. pseudomallei*.

Tuesday 15 December 2020

S11: Community and health system research for malaria elimination

12.30-14.00hr

Room E

Chairperson: Suparat Phuanukoonnon

Invited speaker:

1. Reported acceptability and feasibility of mass administration of primaquine in field sites in Thailand and Myanmar
   Daniel Parker
   University of California, Irvine, United States

2. Forest-going, malaria and prophylaxis: preliminary results from a multi-site qualitative study in Cambodia, Laos and Thailand
   Christopher Pell
   Amsterdam Institute for Global Health and Development, Netherlands

3. Understanding malaria preventive practices among border population in western Thailand: association between migration patterns and malaria prevention
   Suparat Phuanukoonnon
   Faculty of Tropical Medicine, Mahidol University, Thailand

Title: Reported acceptability and feasibility of mass administration of primaquine in field sites in Thailand and Myanmar

Author: Daniel Parker (Presenter), University of California, Irvine, United States

Background: All nations of the Greater Mekong Subregion have committed to eliminating malaria by the year 2030. The primary focus of most efforts has been *Plasmodium falciparum* malaria. However, *P. vivax* malaria remains a major contributor to overall malaria morbidity in the region and if all malaria is to be eliminated, this species must also be targeted. Treatment of *P. vivax* is more complicated than for *P. falciparum* because of the dormant liver stage, requiring radical cure (with primaquine or tafenoquine) for curative treatment. Here I will present results from a mixed methods social science study in villages targeted for mass administration of primaquine.

Study Design & Methods: A mixed methods approach was used, including qualititative interviews and focus group discussions, as well as household surveys. Questions in both surveys and interviews focused on knowledge, attitudes, and practice with regard to malaria and malaria treatment. Furthermore, participants were asked about previous adherence to primaquine and likelihood of participating in mass administration of primaquine.

Results: Most participants noted that malaria had been a major contributor to morbidity and mortality in the past, but also that the burden of this disease has decreased. Most participants acknowledged that they ceased taking primaquine after feeling better, following a bout of malaria and subsequent diagnosis. Participants agreed that mass administration could be useful and the majority of adults agreed to participate, with a smaller proportion agreeing for their children to participate. Several community members voiced concerns and questions regarding side effects of primaquine.

Conclusions: Mass administration with primaquine appears feasible, given ample community education and engagement. It will be important to address concerns and side effects related to the drug. Collaboration between villagers, migrants, and public health authorities will likely be key to success of such targeted efforts.

Title: Forest-going, malaria and prophylaxis: preliminary results from a multi-site qualitative study in Cambodia, Laos and Thailand

Author: Christopher Pell (Presenter), Amsterdam Institute for Global Health and Development, Netherlands
Co-authors: Monnaphat Jongdeepaisal, Mom Ean, Panarasri Khonputsa, Soulixay Inthasone, James Callery Tom Peto, Lorenz Von Seidlein, Rupam Tripura, Richard Maude

Background: Despite recent declines in malaria incidence, forested zones are recognized as an important setting for continued transmission in the Greater Mekong Sub-region (GMS). Forest-going presents challenges to traditional prevention and control approaches, such as insecticide-treated bed or hammock nets. Prophylaxis targeted at forest-goers is one supplementary intervention, but little is known about the acceptability or feasibility of this approach. This presentation draws on the preliminary findings of a multi-site qualitative study of acceptability and implementation challenges of forest-goer prophylaxis.

Study Design & Methods: In-depth interviews with forest-goers, health care providers, study staff and policy stakeholders were conducted in Cambodia, Laos and Thailand. In Cambodia, interviews were conducted with participants in a trial of forest-goer prophylaxis. Interviews were conducted by trained local researchers, transcribed and translated to English for qualitative content analysis.

Results: Preliminary findings highlight the heterogeneity of forest-going, with purpose, timing, duration and group composition varying across individuals, settings and over the seasons. Forest-goers expressed concern about possible malaria infection – often based on past, sometimes frequent bouts of illness. Trial participants were enthusiastic about participating in the study and reported high levels of adherence, which was also indicated by pill-counts. Health providers raised concerns about implications for bednet use, adherence/sharing medicine in real-life circumstances (which was not reported under trial conditions). Village malaria workers were described as the main provider for malaria diagnosis and treatment.

Conclusions: Under trial conditions, malaria prophylaxis was well received by forest-goers. Further research is needed to assist in adapting implementation to local circumstances and ensuring adherence.

Title: Understanding malaria preventive practices among border population in western Thailand: association between migration pattern and malaria prevention

Author: Suparat Phuanukoonnon (Presenter) Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Siriporn Yongchaitrakul, Daniel Parker, Pratap Singhasivanon, Liwang Cui, Jetsumon Sattabongkot

Background: Endemic malaria in Thailand remains persistent along international borders, however, malaria preventive practices among the border population are not well understood. This study aims to describe malaria prevention practices in relation to migration patterns among the border population in Western Thailand.

Study Design & Methods: The study was a cross-sectional study using a monthly movement activity calendar. The study was conducted in two ICEMR villages (Nong Bua and Suan Oi) of Tha Song Yang District from March to April 2019. Data were analyzed using descriptive analysis in SPSS® Statistics program, version 23.

Results: Of 385 participants, in a month, 79.1% did not travel, 12.5% travelled internally and 8.4% cross the Thai-Myanmar border. Of those who crossed border, 17.1% travelled more frequent than 14 days in a month and 23.1% stayed overnight in Myanmar. When crossing border, 20.4% did not prevent themselves from mosquito biting, which was higher than 9.8% of those who did not cross border. Most common preventive practice was sleeping under bed-net (cross-border 66.7% vs not cross-border 91%). Other control methods (repellent, wearing long- sleeve shirts or pants, repelling mosquitos with smoke from fire) were of small percentages such as fabric barrier was second common method, accounted 5%. When crossing border, 54.7% of those stayed overnight in Myanmar slept under bed net, and the percentages of those sleep under bed net when cross border between male and female was quite similar (male 66.1% vs female 68.3%).

Conclusions: The cross-border movements affected malaria preventive practices in particular to the use of bed net.Keywords: Pattern of movement, Malaria preventive practice, Border population, Western Thailand

Tuesday 15 December 2020

S12: Free Paper II: COVID-19 and bacterial related diseases

14.10-15.40hr

Room A

Chairpersons:

1. Pornpan Pumirat
2. Muthita Vanaporn

Speakers:

1. Anosmia and ageusia are characteristic to COVID-19: a case report
   Hisham Ahmed Imad
   Mahidol-Osaka Center for Infectious Diseases, Thailand

2. Modelling the optimal timeliness and coverage of contact tracing and containment for the COVID-19 epidemic control in Thailand
   Parinda Wattanasri
   Centre for Global Health and Tropical Medicine, Nuffield Department of Medicine, University of Oxford, United Kingdom

3. Effects of COVID-19 government travel restrictions on mobility in a rural area along the Thai-Myanmar border
   Peter Haddawy
   Mahidol University, Thailand

4. Epidemiology of melioidosis: a 62 months' retrospective study from a teaching hospital in Kuala Lumpur, Malaysia
   Vanitha Mariappan
   Universiti Kebangsaan Malaysia, Malaysia

5. Human–animal–water-source interactions and leptospirosis in Thailand
   Udomsak Narkkul
   Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand

6. Decision making, consent and perceptions of research: a qualitative case study from Northern Thailand
   Nipaphan Kanthawang
   Mahidol-Oxford Tropical Medicine Research Unit, Thailand

7. UHPLC-ESI-QTOF-MS/MS-based molecular networking guided isolation and dereplication of antimicrobial natural products of *Ventilago denticulate*
   Muhaiminatul Azizah
   Chulabhorn Graduate Institute, Chemical Biology Program, Chulabhorn Royal Academy, Thailand

8. A comparison of in vitro activity of flomoxef and current broad-spectrum antimicrobial agents against extended-spectrum β-lactamase-producing *Escherichia coli*
   Soo Tein Ngoi
   University of Malaya, Malaysia

9. A qualitative case study of vulnerability and agency in research participants' daily lives and their experiences of research
   Rachel Greer
   MORU, United Kingdom

Title: Anosmia and Ageusia are characteristic to COVID-19: a case report

Author: Hisham Ahmed Imad (Presenter), Mahidol-Osaka Center for Infectious Diseases, Thailand
Co-author: Rajib Kumar Dey, Abdullah Isneen Hilmy, Ali Zaadhee, Zaidhoon Jaleel, Ahmed Zooshan, Afa Ibrahim, Azna Waheed, Saifullah Waseel, Mariyam Hishma, Mariyam Naseem, Mariyam Shahana Mufeed, Mihunath Mustafa, Dhunya Thaufeeq, Rania Nabil, Abdul Azeez Yoosuf, Ali Nazeem, Ali Abdulla Latheef

Background: A novel pathogen with pandemic potential was detected in early January 2020. This was a respiratory virus identified as severe acute respiratory syndrome coronavirus 2, which causes coronavirus diseases 19. The main modes of transmission are by contact and droplet transmission including aerosolization of the virus. This highly infectious respiratory virus causes pneumonia and infects all age groups. Severe cases subsequently develop other organopathy and death. Individuals at risk of a severe infection include adults over the age of 65 years, male gender, and those with underlying comorbidities. The average incubation period is five days and the common manifestations include fever, coryza, cough, anosmia, ageusia, fatigue, and rash. The hematological profile included leukopenia, lymphopenia, and thrombocytopenia. Diagnosis is made with molecular techniques. Herein, we describe the clinical progression and findings.

Study Design & Methods: An informed consent was obtained before obtaining the clinical and laboratory data from the medical chart at a center established for treating COVID-19 cases in the Maldives.

Results: Our case presented with complaints of fever, and worsening of cough. The vital signs were temperature of 400C, a pulse of 101beats per minute, blood pressure of 120/80 mmHg, and an increased respiratory rate of 30 breaths per minute. Other findings included a decreased oxygen saturation of 89% in room air and fine crepitation’s on auscultation.

Conclusions: COVID-19 causes atypical pneumonia with a hematological profile consistent with a viral etiology. Symptoms of anosmia and ageusia seem to be characteristic of COVID-19. Fatigue and cough persisted even with the resolution of radiological and findings. Acknowledgment: We would like to express our sincere appreciation to all the front-liners across the globe for their bravery and dedication in combating this unprecedented event in our present lifetime. In addition, to all the staff working at the COVID-19 makes-shift facility and everyone at the multiagency-taskforce overseeing the management of the current epidemic outbreak in the Maldives.

Title: Modelling the optimal timeliness and coverage of contact tracing and containment for the COVID-19 epidemic control in Thailand

Author: Parinda Wattanasri (Presenter), Centre for Global Health and Tropical Medicine, Nuffield Department of Medicine, University of Oxford, United Kingdom
Co-authors: Wirichada Pan-ngum, Panithee Thammawijaya, Lisa White

Background: Proactive contact tracing and containment are critical interventions to achieve the COVID-19 epidemic control goal. Tracing delays with inadequate coverage can compromise the operational efficacy of the contact tracing. Additionally, determining the appropriate level of investment in contact tracing is challenging for public health authorities. We aimed to illustrate the optimal level of these critical features for a successful contact tracing.

Study Design & Methods: We developed an SEIR model of COVID-19 transmission with contact tracing interventions in the Thai population. We displayed the simplified workflow of contact tracing and containment interventions through the model. We then simulated different timeliness and coverage levels to identify the optimal level to control the COVID-19 epidemic in Thailand. We also monitored the quarantine and hospitalisation numbers for guiding quarantine, and hospital capacity need in each scenario.

Results: We found that both timeliness and coverage of the procedures had significant effects on reducing the transmission. Timeliness had the most impact on the interventions. The number of cases rapidly declined with minimising tracing delays. When contact tracers detected and isolated cases within two days of infection, coverage more than 50% was enough to control the outbreak, however, if they delayed the intervention until day five, the transmission would be under controlled when the coverage reached 100%.

Conclusions: Finding contact quickly with optimal coverage are the main features of successful contact tracing and containment measures. Investing in strengthening preparedness and contact tracing means to reach an adequate level in controlling the outbreak could prevent further transmission, avoid overloaded quarantine and hospital capacity, and mitigate the disruptive impact of stringent measures on a whole population. We could enhance the timeliness and coverage of contact tracing by investing in improving public health capacities and workforce. Combining mathematical modelling with epidemiology is also a crucial part of creating an efficient public health tool. Multidisciplinary approaches are the key to tackle the novel contagious disease.

Title: Effects of COVID-19 government travel restrictions on mobility in a rural area along the Thai-Myanmar border

Author: Peter Haddawy (Presenter), Mahidol University, Thailand
Co-authors: Saranath Lawpoolsri, Chaitawat Sa-ngamuang, Myat Su Yin, Thomas Barkowsky, Anuwat Wiratsudakul, Jaranit Kaewkungwal, Amnat Khamsiriwatchara, Patiwat Sa-angchai, Jetsumon Sattabongkot, Liwang Cui

Background: Thailand is among the top five countries with effective COVID-19 transmission control. This study examines how news of presence of COVID-19 in Thailand, as well as varying levels of government restriction on movement, affected human mobility in a rural Thai population along the border with Myanmar.

Study Design & Methods: This study makes use of mobility data collected using a smartphone app. Between November 2019 and June 2020, four major events concerning information dissemination or government intervention give rise to five time intervals of analysis. Radius of gyration is used to analyze movement in each interval, and movement during government-imposed curfew. Human mobility network visualization is used to identify changes in travel patterns between main geographic locations of activity. Cross-border mobility analysis highlights potential for intervillage and intercountry disease transmission.

Results: Inter-village and cross-border movement was common in the pre-COVID-19 period. Radius of gyration and cross-border trips decreased following news of the first imported cases. During the government lockdown period, radius of gyration was reduced by more than 90% and cross-border movement was limited to short-distance trips. Human mobility was nearly back to normal after relaxation of the lockdown.

Conclusions: This study provides insight into the impact of the government lockdown policy on an area with extremely low socio-economic status, poor healthcare resources, and highly active cross-border movement. The lockdown had a great impact on reducing individual mobility, including cross-border movement. The quick return to normal mobility after relaxation of the lockdown implies that close monitoring of disease should be continued to prevent a second wave.

Title: The epidemiology of melioidosis: a 62-month retrospective study from a teaching hospital in Kuala Lumpur, Malaysia

Author: Vanitha Mariappan (Presenter), Universiti Kebangsaan Malaysia, Malaysia
Co-authors: Renuga Devi, Sockalingam, Kumutha Malar Vellasamy, Jamuna Vedivelu, Rukumani Devi Velayuthan

Background: *Burkholderia pseudomallei* is the causative agent of melioidosis, an emerging infectious disease, endemic in Southeast Asia and northern Australia. Current global reports estimated 165,000 cases with the predicted fatality of 54.3% annually.

Study Design & Methods: Based on our descriptive, retrospective study (November 2013 - December 2017), there were 86 melioidosis-confirmed cases from University Malaya Medical Centre, Kuala Lumpur (a teaching hospital). The antimicrobial susceptibility pattern of *B.pseudomallei* and demographic trend of melioidosis patients including age, gender, race, nature of the specimen, and monthly distribution of cases were evaluated.

Results: The male-to-female ratio was 1:0.265, and the mean age was 49.07 (±17.08) years with an average of 1.39 cases per month. Majority of the patients were between 41 - 60 year-old (51.2%), while three pediatric patients aged 2, 14 and 16 year-olds were identified. Fifty-percent of the patients were of Malay descendant, while Chinese and Indian made up to 19.77% and 26.74%, respectively and the remaining 3.75% comprised of foreigners. Of the 86 confirmed melioidosis cases (79 patients with seven relapse cases), B.pseudomallei was isolated from blood, swab samples, respiratory fluid and urine samples (53, 34, 18 and 2, respectively). Of the 79 patients, 22 (27.8%) patients died (12 with diabetes). All the isolates were 100% susceptible to chloramphenicol, imipenem, piperacillin-tazobactam, and tetracycline. In contrast, 100% of the isolates were resistant to gentamicin, and polymyxin B.
Conclusions: It is important to take note that melioidosis is expanding in endemicity around Malaysia. Control of the disease requires close monitoring, improved clinical laboratory standards and aggressive therapy.

Title: Human–animal–water-source interactions and leptospirosis in Thailand

Author: Udomsak Narkkul (Presenter), Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: James Rudge, Janjira Thaipadungpanit, Metawee Thongdee, Natachai Srisawat, Rungrawee Pawarana, Wirichada Pan-ngum

Background: Leptospirosis is an important zoonotic disease worldwide, with the greatest impact in developing countries. In Thailand, leptospirosis is primarily associated with those who work in agricultural occupations. Leptospirosis control is hampered by a poor understanding of the complex interactions between humans, animal reservoirs, Leptospira, and the variable spatial environment in which these factors coexist. We aimed to address key knowledge gaps concerning leptospirosis disease dynamics and the human–animal–water-source interface in two high-risk areas in Thailand.

Study Design & Methods: We conducted a cross-sectional survey among 746 study participants in two high-risk areas for leptospirosis in Thailand: Sisaket (SSK) and Nakhon Si Thammarat (NST). Interactions among humans, animals and water sources were quantified and analyzed. Reported cases from 2013–2017 were matched to the survey data for association analysis. The matched number of cases in SSK was almost ten-times that in NST (29 vs 3).

Results: Participants with occupations related to animals or environmental water and those who consumed water from more than two sources were more likely to have been infected with leptospirosis, with adjusted odds ratios 4.31 (95%CI, 1.17 – 15.83) and 10.74 (95% CI, 2.28 – 50.53), respectively. Some animal species were more likely to be present within households in NST and SKK, e.g. chickens and domestic pets. In SSK, households generally consumed water from shared sources, and the use of surface water was common. In NST, most households had their own wells, while the most common water sources were groundwater and waterfalls.

Conclusions: This study demonstrated the different patterns of interactions among hosts, animals, and water sources between two high-risk settings for leptospirosis. Understanding specific water-source sharing networks and human–animal contact patterns is useful when designing national and area-specific control programmes to prevent and control leptospirosis outbreaks.

Title: Decision making, consent and perceptions of research: a qualitative case study from northern Thailand

Author: Nipaphan Kanthawang (Presenter), Mahidol-Oxford Tropical Medicine Research Unit, Thailand
Co-authors: Phaikyeong Cheah, Rachel Greer

Background: Deciding whether to take part in research or not can be influenced by many factors such as peoples' perception of research, the risks and benefits involved, and social and cultural factors. Little is known about how these decisions are made in the context of northern Thailand. Our study aims to understand the background, social and cultural factors involved in the decision making process of women and children taking part in a case study of scrub typhus research in Chiang Rai, Thailand.

Study Design & Methods: Research participants, their family members, researchers and community leaders linked to the scrub typhus studies were interviewed in 42 semi-structured interviews. We explored how women and caregivers made decisions, gave consent and perceived research, as part of a wider qualitative study exploring vulnerability in research.

Results: We found that most women decided to participate in research on their own, some involved their families. Common reasons to join were thinking that the research would benefit them or their family, often through providing medical care, and that it would help others in the future. Reasons not to participate in research included a lack of time and inconveniences for care givers. Researchers felt that the relationship between the participant and the researcher, including trust and being considerate, influenced decision making. The consent process could be more challenging for those who were illiterate or unable to speak Thai fluently. Family members or people in the community helped to translate for them, although the amount of information translated varied.

Conclusions: Most women decided to participate in research alone. Social and cultural factors affected people's decision making, as well as perceptions of research. Overall people had positive feelings towards research.

Title: UHPLC-ESI-QTOF-MS/MS-Based Molecular Networking Guided Isolation and Dereplication of Antimicrobial Natural Products of *Ventilago denticulata*

Author: Muhaiminatul Azizah (Presenter), Chulabhorn Graduate Institute, Chemical Biology Program, Chulabhorn Royal Academy, Thailand
Co-authors: Patcharee Pripdeevech, Tawatchai Thongkongkaew, Chulabhorn Mahidol, Somsak Ruchirawat, Prasat Kittakoop

Background: The plant, *Ventilago denticulata*, is an herb widely used to treat wound infection, suggesting that it is rich in antimicrobial agents. The purpose of this study is to explore antimicrobial agents in crude extracts and fractions of *V. denticulata*.

Study Design & Methods: Analysis by UHPLC-ESI-QTOF-MS/MS technique, as well as by a molecular networking, led to the isolation and characterization of antibacterial and antifungal natural products in *V. denticulata.*

Results: Nine antimicrobial agents in *V. denticulata* were structurally characterized by analysis of NMR and MS, and they were rhamnazin 3-rhamninoside, catharticin or rhamnocitrin 3-rhamninoside, xanthorhamnin B or rhamnetin 3-rhamninoside, kaempferol 3-rhamninoside and flavovilloside or quercetin 3-rhamninoside, lupeol, and ventilatones A-C. Among the isolated compounds, ventilatone C was a new compound. Moreover, a few natural products including kaempferol, chrysoeriol, isopimpinellin, rhamnetin, luteolin, emodin, rhamnocitrin, ventilagodenin A, (+)-(R)-ventilagolin, rhamnazin and mukurozidiol, were tentatively identified in extracts of *V. denticulata*, and these compounds were proposed to be the active antimicrobial agents in this plant.

Conclusions: Mass spectrometry-based molecular networking not only identifies known metabolites in complex mixtures, but also suggests the presence of related analogues. The presence of many antibacterial and antifungal compounds in the plant, *V. denticulata*, supports the traditional use of this plant as an herbal medicine for the treatment of wound infection. This work also demonstrates that the molecular networking guided isolation and dereplication could assist the identification of antibacterial and antifungal agents in extracts of a plant.

Title: A comparison of *in vitro* activity of flomoxef and current broad-spectrum antimicrobial agents against extended-spectrum Î²-lactamase-producing *Escherichia coli*

Author: Soo Tein Ngoi (Presenter), University of Malaya, Malaysia
Co-authors: Cindy Shuan Ju Teh, Ramliza Ramli, Azian Harun, Tengku Zetty Maztura Tengku Jamaluddin, Anis Ahmed Khan, Rina Karunakaran, Kartini Abdul Jabar, Sharifah Azura Salleh, Zalina Ismail, Victor Kok Eow Lim, Sazaly AbuBakar, Kin Chong Leong
Zalina Ismail, Loong Hua Tee, Sharifah Azura Salleh, Rina Karunakaran, Kin Chong Leong, Loong Hua Tee. Sasheela Ponnampalavanar

Background: Surgical site infections (SSIs) constituted one of the major problems associated with hospital-acquired infections (HAIs). Increasing prevalence of extended-spectrum Î²-lactamase (ESBL)-producing *Escherichia coli* (ESBL-EC) poses a great threat to patients undergoing surgery in hospitals. We aim to evaluate the *in vitro* efficacy of flomoxef against ESBL-EC associated with SSIs in Peninsular Malaysia.

Study Design & Methods: A total of 111 ESBL-EC strains were collected from five hospitals located at North, Central, and South Malaysia, 24 of which were associated with SSIs. All strains were subjected to disk diffusion assay to determine their susceptibility towards flomoxef, cephalosporin, carbapenem, monobactam, Î²-lactamase inhibitor, and fluoroquinolone antibiotics.

Results: High rates of resistance towards cefpodoxime (100%), cefotaxime (99%), ceftriaxone (98%), aztreonam (57%), ciprofloxacin (56%), and cefepime (51%) were observed among all ESBL-EC. Reduced susceptibility towards cefepime (42%), amoxicillin-clavulanate (32%), ceftazidime (20%), and aztreonam (19%) were relatively high. When compared to isolates from non-surgical sites, the SSI-ESBL strains showed higher rates of non-susceptibility towards cefoxitin, amoxicillin-clavulanate, aztreonam, imipenem, and flomoxef. All ESBL-EC were largely susceptible to meropenem (100%), ertapenem (100%) and flomoxef (95%).

Conclusions: The *in vitro* efficacy of flomoxef is comparable to that of carbapenems and higher than cephalosporins, fluoroquinolone, and Î²-lactamase inhibitors.

Title: A qualitative case study of vulnerability and agency in research participants' daily lives and their experiences of research

Author: Rachel Greer (Presenter), MORU, United Kingdom
Co-authors: Maureen Kelley, Nipaphan Kanthawang, Jennifer Roest, Phaik Yeong Cheah

Background: Research participants are often classed as vulnerable populations in order to protect participants from exploitation. However, population-based assessments of vulnerability can result in the exclusion of certain groups who might benefit from research, such as children or migrants. Research participation may result in hidden harms when vulnerabilities of daily living are not taken into account. We conducted a research ethics case study in Chiangrai, Thailand to better understand research vulnerability in the context of participants' daily lives, and in their own words.

Study Design & Methods: We conducted 42 semi-structured interviews with research participants enrolled in two linked scrub typhus studies, their family members, researchers and key community informants. Participants in the scrub typhus studies were primarily from ethnic minority groups, some spoke limited Thai and a few had no legal status.

Results: The inability to speak Thai, lack of education, lack of legal status and living remotely contributed to other vulnerabilities resulting in more challenging access to healthcare and unstable employment. Research participants expressed their challenges in different ways; from talking openly about them, describing them as part of normal life, to not having any. Researchers and key informants most commonly described hill tribes, migrants and the poor as being vulnerable due to their circumstances. These vulnerabilities feature prominently in the perception of benefits and burdens of research. For example access to health care and gaining knowledge were considered benefits of research and the main burdens were related to follow-up visits. Participants showed remarkable resilience and agency in navigating these daily challenges, although agency could be constrained by circumstances.

Conclusions: Participants described vulnerabilities in relation to their circumstances and opportunities. Despite the additional burdens of taking part in research, participants felt they benefited overall.

Tuesday 15 December 2020

S13: Genetic and epidemiological determinants of malaria risk

14.10-15.40hr

Room B

Chairperson: Mallika Imwong

Invited speakers:

1. Impact of malaria elimination on immunity and risk of malaria rebound in Myanmar
   Aung Pyae Phyo
   Myanmar Oxford Clinical Research Unit, Myanmar

2. The protective effect of G6PD deficiency against severe malaria in Africa
   James Watson
   Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit

3. The risk of hemolysis in glucose-6-phosphate dehydrogenase deficiency: genotype-phenotype association analysis
   Usa Boonyuen
   Department of Molecular Tropical Medicine and Genetics, Faculty of Tropical Medicine, Mahidol University

Title: Impact of malaria elimination on immunity and risk of malaria rebound in Myanmar

Author: Aung Pyae Phyo (Presenter), Myanmar Oxford Clinical Research Unit, Myanmar
Co-authors: Katherine O'Flaherty, Francois Nosten, Freya J.I. Fowkes

Background: One potential concern of large scale intensive intervention project for malaria elimination, particularly mass drug administration (MDA), is malaria rebound after successful elimination, which is hypothesized to be due to loss of naturally acquired malaria immunity. However, exact timelines for the immune decay and the rebound is yet to be explored, due to the paucity of quantifiable data from studies assessing both the impact of MDA and its effect on malaria immunity.

Study Design & Methods: Using the data from malaria elimination pilot project on the Myanmar-Thailand border, the impact of malaria elimination measures (including MDA) on malaria immunity and how this predicts epidemiological patterns of infection over time is quantified.

Results: MDA was associated with a 12-fold reduction in the odds of PCR-detectable *P. falciparum* carriage over a 24-month follow-up period. Antimalarial IgG in response to conserved merozoite antigens (PfMSP2 and PfAMA1) was measured at three monthly surveys for 24-months (n samples = 10,520, n participants = 2,810). Multivariable mixed-effects linear and logistic regression were performed to determine (i) the temporal changes to antimalarial IgG, and (ii) the effects of IgG on *P. falciparum* infection before and after MDA. Throughout the study, IgG levels and seroprevalence fluctuated insignificantly and is varied by village but were relatively maintained over the 24-months follow-up period. In adjusted analyses, IgG responses were not associated with the odds of *P. falciparum* infection where effect modification for time (before and after MDA) was included.

Conclusions: These findings indicate that immediately following MDA, anti-merozoite IgG levels do not significantly decline despite the elimination of *P. falciparum* reservoirs, and are not associated with individual odds of *P. falciparum* infection after MDA. Future surveys are being planned to determine the long-term impact of MDA on acquired antimalarial antibody responses, and whether any changes are associated with higher risk of reintroduction or rebound.

Title: The protective effect of G6PD deficiency against severe malaria in Africa

Author: James Watson (Presenter), Mahidol Oxford Tropical Medicine Research Unit, Thailand
Co-author: Nicholas White

Background: Malaria has substantially affected the evolution of the human genome. Glucose-6-phosphate dehydrogenase (G6PD) deficiency, the most common enzymopathy of humans, is prevalent in all areas where malaria is or was endemic. Although whole-genome data from large patient cohorts combined with accurate haplotype imputation have advanced understanding of the relationship between many human genetic polymorphisms and the risk of severe falciparum malaria, the protective effect of G6PD deficiency has remained elusive and controversial.

Study Design & Methods: A causal model of severe malarial disease was used to assess the relationship between G6PD deficiency and severe malaria in a combined series of 4,667 Gambian and Kenyan children clinically diagnosed with severe malaria along with 7,210 healthy population controls.

Results: We show that G6PD deficiency is associated with reduced severity of illness in *P. falciparum* infection.

Conclusions: The strong association between phenotypic G6PD deficiency and reduced disease severity is obscured by the complex relationship with severe anaemia. Severe anaemia is part of the case definition of severe malaria and this biases genetic association studies.

Title: The risk of hemolysis in glucose-6-phosphate dehydrogenase deficiency: genotype-phenotype association analysis

Author: Usa Boonyuen (Presenter), Mahidol University, Thailand

Background: Glucose-6-phosphate dehydrogenase (G6PD) deficiency is an inherited genetic defect and the most common enzymopathy, affecting approximately 500 million people worldwide with greater than 200 identified variants. G6PD-deficient individuals have an increased susceptibility to hemolysis upon exposure to oxidative agents, including primaquine and tafenoquine which are the only medications effective for radical cure of *P. vivax* and *P. ovale*. Hemolytic toxicity of G6PD deficiency depends on two major factors; the level of G6PD activity which is determined by G6PD genotype and the exposure to oxidative stress.

Study Design & Methods: Biochemical and structural characterization of G6PD variants provided information regarding the association between phenotype and genotype.

Results: Most of natural G6PD mutations, especially Class II variants, are catalytically active but their structural instability is largely responsible for a significant decrease in the catalytic efficiency of the enzymes, contributing to severe enzyme deficiency observed in the clinical phenotypes. This also reflects the response of each G6PD variant to the oxidative stress. It was observed that an apparent non-deficient genotype does not necessarily imply a normal phenotype.

Conclusions: Therefore, the information on relationship between phenotype and genotype is of great importance to improve safety and clinical outcomes of malaria treatment using primaquine and tafenoquine.

Tuesday 15 December 2020

S14: Free Paper III: Medical entomology

14.10-15.40hr

Room C

Chairpersons:

1. Ronald Enrique Morales Vargas
2. Jiraporn Ruangsittichai

Speakers:

1. Wing morphometrics as a tool for identification of blow flies, *Lucilia* (Diptera: Calliphoridae)
   Rutchanon Jitaree
   Department of Parasitology, Faculty of Medicine, Chiang Mai University, Thailand

2. Collection performance of the new BG-Pro mosquito traps in various locations around the world
   Jennifer McCaw
   Biogents AG, Germany

3. Vector control in Indo-Pacific: developing a toolbox and improving access
   Fred Yeomans
   IVCC, United Kingdom

4. Utility of hot spot maps in local dengue surveillance in Quezon City, Philippines
   John Robert Medina
   Department of Epidemiology and Biostatistics, College of Public Health, University of the Philippine, Philippines

5. Characterization and functional analyses of dengue-specific memory CD8 t cells in healthy Thai subjects with HLA-B*38:02 allele
   Laxmi Gurung
   Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

6. Accuracy of dengue, chikungunya, and zika diagnoses by primary healthcare physicians in Tegucigalpa, Honduras
   Maria Fernanda Avila Mejia
   National Yang-Ming University, Taiwan

Title: Wing morphometrics as a tool for identification of blow flies, *Lucilia* (Diptera: Calliphoridae)

Author: Rutchanon Jitaree (Presenter), Department of Parasitology, Faculty of Medicine, Chiang Mai University, Thailand
Co-authors: Jens Amendt, Kabkaew L. Sukontason, Kom Sukontason, Kwankamol Limsopatham, Nina Feddern, Pradya Somboon, Sangob Sanit

Introduction: Blow flies of the genera *Lucilia* Robineau-Desvoidy are of forensic importance worldwide. Before being used in forensic investigations, correct species identification is an essential initial step. Although morphological and molecular techniques have been commonly utilized for species identification, some limitations of both methods have been reported. Since identification using wing morphometric analysis has been increasingly applied in the last few decades for many insects, including flies, the aim of this study was to determine if it could be used to identify *Lucilia* species of forensic importance.

Methods: Three Thailand species of *Lucilia*, *L. cuprina* (Wiedemann) (n=50), *L. porphyrina* (Walker) (n=19), *L. sinensis* (Aubertin) (n=10) and two Swiss species, *L. caesar* (Linnaeus) (n=78) and *L. illustris* (Meigen) (n=76) were investigated. The right wings of 233 specimens were flattened by slide-mounting, photographed, landmark digitized and analyzed for size and shape variation. The unweighted pair group method with arithmetic mean (UPGMA) dendrogram was constructed to determine the phenetic relationships of wing shape among each species. SPSS V.22.0 and MorphoJ were used for statistical analysis.

Results: Wing size differed significantly between the five species (Independent *t-test*, $P < 0.05$), except for comparison of *L. porphyrina – L. illustris*. Wing shape differed significantly between all five species ($P < 0.0001$), and *L. porphyrina* was most clearly separated from the other species. Interestingly, the percentage of correctly classified specimens are highly from 85.53 to 100 and the UPGMA dendrogram obviously revealed their closely related species.

Conclusion: Wing morphometrics is reliable method for identifying the five species of *Lucilia* of forensic importance. However, only wing shape data are recommended for use. Increasing the number of specimens and other *Lucilia* species merits further investigation.

Title: Collection performance of the new BG-Pro mosquito traps in various locations around the world

Author: Jennifer McCaw (Presenter), Biogents AG, Germany
Co-authors: Alvaro E. Eiras, Caro Degener

Background: CDC light traps have been in use for decades since their introduction in 1962 (Sudia & Chamberlain). They were the first portable traps that could easily be operated in almost any field setting and allowed live capture of mosquitoes, which is especially important for arbovirus isolation. A standard CDC light trap consists of plastic cylinder containing a motor unit with 4-bladed fan to draw in approaching mosquitoes, incandescent light, lid and catch bag. The fan and light are powered by a 6V battery. Light alone is not a strong attractant but when traps are supplied with CO2, collection rates usually increase significantly.

Study Design & Methods: Biogents has developed and tested a new CDC style trap that uses a novel catch bag and a 3-bladed fan. The prototype incorporated the same style lid and incandescent light as the standard CDC miniature light trap. The novel catch bag has a conical shape and an airtight bottom part that creates a different airflow around the trap compared to standard CDC traps. The 3-bladed fan is waterproof and can be powered by a 6V as well as a 12V battery. While moving a higher air volume even at 6V, the fan draws less amperage compared to the standard CDC fan. The lower power consumption will increase battery life by 30-40%. Due to a lower rotational frequency and the design of the blade the sucked-in mosquitoes are also better preserved.

Results: The performance of the new prototype was compared to the standard CDC miniature light trap and EVS trap in two locations in the US and Germany. The new prototype collected more species and more total mosquitoes than the CDC or EVS traps.

Conclusions: We hier with present a new and improved tool for mosquito surveillance.

Title: Vector control in Indo-Pacific: developing a toolbox and improving access

Author: Fred Yeomans (Presenter), IVCC, United Kingdom

Background: One of the main principles of malaria elimination should be to move away from a single intervention and deploy a set of interventions tailored for the setting. There is an urgent need to move beyond over reliance on mass free distribution of LLINs amongst forest goers in the Greater Mekong Subregion and for malaria transmission in and around villages in Papua New Guinea, and provide complementary tools and different points of access. Funded by the Australian Government's DFAT, IVCC's Indo-Pacific Initiative (IPI) aims to capitalize on IVCC's work in Africa to develop and support delivery of new vector control tools to combat the various unique challenges hindering the progress of malaria elimination in the region such as outdoor biting, vector diversity and hard-to-reach at-risk populations.

Study Design & Methods: Established in 2018, IPI commissioned three landscape reports on technical, regulatory and market access challenges and opportunities related to vector control in the region. From this baseline, two projects have been developed, one in the GMS to develop and test products for "Forest Packs" for forest-going populations; and the other in Papua New Guinea to build vector control testing and evaluation capacity and begin testing of vector control interventions not previously or recently used in the country. The BITE project (Bite Interruption Towards Elimination) in Thailand and Cambodia is a partnership led by University of California San Francisco's Malaria Elimination Initiative, including Cambodia CNM, AFRIMS, Kasetsart University, University of Notre Dame, Malaria Consortium, Swiss TPH and the Ifakara Health Institute. It aims to test Spatial Repellents, Insecticide Treated Clothing and Topical Repellents; semi-field evaluations by AFRIMS and Kasetsart University are underway with field evaluations among forest rangers, forest-goers and forest-dwellers in Mondolkiri province, Cambodia, scheduled to begin in 2021. The NATNAT project (Newly Adapted Tools Network Against mosquito-borne disease Transmission in PNG) is a partnership comprising the PNG Institute of Medical Research, Burnet Institute and James Cook University, and is focused on testing the efficacy, feasibility and acceptability of complimenting LLIN distribution with IRS, Larval Source Management and Spatial Repellents for the village peri-domestic environment. Both projects will include modelling by Imperial College London and Swiss TPH to model the impact of new vector control tools on malaria transmission.

Results: The trials are still in progress and so no results are available yet. The purpose of this oral presentation is to raise awareness of this activity and continue to build links with relevant stakeholders in the region. Preliminary findings of the trials in GMS and PNG will be available in 2021.

Conclusions: In this uncertain political, social and economic era of pandemic response, the IVCC IPI is working with partners to enable programs to adopt evidence based integrated vector control programs tailored to address local needs and settings.

Title: Utility of hot spot maps in local dengue surveillance in Quezon City, Philippines

Author: John Robert Medina (Presenter), Department of Epidemiology and Biostatistics, College of Public Health, University of the Philippine, Philippines
Co-authors: Chris Erwin Mercado, Kim Ian Tiu, Rolando Cruz, Melvin Abrigo, Khew Ee Hung, Flavio Furukawa, Shin'ya Kawamura, Masami Kaneko Ernesto, Jr. Gregorio, Paul Michael Hernandez, Nonaka Daisuke, Fernando, Jr. Garcia, Richard Maude, Jun Kobayashi

Background: Quezon City, a highly urbanized city in Metropolitan Manila, has long been facing dengue as a perennial public health concern. Surveillance is one of the key strategies being implemented by the Dengue Prevention and Control Program at the national and local level. Under the current surveillance system, dengue is being reported weekly on an all-case basis, i.e. probable and suspected cases are reported. In recent years, geographic information system has been adapted in routine surveillance procedures by some localities including Quezon City. However, maps that visualize number of cases or disease incidence rely on subjective interpretation. Performing further spatial statistical analyses may be helpful in addressing such limitation. Hence, the utility of integrating global clustering analysis and local cluster detection that generates hot spot maps was demonstrated in this paper.

Study Design & Methods: This is a retrospective study that involved spatial analysis of reported dengue cases in Quezon City from January 2010 to December 2017. The surveillance data was provided by the Quezon City Epidemiology and Surveillance Unit (QESU). Getis Ord General G statistics was used to determine if clustering is present in the study area, while Getis-Ord Local General Gi* was used to locate dengue hot spots.

Results: Spatial heterogeneity was observed over the years. The spatial distribution of reported dengue cases was varying greatly across years as observed in the incidence maps. Statistically significant global clustering of reported dengue cases was observed from 2011 to 2015. The spatial distribution of high incidence in the dataset is more spatially clustered than would be expected if underlying spatial processes were truly random. The highest number of hot spots was identified in 2012 with nine hot spots, while the lowest was in 2016 with only three hot spots. From 2010 to 2017, 18 villages were identified as hot spots. Dengue hot spot instability was evident across years.

Conclusions: Identification of statistically significant hot spots can assist in directing efforts towards the containment of dengue, which can be made more targeted, tailored-fit, and time-effective. It can also help in the allocation of financial and human resources in times of outbreak. Employing cluster analysis and local cluster detection in the routine surveillance procedures may be helpful not only in disease control but also in public health planning, monitoring, and evaluation.

Title: Characterization and functional analyses of dengue-specific memory CD8 t cells in healthy Thai subjects with HLA-B*38:02 allele

Author: Laxmi Gurung (Presenter), Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
Co-author: Jaturong Sewatanon

Background: Dengue virus (DENV) infection is a global public health burden. According to the World Health Organization (WHO), about 3.9 billion people are living in the areas at risk of having dengue and approximately 50,000-150,000 dengue cases have been reported in Thailand annually. At present, there is no effective vaccine against DENV. The robust CD8 T cell responses are associated with a lower risk of severe dengue. However, the protective role of dengue-specific memory CD8 T cells is still unclear. Recently, our laboratory has identified a novel DENV NS3 epitope (NS3296-304), which induced a high level of interferon-gamma (IFN-g) producing CD8 T cells upon peptide stimulation and this epitope binds to the HLA-B*38:02 allele in this person. Interestingly, this person has never been diagnosed with dengue illness. Therefore, we hypothesized that individuals with HLA-B*38:02 allele could develop dengue-specific memory CD8 T cells that contribute to protective immunity during subsequent dengue virus infection.

Study Design & Methods: This project aims to characterize dengue-specific memory CD8 T cells in Thai people with HLA-B*38:02 allele. Peripheral blood mononuclear cells (PBMCs) were isolated from 8 regular blood donors at Siriraj Blood Bank and had been tested to have HLA-B*38 by serology method. The PBMCs was stimulated by the DENV NS3296-304 peptide for 6 hours before flow cytometry analyses for tetramer, surface markers, and intracellular cytokines. Moreover, enzyme-linked immunosorbent assay (ELISA) for antibodies (IgG) against DENV, Japanese encephalitis virus (JEV), and Zika virus (ZIKV) were performed to determine whether these study subjects have been exposed to these flaviviruses.

Results: Tetramer+ CD8 T cells were detected in all study subjects with an average of 0.33% of CD8 cells. The majority of these tetramer+ CD8 T cells were effector memory (CCR7-CD45RA-) with an average of 54.7 %. Low level of IFN-g and TNF-a production was observed after 6-hours of DENV-NS3-peptide stimulation but surprisingly not significantly higher than the unstimulated cells. All study subjects contained anti-DENV IgG in their plasma and some also had anti-ZIKV IgG.

Conclusions: In conclusion, the findings suggest that dengue-specific CD8 T cells can be detected in all study subjects who have been exposed to DENV. However, further investigation would be required for their functions that might contribute to protective immunity against DENV infection.

Title: Accuracy of dengue, chikungunya, and zika diagnoses by primary healthcare physicians in Tegucigalpa, Honduras

Author: Maria Fernanda Avila Mejia (Presenter), National Yang-Ming University, Taiwan
Co-authors: Chyong-Mei Chen, Pei-Yun Shu, Dar-Der Ji

Background: Arboviruses are a worldwide health burden. In Honduras, Dengue, Chikungunya, and Zika are co-endemic. These infections share similar clinical and epidemiological behavior complicating the differential diagnosis. The surveillance done by the Ministry of Health is mostly passive and relies on reported physician diagnoses that are not frequently laboratory confirmed.

Study Design & Methods: We conducted a cross-sectional study with convenience sampling from June to September in 2016 and 2017. Clinical data and capillary blood samples from 415 arboviral cases and a control of 248 febrile cases were collected on Whatman 903 filter paper. Viral RNA was extracted from a 6-mm dried blood spot. The samples were confirmed by RT-qPCR and sequencing.

Results: In 2016, the sensitivity of Dengue clinical diagnosis was 42.9% while Zika was 22.4%. In 2017, Dengue sensitivity was 93.1% and Zika dropped to 0%. In both years, Chikungunya sensitivity remained 0%. 372 (90.12%) of all clinically diagnosed arboviral cases fitted one or more case definitions. In 2016 during Epiweek 37, physicians were unaware of a viral switch from Dengue to Zika and kept diagnosing these cases as Dengue. Similarly, in 2017 from Epiweek 26 to Epiweek 28, a Zika outbreak was mistaken for Dengue.

Conclusions: Physicians based their diagnoses according to Honduran MOH case definitions. These criteria help to identify arboviral cases but are not enough to differentiate between these arboviruses. There is the need to improve arboviral diagnoses since differential diagnosis without laboratory confirmation is challenging. This results in erroneous disease estimates that can affect public health interventions.

Tuesday 15 December 2020

S15: Updates on HIV Prevention

14.10-15.40hr

Room D

Chairpersons**:**

1. Punnee Pitisuttithum
2. Eileen Dunne

Invited speakers**:**

1. Injectable long**-**acting cabotegravir**-**an HIV prevention alternative?
   Chaiwat Ungsedhapand
   *Thailand Ministry of Public Health **-** U.S. Centers for Disease Control and Prevention Collaboration, Thailand*

2. PrEP implementation and demand generation in Thailand
   Chomnad Manopaiboon
   Centers for Disease Control and Prevention, Thailand, Thailand

3. Combination HIV prevention services among young men and transgender women selling or trading sex in Thailand, the COPE4 study
   Andrew Hickey
   Division of HIV/AIDS Prevention, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia, United States

4. Assessing biological risk of HIV transmission in transgender women
   Alexandra Schuetz
   *MHRP**-**AFRIMS, Thailand*

Title: Injectable long-acting cabotegravir—an HIV Prevention alternative?

Author: Chaiwat Ungsedhapand (Presenter), Thailand Ministry of Public Health - U.S. Centers for Disease Control and Prevention Collaboration, Thailand

Background: Pre-exposure prophylaxis (PrEP) is an HIV prevention method in which HIV-negative people use antiretroviral drug to protect themselves from getting HIV. To date, only oral tenofovir disoproxil fumarate/emtricitabine (TDF/FTC) has been approved for all populations. Recently, oral tenofovir alafenamide/emtricitabine/ (TAF/FTC) was approved by the US FDA for daily use for men who have sex with men (MSM) and transgender women (TGW).

Study Design & Methods: Long-acting injectable cabotegravir (CAB-LA) is an antiretroviral developed and formulated as an injectable for both HIV treatment and HIV prevention. There are two large-scale randomized, controlled, double-blind study comparing the safety and efficacy of CAB-LA injected once every 8 weeks to daily TDF/FTC for HIV prevention in MSM, TGW (HPTN 083), and women (HPTN 084) at risk of HIV infection.

Results: For HPTN 083 study, an independent Data and Safety Monitoring Board (DSMB) that reviewed interim study data found that both PrEP regimens safely and effectively prevented HIV acquisition in the study population. The final data analysis based on a more extensive analysis of interim data has shown that a total of 52 participants have HIV infections, 13 and 39 participants acquired HIV in the CAB-LA arm and TDF/FTC arm, respectively (incidence rate 0.41% and 1.22%, respectively). The hazard ratio for the CAB-LA versus TDF/FTC arms is 0.34 (95% CI 0.18-0.62), corresponding to a 66% reduction in incident HIV infections in CAB-LA group. HPTN 084 study results are expected in 2023.

Conclusions: Ultimately, the results of these long-acting injectable PrEP trials will help guide next steps for alternative HIV prevention option.

Title: PrEP implementation and demand generation in Thailand

Author: Chomnad Manopaiboon (Presenter), Centers for Disease Control and Prevention, Thailand, Thailand

Background: The Thai government has demonstrated active ownership in providing PrEP services to key populations and others who are at risk of HIV. Thailand National Prevention and Treatment guidelines have endorsed PrEP as part of a comprehensive HIV prevention package since 2014, leading to the development of the national PrEP implementation guideline in 2018.

Study Design & Methods: Starting in October 2019, the National Health Security Office (NHSO) approved the inclusion of the PrEP pilot service in the HIV universal health care coverage with a quota for 2,000 PrEP users, aiming to scale up the service for all who can benefit from PrEP. Additionally, a web-based platform has been developed to monitor national PrEP use and uptake.

Results: Despite a favorable policy environment, PrEP services are not currently widely accessed and drugs have been offered at low or no cost as part of government and external donor-supported demonstration projects and research activities. PrEP service delivery in Thailand are provided mainly by key population-led PrEP program and government-based PrEP providers. As of May 2020, program data showed 12,713 accessed PrEP, accounting for 9% of estimated 2020 country's PrEP target. PrEP demand creation has been sporadically implemented through several social media channels, websites, and community-based outreach. There is neither a concerted effort at the national level to promote PrEP nor a government budget specifically allocated for this activity.

Conclusions: As Thailand moves forward to end AIDS by 2030, demand creation and scaling up access to PrEP should be considered and included in HIV prevention discussions to create an effective national PrEP program.

Title: Combination HIV prevention services among young men and transgender women selling or trading sex in Thailand, the COPE4 study

Author: Andrew Hickey (Present), Division of HIV/AIDS Prevention, U.S. Centers for Disease Control and Prevention, Atlanta, Georgia, United States

Background: Thai young men (YMSM) and transgender women (YTGW) who sell and trade sex with other men are at much greater risk for HIV/STI acquisition and transmission compared to the general population. Understanding the factors associated with HIV/STI transmission within these communities can be used to improve targeted prevention interventions and better understand what services are important to consider for HIV prevention packages offered to high risk vulnerable populations.

Study Design & Methods: YMSM and YTGW in Bangkok and Pattaya, Thailand that reported sex work (within the last 12 months) and aged 18-26 years were enrolled in a mixed methods study (COPE4) offering all participants combination HIV prevention support services with the option of starting/stopping HIV pre-exposure prophylaxis (PrEP) while on the study. At enrollment and every 3 months thereafter (standard follow up), participants were provided combination HIV prevention counseling and testing services, including sexual health assessment, review PrEP eligibility, access to free condoms and lube, testing for HIV and syphilis (rapid tests) as well as rectal Neisseria gonorrhoeae and Chlamydia trachomatis (by nucleic acid amplification from rectal swab samples) in accordance to Thailand national standards. Participants also completed computer assisted self-assessment at each 3-month standard visit.

Results: Overall, 900 YMSM and YTGW were enrolled and followed for at least 12 months (up to 24 months). At the baseline study visit, 44 (4.9%) had HIV infection, 79 (9.2%) had syphilis, 42 (4.9%) had rectal gonorrhea and 123 (24.4%) had rectal chlamydia. Among participants on study for at least 12 months (n=827), the majority started PrEP within one week of enrollment (n=516, 62%) and 92%-98% of participants consistently self-reported (weekly SMS survey) at least 4 doses of PrEP within the preceding 7 days. Further, more than 75% of eligible participants returned for a standard visit at 24 months and more than 85% of participants that initially chose to take PrEP continued on PrEP at the 12 month visit.

Conclusions: Both YMSM and YTGW that sell/trade sex are at substantial risk of HIV and other STI infections as evidenced by the high prevalence of infections observed at the enrollment visit. However, high risk Thai YMSM and YTGW participants engaged in combination HIV prevention services, with high uptake, adherence, and persistence with HIV PrEP over at least 12 months of follow up.

Title: Assessing biological risk of HIV transmission in transgender women

Author: Alexandra Schuetz, on behalf of the SEARCH 011/RV304 study team (Presenter), MHRP-AFRIMS, Thailand

Background: Transgender women (TGW) have been disproportionally affected by HIV infection, with a global pooled estimated HIV prevalence among TGW of 19.1%, and the odds of being HIV positive 50 times that of all reproductive-age adults in low/middle income countries. Those high HIV infection rates in TGW are often attributed to high rates of poor access to healthcare due to stigmatization, discrimination, or criminalization in some settings, high burden of mental health problems, and substance use.

Study Design & Methods: However, data are scarce regarding potential underlying biological mechanisms of HIV transmission in TGW. Usage of exogenous hormones, especially in supraphysiologic doses, could modulate the expression of the CCR5 co-receptor and/or cytokine/chemokine secretion which could impact HIV acquisition. In addition, injectable synthetic fillers that allow for feminization, and undergoing gender affirmation surgery (GAS), by re-constructing a neo-vagina through penile skin inversion, scrotal or sigmoid colon grafts, may affect the risk of HIV transmission by potentially increasing systemic and/or local immune activation. Current data are limited, but there are studies underway in Thailand and the US to assess the biological risk of HIV transmission in TGW.

Results: We conducted a cross-sectional study in Thailand of HIV-negative volunteers including 10 TGW post GAS taking gender affirming hormone treatment, 10 cis women (CW) not taking hormonal contraceptives, and 10 MSM to assess the potential biological risk of HIV transmission in TGW compared to CW and MSM. All volunteers underwent a detailed medical history, physical examination, and phlebotomy, with optional gut biopsy, lymph node biopsy, and vaginal/neo-vaginal and/or rectal secretion collection.

Conclusions: We assessed peripheral and mucosal immune activation markers, and CCR5 expression as well as gut, vaginal/neo-vaginal microbiome profiles to evaluate the impact of gender affirming hormone treatment, injectable fillers and GAS in TGW.

Tuesday 15 December 2020

S16: COVID-19 case management (Thai/Eng session)

14.10-15.40hr

Room E

Chairperson: Weerawat Manosuthi

Invited speakers:

1. Adult: infection control: care and treatment (no abstract)
   Weerawat Manosuthi and Lantharita Charoenpong
   Ministry of Public Health, Thailand

2. Pediatric: infection control in pediatric (no abstract)
   Visal Moolasart and Chaisiri Srijareonvijit
   Ministry of Public Health, Thailand

3. Nursing care of critically ill COVID-19 in intensive care unit (no abstracts)
   - Nursing care for patients on respirator
     Rasamee Srico
     Ministry of Public Health, Thailand

   - Nursing care for adult and pediatric
     Putthiporn Limpanadusadee
     Ministry of Public Health, Thailand

   - Site visit
     Somtavil Umpornareekul
     Ministry of Public Health, Thailand

Tuesday 15 December 2020

S17: Perspectives on COVID-19 research, surveillance, and treatments

15.40-17.10hr

Room A

Chairperson: Anthony Jones

Invited speakers:

1. Impact of COVID-19 on the Armed Forces of the Philippines medical research and their role in the public health response
   Paula Corazon Diones
   Philippines-AFRIMS Virology Research Unit, Philippines

2. Evolution of a COVID-19 pandemic response: from the emergence of the disease to current priorities
   Anthony Jones
   Armed Forces Research Institute of Medical Sciences, Thailand

3. Evolvability of COVID-19 and its impact on genomic surveillance
   Thanat Chookajorn
   Faculty of Tropical Medicine, Mahidol University, Thailand

4. Management in COVID-19 confirmed patients, Thai perspective
   Krittaecho Siripassorn
   Bamrasnaradura Infectious Disease Institute, Ministry of Public Health, Thailand

Title: Impact of COVID-19 on the Armed Forces of the Philippines Medical Research and their role in the public health response

Author: Paula Corazon Diones (Presenter), Philippines-AFRIMS Virology Research Unit, Philippines

Background: The first SARS-CoV-2 case was confirmed on 30 Jan 2020 and community transmission documented on 05 March 2020 in the Philippines. As of 4 Sept 2020, there are already 228,403 confirmed COVID-19 cases in the Philippines with 3,688 deaths. The Armed Forces of the Philippines-Armed Forces Research Institute of Medical Sciences (AFP-AFRIMS) Collaborative Molecular Laboratory, being the only molecular laboratory capable of performing COVID-19 PCR testing within the Philippine military hospital network, was confronted with the task of supporting the AFP in detecting COVID-19 cases among active duty personnel and their dependents. Here, we describe an overview of our SARS-CoV-2 public health response and its impact on other ongoing medical researches.

Study Design & Methods: To combat COVID-19 among the Philippine military population, the following measures were done at the AFP in collaboration with AFRIMS: (1) Technical assistance on setting up of the COVID laboratory by initially assisting in sample testing and sharing our expertise in the design, equipment and laboratory consumables required in setting up an extension laboratory specific for COVID-19 testing, as well as training AFP laboratory personnel in biosafety and biosecurity procedures (2) Training of AFP personnel in the performance of manual and automated PCR techniques for SARS-CoV-2 (3) support in establishing a workflow for COVID-19 including specimen collection, transport and processing.

Results: Through the collaborative efforts of AFRIMS and the VLMC-AFPHSC, the Philippines Department of Health granted Level 5 accreditation for the AFP-AFRIMS Collaborative Molecular Laboratory for COVID-19 testing on 11 April 20. More than nine (9) AFP personnel were trained to augment current laboratory capability and an efficient workflow and referral system with other military hospital units were established. From 14 Apr 20 up to 15 Aug 20, 12,440 active duty personnel, dependents and authorized civilians were tested with 771 (6%) positive for SARS-CoV-2. Positive cases were predominantly military (67%). Most of the ongoing research projects were put on hold temporarily to prioritize SARS-CoV-2 testing but there are plans and mitigation measures in place to gradually resume these projects.

Conclusions: This shows the successful results of the more than 10 years strong collaboration between AFRIMS and the AFP in detecting, testing, monitoring and controlling emerging and re-emerging diseases.

Title: Evolution of a COVID-19 pandemic response: from the emergence of the disease to current priorities.

Author: Anthony Jones (Presenter), Armed Forces Research Institute of Medical Sciences, Thailand
Co-authors: Chonticha Klungthong, Taweewun Hunsawong, Stefan Fernandez

Background: With the emergence of SARS-CoV-2, USAMD-AFRIMS played an integral supporting role in the early days of the outbreak where testing kits were extremely limited. As the pandemic progressed, USAMD-AFRIMS continued to develop their support capacities to include a variety of diagnostic, surveillance, and epidemiological tools in anticipation of shifting priorities as the COVID-19 pandemic progressed.

Study Design & Methods: AFRIMS Virology utilized the WHO Berlin COVID-19 RT-PCR assay during the initial emergence of SARS-CoV-2. As the focus shifted to epidemiology, Illumina Miseq Next Generation Sequencing was used to determine the genomic phylogeny of isolated SARS-CoV-2 viruses, in addition to the development of EIA, PRNT, and RVP to screen for seroprevalence among our study populations.

Results: During the initial period of the outbreak, AFRIMS performed 240 PCR assays and supplied 500 screening kits to partners in Thailand, Nepal, Bhutan, and the Philippines. In March, AFRIMS Virology shifted priorities to providing genomic phylogenetic data for 52 viral isolates as part of the COVID-19 Network Investigations Alliance (CONI). Finally, upon the commissioning of the AFRIMS BSL-3 for SARS-CoV-2 work, AFRIMS Virology focused on validation of EIA and neutralization assays for upcoming seroprevalence studies.

Conclusions: AFRIMS Virology's past, present, and continuing support of US, Thai, and regional partners, in addressing the concerns of COVID-19, has not only contributed to ensuring positive public health outcomes in the face of a pandemic but also has provided valuable lessons and data that can be utilized in the preparation of future public health emergencies should they arise.

Title: Evolvability of COVID-19 and its impact on genomic surveillance

Author: Thanat Chookajorn (Presenter), Mahidol University, Thailand

Background: The COVID-19 pandemic has presented the research community with a series of real-time evolutionary events, unprecedentedly monitored at a genomic scale worldwide. Months after the first outbreak, SARS-CoV-2, the etiological RNA virus of COVID-19, has accumulated a series of mutations, generating hundreds of lineages that could be traced to countries of origin and major spreading events. Genomic investigations of SARS-CoV-2 in Thailand using an ARTIC-based multiplex enrichment method have revealed multiple introduction events into the country. A virus population, supposedly imported in January of 2020, has expanded into a Thai-specific lineage by means of local transmission. However, this Thai-specific lineage, scientifically designated A.6, appears to undergo lineage extinction, which confirms the end of the first COVID-19 wave in Thailand. Still, the prolonged evolving nature of the virus pandemic has generated multiple sub-lineages on the global scale. These ongoing evolutionary phenomena have become an invaluable tool for determining the source of re-positive cases and for assisting disease investigation in Thailand. These tools and their impacts will be discussed.

Title: Management in COVID-19 confirmed patients, Thai perspective

Author: Krittaecho Siripassorn (Presenter), Bamrasnaradura Infectious Disease Institute, Ministry of Public Health, Thailand

Background: The COVID-19 outbreak in Thailand occurred in March 2020. During that period, there was no any approved medication for patients infected with SARS-CoV-2.

Study Design & Methods: This presentation reviewed the Thai Regulations and guidance/policy of management COVID-19 confirmed patients in Thailand. And evidence-based treatment from the outbreak.

Results: After the first confirmed COVID-19 infected patients in Thailand was reported in Jan 2020, the outbreak started on Mar 2020. To respond and control the outbreak, the Communicable Diseases Act, B.E. 2558 (2015) was mandated and the Department of Medical Services, MOPH issued first guidance in Mar 2020. It mainly included quarantine policy, face mask plus social distancing campaign, and antiviral therapy for confirmed patients.

Conclusions: Cooperative management during the outbreak, and discipline of Thai people, include infected patients to follow the guidance from authority could control the outbreak in May 2020.

Tuesday 15 December 2020

S18: Elimination of *P. falciparum* from Kayin State (Myanmar)

15.40-17.10hr

Room B

Chairperson**:** Francois Nosten

Invited speakers**:**

1. Progress towards *P. falciparum* malaria in Kayin State
   Jade Rae
   Shoklo Malaria Research Unit (SMRU), Thailand

2. Artemisinin resistance markers during elimination of *P. falciparum* in Kayin State
   Aung Myint Thu
   Shoklo Malaria Research Unit (SMRU), Thailand

3. Importance of community engagement for malaria elimination (no abstract)
   Saw Winn
   Shoklo Malaria Research Unit (SMRU), Thailand

4. Environment analysis and surveillance to improve malaria elimination strategy**:** the EASIMES (no abstract)
   Jordi Landier
   Aix Marseille Univ, INSERM, IRD, SESSTIM, Marseille, France

Title: Progress towards *P. falciparum* malaria in Kayin State

Author: Jade Rae (Presenter), Shoklo Malaria Research Unit (SMRU), Thailand

Background: The global burden of malaria has decreased dramatically since the year 2000, resulting in substantial reductions in the transmission intensity, and spatial distribution of malaria. Since 2014, the Malaria Elimination Task Force (METF) programme has operated a vast network of malaria posts across Kayin State, in the East of Myanmar in response to high *P. falciparum* transmission and the ongoing threat of antimalarial drug resistance. For elimination in the METF programme, and malaria elimination programmes globally, it is essential that interventions are targeted based on the risk of ongoing transmission, and that cases continue to be diagnosed early to ensure treatment is delivered to interrupt transmission.

Study Design & Methods: To provide an overview of the progress towards *P. falciparum* elimination, the long-term impacts of mass drug administration, and the spatio-temporal trends of transmission, data collected throughout the METF programme was analysed using descriptive statistics, regression modelling and ArcGIS mapping software. To determine the diagnostic capabilities of the malaria posts when approaching elimination, the relationship between rapid diagnostic testing rates and declining incidence was investigated using regression modelling techniques.

Results: Progress towards the elimination of *P. falciparum* malaria has resulted in a 96.8% reduction in the yearly incidence per 1,000-person years since the programmes commencement, now with 1,110 malaria posts out of 1,198 malaria posts reporting no *P. falciparum* cases. The spatio-temporal evaluation of ongoing transmission revealed heterogeneity in the distribution of malaria risk across space and time, highlighting the need for strategically targeted interventions, particularly when approaching elimination targets.

Conclusions: The METF programme has seen dramatic declines in *P. falciparum* malaria since its inception. By ensuring uninterrupted test and treatment availability to population at-risk of malaria, and by identifying locations where targeted interventions could assist in reducing ongoing transmission using spatio-temporal analysis, elimination targets can be met.

Title: Artemisinin resistance markers during elimination of *P. falciparum* in Kayin State

Author: Aung Myint Thu (Presenter), Shoklo Malaria Research Unit, Myanmar

Background: *P.falciparum (P.f)* malaria parasite that carry Kelch 13 (K13) mutations are reported since 2003 on the Thailand-Myanmar border. There has been rising concern on the spread of artemisinin resistance in Eastern Myanmar where it shares the border along with the western part of Thailand and intense malaria elimination implementation are deployed including large scale community-based malaria diagnosis and treatment and targeted mass drug administration (MDA) at hotspot villages.

Study Design & Methods: In this observational study 2,806 *P.f* samples confirmed by rapid diagnostic test (RDT) from >300 sites/villages in 4 townships of the Eastern part of Myanmar from 2014 to 2018 were analyzed.

Results: Overall K13 mutant parasite prevalence was 59% (1,665/2,806) and most common mutants were F446I (14%), P441L (14%) while C580Y was < 3%. Of 53 villages with MDA intervention, 338 samples were from the period before MDA interventions (median months = 7 (IQR 2 – 12) and 487 samples were from the post MDA period, median months = 14 (IQR 7-17). K13 mutant proportion decreased about 10% from 62% to 54% after MDA. C580Y allele was found in < 1% in post MDA period compared to 4% before MDA ($P<0.05$, 95% CI 0.531-0.937).

Conclusions: Our observational study found that targeted mass drug administration using dihydroartemisinin-piperaquine in addition to the use of artemether-lumefantrine in passive case treatment at falciparum hotspots did not increase the artemisinin resistance K13 mutant parasites in Eastern Myanmar.

Tuesday 15 December 2020

S19: The current landscape of tropical diseases vaccine

15.40-17.10hr

Room C

Chairpersons**:**

1. Punnee Pitisuttithum
2. Jerome Kim

Invited speakers**:**

1. Enteric disease vaccine (no abstract)
   Jerome Kim
   The International Vaccine Institute (IVI)

2. Chikungunya vaccine (no abstract)
   Anh Wartel
   The International Vaccine Institute (IVI)

3. HIV cure developments
   Eugene Kroon
   SEARCH, Institute of HIV Research and Innovation, Thailand

Title: HIV cure developments

Author: Eugene Kroon (Presenter), SEARCH, Institute of HIV Research and Innovation, Thailand

Background: HIV cure is a desirable goal for individuals living with HIV who face stigma and life-long antiretroviral therapy (ART), while treatment costs pose a significant challenge to national health programs and donors. Eliminating all cells capable of producing HIV seems a near unattainable goal with current therapies and a more achievable goal may be HIV remission. Therapeutic vaccines aim to enable the host immune response to control HIV after ART interruption.

Study Design & Methods: Individuals treated since acute HIV infection (AHI) achieve significantly smaller HIV reservoirs, preserved immune function and little viral escape and are therefore targeted for early intervention therapy studies in humans. Interventions to date include latency reversing agents, broadly neutralizing antibodies, therapeutic vaccines, and gene editing.

Results: None of the single interventions applied to date, including therapeutic vaccines, have induced long-term HIV remission in human randomized controlled trials. However, in non-human primates, combinations of vaccines inducing broad immune responses with latency reversal and/or immune modulation and/or broadly neutralizing antibodies have induced long-term HIV remission in a significant number of monkeys.

Conclusions: In order to achieve long-term HIV remission in humans therapeutic vaccines will likely need to be combined with other modalities in placebo controlled trials with treatment interruption. Given the risks and uncertainties associated with these early stage trials, it is critical that community participation and social science studies inform the conduct of these trials.

Tuesday 15 December 2020

S20: Melioidosis: targeting the sources of infection

15.40-17.10hr

Room D

Chairperson: Matthew Reed

Invited speakers:

1. *Burkholderia pseudomallei* in soil and water
   Alain Pierret
   French Research Institute for Sustainable Development (IRD), Lao PDR

2. Co-evolutionary signals from *Burkholderia pseudomallei* population genomics highlight its survival strategy in a hostile environment
   Claire Chewapreecha
   Mahidol-Oxford Tropical Medicine Research Unit, Thailand

3. Melioidosis in animals
   Matthew Reed
   Armed Forces Research Institute for Medical Sciences, Thailand

4. Melioidosis prevention strategies
   Direk Limmathurotsakul
   Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand

Title: *Burkholderia pseudomallei* in soil and water

Author: Alain Pierret (Presenter), French Research Institute for Sustainable Development (IRD), Lao PDR

Background: Melioidosis, a severe infection caused by the environmental bacterium, *Burkholderia pseudomallei*, is being recognized increasingly frequently throughout the tropics. Both the disease and the causative organism are distributed unevenly within endemic areas, but the factors that determine such an uneven distribution and the true burden of melioidosis remain poorly understood. Most recent studies suggest that rainfall, soil moisture, temperature and soil type determine, to a large extent, the presence of *B. pseudomallei*.

Study Design & Methods: In this presentation, we provide a concise overview of current knowledge on the environmental factors that appear to influence the occurrence and spread of *B. pseudomallei* in the environment, with a focus on recent observations of soils and surface waters in Lao PDR.

Results: The studies reviewed in this presentation clearly show that *B. pseudomallei* seems to be associated with some soil types / soil properties and that its presence in surface waters is influenced by seasonal climatic conditions. Our work also demonstrates that *B. pseudomallei* can occur at soil depths well below 30 cm.

Conclusions: This mini-review confirms the importance of several environmental factors as potential determinants of the occurrence and dissemination of *B. pseudomallei* and outlines new directions to be explored further to better understand the physico-chemical conditions that favor the persistence of this pathogen in the environment.

Title: Co-evolutionary signals from *Burkholderia pseudomallei* population genomics highlight its survival strategy in a hostile environment

Author: Claire Chewapreecha (Presenter), Mahidol-Oxford Tropical Medicine Research Unit, Thailand

Background: The soil bacterium *Burkholderia pseudomallei* is the causative agent of melioidosis and a significant cause of human morbidity and mortality in many tropical and sub-tropical countries. The species notoriously survives harsh environmental conditions but the genetic architecture for these adaptations remains unclear. However, progress towards a better understanding of the evolution and adaptation of this species has been impeded by its large and complex gene repertoire, with at least two large chromosomes, multiple genomic islands, and paralogous genes.

Study Design & Methods: A hypothesis-free co-selection analysis, known as genome-wide epistasis and co-selection study (GWES) has recently been used to successfully identify bacterial co-selected loci, many of which matched known gene-gene interacting partners. This prompted us to apply GWES to detect co-evolutionary signals in a collection of 1,136 *B. pseudomallei* isolates and validate our findings on an additional collection of 875 isolates, thereby enabling us to identify loci under recent selective pressure while distinguishing interacting genes from their multiple paralogs. To elucidate the function of the co-selected genes, we integrated the GWES findings with transcriptomic data and gene knockout assays.

Results: We identified a large number of mutation pairs under co-selection in distinct genes and non-coding RNA, of which a majority of signals detected in the discovery dataset can be replicated in the validation dataset (totalling 2,011 genomes). Genes under co-selection are mostly conditionally expressed with a marked correlation in the expression of gene-gene pairs when grown under physical stress conditions. We discovered a putative adhesin (BPSL1661) as a hub of co-selection signals and experimentally confirmed the essential role of BPSL1661 under nutrient deprivation. The gene co-selection network surrounding BPSL1661 likely offers *B. pseudomallei* a selective advantage to survive nutrient limited conditions.

Conclusions: We propose that anthropogenic activities such as pre- and post-harvest crop residue burning have accelerated soil nutrient depletion and may have directly contributed to the preferential survival of *B. pseudomallei* over other relatively benign soil microorganisms. This is expected to lead to a consequent increase in the incidence of melioidosis should the “slash-and-burn” practices continue to expand.

Title: Melioidosis in animals

Author: Matthew Reed (Presenter), AFRIMS, Thailand

Background: *Burkholderia pseudomallei*, the saprophytic bacteria that causes human Melioidosis, is responsible for 89,000 deaths globally per year. The bacteria is also unique in its ability to infect a multitude of species. Human cases are well characterized, with established risk factors, diagnosis and treatment protocols; however, the significance of animal disease and its role in environmental contamination and human transmission is not well understood.

Study Design & Methods: In this presentation, existing published research is collated to evaluate the current state of knowledge of Melioidosis in animals, approximate its role in environmental contamination and subsequent human transmission, and propose biosecurity practices aimed to reduce disease risk for people associated with livestock. Finally, knowledge gaps are highlighted and presented as opportunities for future research.

Results: *B. pseudomallei* has been detected in dozens of animal species, with a range of clinical presentation to from multisystemic organ failure to asymptomatic disease. Animal transportation has been suggested as the cause of several human Melioidosis outbreaks in non-endemic areas. Bacterial shedding has been confirmed from animal feces, urine, saliva, wound discharge and from fluids during parturition. There is scant published data on surveillance of the bacteria among livestock and wildlife; however, nonpublished work by AFRIMS has found seroprevalence of about 1% in Thailand livestock. Risk factors of disease transmission appears similar to those suggested by human cases. Biosecurity practices, typical of those to control most infectious diseases of livestock, should warrant significant reduction in disease risk when fully implemented.

Conclusions: Future studies should focus on the role of environmental contamination by infected livestock and wildlife to identify additional precautions that may be necessary to minimize the role of animal Melioidosis in human disease.

Title: Melioidosis prevention strategies

Author: Direk Limmathurotsakul (Presenter), Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Thailand

Background: In Thailand, evidence-based guidelines for the prevention of melioidosis recommend that residents, rice farmers and visitors should wear protective gear (such as boots and gloves) if direct contact with soil or water is necessary, only drink bottled or boiled water and avoid outdoor exposure to heavy rain or dust clouds. Nonetheless, effectiveness of the recommendations for melioidosis prevention has not been evaluated to date. No melioidosis vaccine is currently available.In a previous focus group study, we identified barriers to adopting recommended preventive behaviours. The main barriers are categorized into five domains: (i) knowledge, (ii) beliefs about consequences, (iii) intention and goals, (iv) environmental context and resources, and (v) social influence. People have little knowledge of melioidosis, believe that there is little or no harm in not adopting the recommended preventive behaviours, and are not inclined to use boots while working in muddy rice fields. Using the Theoretical Domains Framework and the Behaviour Change Wheel, we previously identified intervention options and modes of delivery, and developed a multifaceted prevention programme aimed at changing behaviour to prevent melioidosis, based on the local context in Thailand. We recently conducted a stepped-wedge cluster-randomised controlled trial and showed that diabetic patients who receive a multifaceted prevention programme of melioidosis could have a lower rate of hospital admissions involving infectious diseases, melioidosis and mortality compared to those who did not receive the programme.

Tuesday 15 December 2020

S21: Social, ethical, and behavioral aspects of COVID-19

15.40-17.10hr

Room E

Chairpersons:

1. Phaik Yeong Cheah
2. Wirichada Pan-ngum

Invited speakers:

1. Economic and social impacts of COVID-19 public health measures: results from an online survey in five countries
   Anne Osterrieder
   Mahidol Oxford Tropical Medicine Research Unit, United Kingdom

2. Perspectives on public health interventions in the management of the COVID-19 pandemic in Thailand
   Wirichada Pan-ngum
   Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand

3. "Black Death, maintaining one's role and acceptance" The lived experience of COVID-19 among Thai people during the lock down period (no abstract)
   Bhensri Naemiratch
   Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand

4. Perceptions of COVID-19 public health measures: a mixed methods study from Malaysia
   Phaik Kin Cheah
   Universiti Tunku Abdul Rahman, Malaysia

Title: Economic and social impacts of COVID-19 public health measures: results from an online survey in five countries

Author: Anne Osterrieder (Presenter), Mahidol Oxford Tropical Medicine Research Unit, United Kingdom
Co-authors: Wirichada Pan-ngum, Natinee Kulpijit, Mira Leonie Schneiders, Miha Orazem, Phaik Kin Cheah, Urh Groselj, Bhensri Naemiratch, Giulia Cuman, Constance Mackworth-Young, Rita Chanviriyavuth, Supa-at Asarath, Darlene Ongkili, Ksenija Perkovic, Supanat Ruangkajorn, Mavuto Mukaka, Lenart Skof, Phee-Kheng Cheah, Naomi Waithira, Pimnara Peerawaranun, Phaik Yeong Cheah, Margherita Silan, Tassawan Poomchaichote

Background: Non-pharmaceutical interventions like quarantine, lockdown or social distancing are essential to mitigate the COVID-19 pandemic. To understand their impact on different social groups, we conducted an anonymous online survey in Thailand, Malaysia, the United Kingdom, Italy and Slovenia.

Study Design & Methods: Between 1st May and 30th June 2020, 5,058 respondents completed the survey. Post-stratification weighting was applied, and data was analysed using Stata 15.0 software.

Results: Overall, factors associated with worse economic impacts were lower education levels, being 65 years or older, living in larger households, having children under 18 in the household, and receiving a flexible or no income. Thailand reported the highest economic impact and Slovenia the lowest. In terms of social impact, respondents were most concerned about the impact of restrictions on their social life, physical health, and mental health and wellbeing. Most respondents from Thailand reported changing their social behaviour voluntarily before government restrictions were introduced. Respondents from Italy and Slovenia, men, people aged 65 years and older, and people with lower levels of understanding of COVID-19 were less likely to report doing so. Self-reported levels of understanding of COVID-19 were lower in Malaysia and Italy, among 18-34 years old, and those with lower education levels. Many respondents reported seeing ‘fake news’ about COVID-19, with differences between countries, education level, and level of understanding being found.

Conclusions: Our results highlight how COVID-19 public health measures impact social groups in different ways. Understanding the factors that contribute to these differences can help to inform future public health interventions.

Title: Perspectives on public health interventions in the management of the COVID-19 pandemic in Thailand

Author: Wirichada Pan-ngum (Presenter), Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Anne Osterrieder, Bhensri Naemiratch, Mavuto Mukaka, Naomi Waithira, Natinee Kulpiji, Noppadon Kannika, Phaik Yeong Cheah, Pimnara Peerawaranun, Rita Chanviriyavuth, Supa-at Asarath, Supanat Ruangkajorn, Tassawan Poomchaichote

Background: Any government needs to react quickly to the pandemic situation and makes decisions on choices of healthcare interventions locally and internationally with little information regarding the perceptions of people and the reactions they may receive during the implementation of those restrictions.

Study Design & Methods: Here, we report an anonymous online survey in Thailand conducted in May 2020 to assess public perceptions of three main interventions in the Thai context: isolation, quarantine and social distancing. A total of 1,020 participants, of whom 52% were women, responded to the survey. Loss of income was the main concern among respondents (>80% for all provinces). Traditional media and social media were the important channels for communication during the pandemic.

Results: A total of 92% of respondents reported that they changed their social behavior even before the implementation of government strategies with 94% reported socially distancing, 97% reported using personal protective equipment such as masks and 95% reported using sanitizer products.

Conclusions: This study showed a high level of cooperation by people with government enforced or voluntarily controls such as quarantine, isolation and social distancing in geographical regions in Thailand. The findings from this study can be inform future government measures to control the pandemic and communication strategies.

Title: Perceptions of COVID-19 public health measures: a mixed methods study from Malaysia

Author: Phaik Kin Cheah (Presenter), Universiti Tunku Abdul Rahman, Malaysia
Co-authors: Naomi Waithira, Anne Osterrieder, Pimnara Peerawaranun, Thashalini Sanjilatheeban, Darlene Ongkili, Mavuto Mukaka, Mira Schneiders, Phaik Yeong Cheah, Phee Kheng Cheah

Background: In response to the global COVID-19 pandemic in March 2020, for the first time in history, Malaysia implemented a Movement Control Order under its Prevention and Control of Infectious Diseases Act 1988. The Movement Control Order involved measures such as the closure of its borders, social distancing, and a partial lockdown that only allowed essential businesses and activities to operate. This study aimed to investigate the perceptions and novel lived experiences among the public and health care workers in Malaysia in response to these public health measures.

Study Design & Methods: This study was conducted during the period of the Movement Control Order, using a mixed method design. A total of 18 in-depth phone interviews were conducted between 2 May and 4 July, 2020 until data saturation was reached. Thematic analysis was conducted. Meanwhile, 827 respondents participated in an online survey conducted from 1 May to 30 June, 2020. Post-stratification weighting was applied, and data was analysed using Stata 15.0 software.

Results: The study found that of those who worked before the COVID-19 pandemic, most continued to work during the pandemic, while two thirds expressed financial and career progression concerns. In addition, those with a fixed salary and benefits/pension were least worried about their loss of earnings compared to those who were on contracts, had no income or other income sources. To cope with the Movement Control Order, most respondents said that the use of internet and online social network was important or very important, and they coped by connecting with others, engaging in new hobbies or learning new skills, finding alternative ways for doing things they loved, practicing self-care, and watching movies or series. Some of the positive outcomes experienced by respondents were spending quality time with family, learning new skills, having new appreciation for relationships and the environment, as well as practicing healthier lifestyles.

Conclusions: This study helps to understand the perceptions and experiences of people in Malaysia living through the first ever Movement Control Order during COVID-19 pandemic. Such insights into lived experiences of COVID-19 related public health measures are important for successfully planning and implementing future non-pharmaceutical interventions.

Tuesday 15 December 2020

S22: **Tropical Disease controls and the COVID-19 pandemic**

17.10-18.40hr

Room A

Chairpersons:
1. Katie Poole-Smith
2. Jodi Fiorenzano

Invited speakers:

1. From count to abundance – applied hierarchical modeling in entomological surveillance
   Patrick Wes McCardle
   AFRIMS Entomology Thailand

2. Vector surveillance in Thailand
   Thanyalak Fansiri
   AFRIMS Thailand

3. Surveillance in the time of COVID: Past, present, and future a case study in Mongolia
   Katie Poole-Smith and Jodi Fiorenzano
   AFRIMS/NAMRU-2 Thailand/Cambodia

4. *Aedes* mosquito surveillance in Phnom Penh, Cambodia; during COVID-19 pandemic
   Didot Prasetyo
   NAMRU-2 Cambodia

Title: From count to abundance – applied hierarchical modeling in entomological surveillance

Author: Patrick McCardle (Presenter), Armed Forces Institute of Medical Sciences, Thailand

Background: The impact of COVID-19 is clearly being felt within the vector surveillance/control community. Many State and local vector control organizations are either diverting resources to COVID-19 surveillance and/or implementing social distancing measures, which can impact community accessibility. This make precision estimates of mosquito abundance more important than ever. Abundance is a fundamental state variable, critically important for determining trends and encounter hazard, but ultimately unobservable (a latent variable). Instead "counts" are substituted as a "measure" of abundance, with accompanying "measurement error". In this presentation, we will look at using a N-mixture model to estimate abundance while accounting for this error. The advantage of this model framework is the ability to estimate the latent variable, abundance, without the necessity of marking and recapturing individuals, a process too resource intense for standard vector surveillance. We will cover the underlying hierarchical model, model assumptions, and impact of assumption violations using simulated data. Then we will illustrate model fitting using Bayesian analysis on real data collected in Kenya from 2008 - 2018.

Title: Vector Surveillance in Thailand

Author: Thanyalak Fansiri (Presenter), USAMD-AFRIMS, Thailand

Background: Mosquitoes and flies are the most common disease vectors in tropical countries and major targets of vector-borne disease surveillance and control activities. Available surveillance data and risk assessment information is essential to facilitate appropriate and timely decisions regarding vector control in high risk areas along borders and in endemic areas. The aim of this study was to monitor population density and abundance of vectors over time to determine risk of disease transmission across Thailand.

Study Design & Methods: Different entomological trapping techniques augmented with CO2 were used in nine Thai provinces. Dengue, chikungunya and Zika vectors were collected indoor during the day time using Biogent sentinel traps. Centers for Disease Control and Prevention miniature light traps were deployed at night to collect vectors of malaria and leishmania. Individual devices were placed in the same location for three consecutive days/nights every two months (2019-2020). Collections were morphologically identified, sexed, and screened for pathogens by PCR.

Results: A total of 2,507 female *Aedes* and 8,520 female Anopheline mosquitoes were collected from 1,001 trap-days and 1,686 trap-nights, respectively. The predominant species were *Ae. aegypti* and *Anopheles minimus*. Approximately 65,000 sand flies from 1,921 trap-nights were majority identified to *Sergentomyia*. Pools were positive for dengue, chikungunya viruses and *Plasmodium* parasites.

Conclusions: Positive detection of pathogens in arthropod vectors is crucial to early detection through vector surveillance. Maintaining this work to inform local vector control operators for immediate vector prevention and control proved to be challenging during COVID-19; we will discuss mitigation methods.

Title: Surveillance in the time of COVID: Past, present, and future a case study in Mongolia

Author: Betty "Katie" Poole-Smith (Presenter), AFRIMS, Thailand

Background: Ectoparasites such as ticks are the primary vectors for pathogens including: Crimean-Congo Hemorrhagic Fever virus, rickettsia, borrelia, tick-borne encephalitis virus, and the emerging Dabie bandavirus formerly known as severe fever with thrombocytopenia syndrome virus (SFTSV). Little to no information is publically available regarding the distribution and prevalence of ticks and tick-borne pathogens or their impact on human populations in Mongolia. To determine the impact of ticks and tick-borne pathogens in Mongolia, Armed Forces Research Institute of Medical Sciences (AFRIMS), Naval Medical Research Unit TWO (NAMRU-2), George Mason University (GMU), National Center for Zoonotic Disease (NCZD), and the Institute of Veterinary Medicine (IVM) have joined together to address these important questions. This study was established in fall 2018 and we initiated tick collections in spring 2019. In 2020, the COVID-19 pandemic began to impact international research studies as limits to travel to country, in-country specimen collections, and specimen shipments were limited. Our tick surveillance studies were some of the first studies impacted by the COVID-19 pandemic as Mongolia implemented an early and particularly robust public health response to COVID-19: tightening border controls in late January, canceling major holidays and associated domestic travel in February, and banning international travel in early March. We will share our lessons learned on adapting tick surveillance to COVID-19 and predictions for surveillance in the near future.

Title: *Aedes* mosquito surveillance in Phnom Penh, Cambodia; during COVID-19 pandemic

Author: Didot Budi Prasetyo (Presenter), U.S. Naval Medical Resarch Unit TWO, Cambodia
Co-authors: Jodi M. Fiorenzano, Nin Noch, Rithea Leang

Background: Multiple vector-borne diseases are endemic and of major public health concern throughout Cambodia. While some mosquito-borne disease such as Malaria have decreased over time, other mosquito-borne diseases such as dengue and chikungunya, which often associated with urban setting, have been steadily increasing. Active mosquito surveillance is labour intensive, time consuming and costly for public health entities. To assess a more sustainable method of mosquito surveillance through community "volunteer" based surveillance methods, to better understand the dynamics mosquito-borne disease, and to inform local government for a better prevention and control strategies in Cambodia, NAMRU-2 conducted routine volunteer-based mosquito surveillance in Phnom Penh city.

Results: From November 2019-August 2020, a total 4,972 mosquitoes were collected from BG GAT traps placed at volunteer's houses. The mosquito genera collected were *Aedes* (58.8%), *Culex* (40.6%), *Anopheles* (0.16%), and others (0.4%). Prior to April 2020 60-80% of volunteers provided surveillance information through surveillance cards. Starting in April 2020, coinciding with the COVID-19 pandemic, the weekly submission of samples decreased significantly due to the COVID-19 response measures such as social distancing and workforce reduction resulting in only 30% of volunteers providing surveillance information.

Conclusions: The findings in this study showed that volunteer based surveillance may be a possibility for future urban mosquito surveillance. However, as we move further into the new "normal" of living, it is not clear if COVID-19 related precautions will continue to affect community involvement in mosquito surveillance.

Tuesday 15 December 2020

S23: Biology of malaria parasite

17.10-18.40hr

Room B

Chairperson: Jacob Baum

Invited speakers

1. Understanding the elusive *P. falciparum* development in liver cells
   Annie Yang
   Radboud University Medical Centre, Netherlands

2. New super-resolution and live imaging routines shed light on blood stage malaria parasites
   Michal Pasternak
   Walter and Eliza Hall Institute of Medical Research, Australia

3. Exploring the druggable landscape of *P. falciparum* gametocytes
   Michael Delves
   London School of Hygiene and Tropical Medicine, United Kingdom

4. Sex-specific genetic screens identify hundreds of *Plasmodium* fertility genes essential for the transmission of malaria parasites
   Claire Sayers
   Umea University, Sweden

Title: Understanding the elusive *P. falciparum* development in liver cells

Author: Annie Yang (Presenter), Radboud University Medical Center, Netherlands
Co-authors: Youri van Waardenburg, Marga van de Vegte-Bolmer, Geert-Jan van Gemert, Wouter Graumans, Johannes de Wilt, Robert Sauerwein

Background: Malaria remains a significant parasitic disease transmitted by mosquitoes resulting in over 220 million clinical cases and half a million deaths annually. With increasing resistance of parasites and mosquitoes to current interventions, there is a pressing need to provide innovative strategies to combat and eradicate this disease. *Plasmodium falciparum (Pf)* parasites are responsible for the highest disease burden. During the initial asymptomatic liver stages, intracellular parasites undergo massive replication before release into the circulation, associated with the emergence of clinical symptoms and complications. Knowledge of *Pf*-liver stage biology is incomplete but essential for rational design of drugs/vaccines. Research is restricted to the use of *in vitro* liver cultures with low parasite infection rates (<0.1-5%) or imperfect animal models. Here we present data regarding the composition of a permissive hepatocyte for parasite development with the aim of improving culture conditions as well as understanding the fundamental biology of this elusive life-stage of malaria parasites.

Study Design & Methods: Freshly isolated primary human hepatocytes were isolated from surgical liver segments, characterized and infected with different *Pf* strains. These strains are from different geographical locations: NF54 (West Africa), NF135 (Cambodia), and NF175 (Nigeria).

Results: *Pf* strains show strong preference for a minority of zone 3 hepatocytes characterized by the particular presence of glutamine synthetase (hGS). Parasite schizont growth is significantly enhanced in these hepatocytes through the hGS uptake early in development.

Conclusions: In conclusion, *Pf* development is strongly determined by the differential metabolic status in hepatocyte subtypes.

Title: New super-resolution and live imaging routines shed light on blood stage malaria parasites

Author: Michal Pasternak (Presenter), Walter and Eliza Hall Institute of Medical Research, Australia
Co-authors: Niall Geoghegan, Julie Verhoef, Cindy Evelyn, Gero Schloetel, Kelly Rogers, Alan Cowman

Background: The very small size of malaria-causing parasites poses a major challenge for subcellular imaging. This could be addressed by super-resolution techniques but their use has been hindered by the parasitesâ€™ sensitivity to light. This sensitivity makes the parasites also very difficult to study by high-resolution live imaging as high light doses interfere with critical processes such as parasite invasion.

Study Design & Methods: To tackle these challenges, we developed new imaging routines. Firstly, we developed a novel Stimulated Emission Depletion (STED) microscopy technique, called guided STED, that allowed us to image particularly sensitive samples with super-resolution. Secondly, we applied lattice-light sheet for live 4D imaging as well as Airyscan detector confocal microscopy to image parasite invasion and development inside the host red blood cell.

Results: The *Plasmodium* parasite is especially sensitive to light during its growth inside the infected red blood cell. At this stage, the parasite uses haemoglobin as its main food source. This leads to release of toxic haem, which is converted into an insoluble crystalline form deposited in the food vacuole. This iron-rich food vacuole undergoes spectacular disintegration when illuminated with high-power lasers such as those required for STED microscopy. This causes major damage to the sample precluding the use of this super-resolution technique. Here we present guided STED, a novel adaptive illumination approach, which identifies the most light-sensitive parts of the infected cell. There, the high-power STED laser is automatically deactivated to prevent local damage. This guided STED nanoscopy approach allows super-resolution imaging of the whole *Plasmodium* life cycle, enabling multicolour imaging of blood-stage malaria parasites with resolutions down to 35 nm without sample destruction. To image the development of live parasites, we used Airyscan confocal microscopy and lattice light-sheet microscopy. The Airyscan allowed us to obtain overnight movies at super-resolution while the lattice light-sheet allowed us to image in 3D and with high temporal resolution dynamic processes such as the parasite invasion.

Conclusions: Together, these techniques gave us insights into dynamic and elusive processes during the parasite life cycle such as parasite invasion, divisions and protein trafficking.

Title: Exploring the druggable landscape of *P. falciparum* gametocytes

Author: Michael Delves (Presenter), London School of Hygiene and Tropical Medicine, United Kingdom

Background: To achieve our ambitious goals of malaria elimination and eradication, interventions that prevent the transmission of the parasite from humans to mosquitoes are essential. Transmission of malaria is mediated by male and female gametocytes that remain dormant in the human host but undergo explosive development within seconds of entering the mosquito. Despite this essential role, due to divergent cell biology, very few antimalarials target gametocytes. Uncovering the drug-targetable cell biology of gametocytes is the first step to developing effective transmission-blocking drugs.

Study Design & Methods:
P. falciparum gametocytes were treated with a panel of 50 transmission-blocking molecules. Their ability to inhibit male gametogenesis was assessed by phenotypic imaging and classified by machine learning analysis.

Results: Diverse chemical scaffolds arrest male gametogenesis giving a range of different inhibition phenotypes that can be clustered and compared computationally. Common phenotypes were frequently observed, suggesting current targetable biology in gametocytes is restricted to several major proteins/pathways.

Conclusions: These data will inform and direct onward detailed mode of action studies for drug development and provide novel tool molecules for the study of gametocyte biology.

Title: Sex-specific genetic screens identify hundreds of *Plasmodium* fertility genes essential for the transmission of malaria parasites

Author: Claire Sayers (Presenter), Umeå University, Sweden
Co-authors: Vikash Pandey, Ondine Duverger, Oliver Billker

Background: Sexual reproduction of malaria parasites is essential for their transmission by mosquitoes. Biological processes required for *Plasmodium* fertility include the formation of gametocytes, their transformation into gametes in response to signals from the mosquito, fertilization in the bloodmeal, meiosis, and the formation of an invasive ookinete. Stage-specific gene expression data suggest that hundreds of parasite genes are uniquely required for sexual reproduction, but previous gene knockout studies have merely scratched the surface of this important aspect of parasite biology.

Study Design & Methods: We have mutagenized *P. berghei* lines making only fertile male or only fertile female gametocytes with barcoded *Plasmo*GEM vectors to screen 1200 targetable genes for sex-specific phenotypes.

Results: Our screens identify hundreds of genes with sex-specific roles. The data recapitulate existing knowledge of *Plasmodium* fertility, identify new likely regulators of the cell cycle and stage-specific metabolism, and assign functions to previously unannotated genes.

Conclusions: For the first time, we are gaining an unbiased picture of the molecular mechanisms of *Plasmodium* fertility at genome-scale, which will lead to a deeper understanding of this novel biology that could serve as targets for transmission blocking drugs or vaccines.

Tuesday 15 December 2020

S24: Dengue control amidst challenges of COVID-19: lessons learned for reduction of future threats

17.10-18.40hr

Room C

Chairperson: James Tibenderana

Invited speakers:

1. Health system and case management challenges during concurrent dengue and COVID-19 outbreaks
   Lucy Lum Chai See
   University of Malaya, Malaysia

2. Myanmar's response to compensate for COVID-19 challenges in dengue control
   Nay Yi Yi Linn
   Ministry of Health and Sports, Myanmar

3. Impact of COVID-19 on a dengue research project in Myanmar
   Hans Overgaard
   Norwegian University of Life Sciences & Khon Kaen University, Thailand

4. *Aedes*-borne diseases: building resilience against future threats
   Leo Braack
   Malaria Consortium, Thailand

Title: Health system and case management challenges during concurrent dengue and COVID19 outbreaks

Author: Lucy Lum (Presenter), University of Malaya, Malaysia

Background: The concurrent dengue and COVID19 outbreaks have posed new challenges to the healthcare system and healthcare workers with one or he other disease slipping through the cracks.

Study Design & Methods: Public health measures to contain these two viral infections are dissimilar. WHO has recommended active surveillance for CoVID-19; governments have introduced lock-down measures and social distancing to prevent local transmission of CoVID-19. While these measures have been successful in the containment of CoVID-19, the lockdown measures left mosquito breeding grounds undisturbed, leading to an increased vector population. 2019 was a record year for dengue and 2020 is set to be even worse for numerous countries in Latin America and Southeast Asia.

Results: Discouraging unnecessary hospital visits might cause a delay in seeking treatment for febrile illnesses particularly during the afebrile phase of dengue where the risk of severe disease is at its highest. Emergency departments have been reorganised to prevent person-to-person transmission of COVID-19 and at the same time permit the efficient consultation for other febrile illnesses. Overlapping clinical signs and symptoms may point towards COVID-19 or dengue in some case series, but on an individual patient level, none of these guarantee a diagnosis of certainty.

Conclusions: Laboratory confirmation of diagnosis is thus mandatory throughout the pandemic, adding another strain to limited resources. Failing to consider COVID-19 because of a positive dengue serology rapid test result has serious implications not only for the patient but also for public health, thus highlighting the urgent need for rapid and sensitive diagnostic tests for SARS-CoV-2.

Title: Myanmar's response to compensate for COVID-19 challenges in dengue control

Author: Nay Yi Yi Linn (Presenter), Ministry of Health and Sports, Myanmar

Background: Dengue is a public health problem in Myanmar and a notifiable disease since 1964. Dengue prevention and control activities are important while all health and community systems are diverted COVID-19. Here we presented national preparedness and response to dengue prevention and control activities that contributed to epidemiological decline amid COVID-19 in early half of 2020.

Study Design & Methods: Data on dengue preparedness and response (larval control activities, fogging, and education sessions) and epidemiological data (dengue cases, deaths, grades, gender, and geographical distribution) were collected and collated from state/region programmes during Jan-June 2020 and compared with Jan-June 2019. These were analyzed and presented in numbers and percentages.

Results: In guidance from Myanmar Ministry of Health and Sports, National Dengue Prevention and Control programme developed National Action Plan early in April 2020 jointly supported by WHO Myanmar and Malaria Consortium. This highlights activities to mitigate the impact of COVID-19. Programme conducted numerous virtual strategic meetings with State/Regional Health Directors and VBDC team leaders, conducted dengue clinical management virtual training to manage DHF cases, and included dengue as a differential diagnosis of COVID-19 in community fever clinics. Essential dengue treatment, prevention and control activities continued like- case detection, case management, dengue risk communication and community engagement, larval control, and fogging. During Jan-June 2020, Dengue Prevention and Control Programme reported 3,130 cases and 22 deaths. In same period in 2019, 6,114 cases and 27 deaths were reported. The case and deaths reported declined by 49% and 19% in 2020 in comparison to 2019, respectively. ~41% of cases and deaths belonged to age group 5-9 years in both periods. Distribution of cases by urban and rural did not vary in each year but death was strikingly higher in rural (91%) in 2020. Cases and deaths did not differ by gender in both years. However, deaths were slightly higher in males (59%) in 2020 vs females (52%) in 2019. Majority of cases were reported as Grade I in 2019 (66%) and 2020 (71%). At the same time, deaths were reported from Grade IV in both years and higher in 2019 (96%) than 2020 (86%). The factors for the decline in dengue cases and deaths amid Covid-19 was primarily due to the implementation of aggressive dengue prevention and control measures starting before the monsoon started and amid COVID-19. Programme did extensive larval control activities in 2020 in comparison to 2019--increase in coverage of wards/villages (by 132%), household coverage (by 138%), and container screening (by 67%) in comparison to 2019. Similarly, programme used 51% more abate in 2020 that resulted in more coverage of wards/village (by 164%), households (by 108%) and population covered (by 128%) but use less abate in school and less coverage by 61%. Due to these measures, in 2020 fogging coverage was much reduced -- in ward/village (by 49%), household (by 66%), schools (by 99%) and population (by 54%). Health education session covered more population (by 225%) in 2020 vs 2019.

Conclusions: In early months of 2020, Myanmar Ministry of Health and Sports was vigilant of approaching monsoon season amid COVID-19. Programme worked with WHO and partners on dengue preparedness plan and implemented dengue prevention and control activities right on time in coordination with local authorities, Public Health Professionals and community involvement. This has contributed in prevention and control of the dengue amid COVID-19.

Title: Impact of COVID-19 on a dengue research project in Myanmar

Author: Hans Overgaard (Presenter), Norwegian University of Life Sciences &Khon Kaen University, Thailand

Background: A cluster randomized controlled trial was designed to reduce dengue incidence and entomological risk factors and to improve knowledge, attitudes and prevention practices, behavior and engagement. The trial includes schools and communities in Yangon, Myanmar applying innovative school-driven vector control approaches adapted to the community context coupled with place-based learning, experiential education and communication for behavioral impact. Baseline data collections and interventions were planned to be implemented when schools start in June 2020. The Covid-19 pandemic caused a complete stop of the project start up due to a nation-wide lockdown, including curfews, school closures, social distancing policies, restrictions on meeting size and closed international borders. Project partners decided to go back to the drawing board and develop a comprehensive background analysis of project implementation using a transdisciplinary holistic approach. First, the trial was postponed one year (start-up in June 2021) and reduced from two years to one year. This presentation attempts to highlight how the pandemic presents new opportunities. The current situation offers strengthened opportunities to improve stakeholder capacity consistent with the overall long-term project aims. Curtailment of travel and limited on-site activity release time for deeper reflection of project assumptions and problem framing, building team and stakeholder capacity, and producing theoretical research outputs. This will improve understanding of underlying factors that may affect trial results and will involve integrating findings from other projects and incorporate theoretical and methodological approaches for operationalizing transdisciplinary research.

Study Design & Methods: CRT

Title: *Aedes*-borne diseases: building resilience against future threats

Author: Leo Braack (Presenter), Malaria Consortium, Thailand
Co-author: Htin Kyaw Thu, James Tibenderana, Jo Lines, Sian Clarke

Background: *Aedes aegypti* is the single most effective vector of disease on our planet, transmitting dengue, Zika, chikungunya, yellow fever and others. Arboviruses are on a rising trend set to overtake malaria as the most important vector-borne challenge in large parts of the world. A research partnership between London School of Hygiene & Tropical Medicine, Malaria Consortium, and regional partners in Africa and Asia, is investigating the state of readiness of affected regions to engage with these threats.

Study Design & Methods: In a mixed-methods approach, a Needs Assessment will be conducted in representative countries in Africa and Asia, to sample policies, practices, constraints and needs associated with a range of arboviral diseases at current and potential medium-term future scenarios. We will undertake literature reviews of published studies on control of *Aedes*-borne diseases, to probe the efficacy of the different methods. We explore the question of what makes a nation "ready" and how does a nation achieve and maintain that state of preparedness?

Results: Results of the Literature Review and in-depth interviews with national disease control authorities, research institutions and other relevant stakeholders will be published in appropriate international peer-reviewed journals.

Conclusions: The conclusions and recommendations of this study are intended to support the international community for realistic trajectories and likely scenarios of arbovirus threats associated with a burgeoning global population, increasing international flow of goods and people including opportunities for pathogen spread, mass migration, climate change and its consequences on favouring vector expansion but also environmental effects such as major disastrous events of floods, drought, and hurricanes.

Tuesday 15 December 2020

S25: Global burden of diabetes, infections, and melioidosis

17.10-18.40hr

Room D

Chairpersons**:**

1. Vanaporn Wuthiekanun
2. Narisara Chantratita

Invited speakers**:**

1. The double burden of diabetes and global infection
   Susanna Dunachie
   University of Oxford, United Kingdom

2. Tactical implementation of melioidosis research in Myanmar Army Medical Corps
   Tin Maung Hlaing
   Defence Services Medical Academy (DSMA), Myanmar

3. Melioidosis in the Lao PDR
   Andrew Simpson
   Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Microbiology Laboratory, Mahosot Hospital, Vientiane, Lao PDR

4. "India is the hotspot for melioidosis**!**" **-** are you serious?
   Chiranjay Mukhopadhyay
   Department of Microbiology, Kasturba Medical College, Manipal, India

Title: The double burden of diabetes and global infection

Author: Susanna Dunachie (Presenter), University of Oxford, United Kingdom

77% of people with diabetes mellitus now live in low and middle-income countries (LMIC), and the incidence of diabetes is accelerating in poorer communities. The majority of people with diabetes are thought to have Type 2 diabetes mellitus (T2DM) although further research on diabetes subtypes in LMIC is needed. Diabetes increases susceptibility to infection and / or worsens outcomes for major global infections such as tuberculosis (TB), dengue, influenza and Gram-negative sepsis including Salmonella species and the neglected tropical disease melioidosis. Melioidosis is caused by the soil bacterium Burkholderia pseudomallei, has a 40% hospitalised case fatality rate in LMIC, and an estimated 89,000 global death toll. People with diabetes have a twelve-fold increased risk of melioidosis compared to non-diabetics, and up to two-thirds of melioidosis patients have T2DM. There is a large overlap between populations at risk of diabetes and those at risk of melioidosis, resulting in an estimated 280 million people with diabetes now living in melioidosis-endemic countries across the world. In addition, people with diabetes bear a disproportionate burden of drug-resistant infections from bacteria with antimicrobial resistance (AMR).This talk will give an overview of what is known about the epidemiology of diabetes and infection, and discuss potential mechanisms for the increased risk of infection, and in particular for the exquisite susceptibility of people with diabetes to melioidosis. International treatment guidelines for T2DM are based on research conducted in high-income countries focussed on preventing adverse cardiovascular outcomes and early death. There is a lack of evidence on which to base treatment guidelines for people living in LMIC, where there is an increased burden of infectious diseases. The literature to date on the impact of treatment on infection risk and outcomes will be discussed. Finally, the role of vaccination of people with diabetes will be discussed. It is noted that a public health vaccine for melioidosis would be targeted at people with diabetes in the first instance, as this group represents a well-defined and accessible population for evaluation of a melioidosis vaccine.

Title: Tactical implementation of melioidosis research in Myanmar Army Medical Corps

Author: Tin Maung Hlaing (Present), DSMA, Myanmar

Background: Melioidosis is one of the serious diseases caused by *Burkholderia pseudomallei*. It was first discovered at the Pathology Laboratory of Rangoon General Hospital (now, Yangon General Hospital) in 1911 in Myanmar. An English Pathologist Captain Alfred Whitmore and C. S. Krishnaswamy from the Indian Medical Service found it in the opium addicts in Rangoon (Yangon). Although it was first discovered in Myanmar, there were not many follow-up research works and reports on Melioidosis.

Study Design & Methods: In the Military Medical Services, Melioidosis is one of the important diseases as it is considered a Tier 1 Select Agent by the United States Centre for Diseases Control and Prevention (CDC). Myanmar Military Medical Corps also listed it under the prioritized diseases. However, there was no significant activity on Melioidosis in Military Medical Practice.

Results: At the turn of 2011, Defence Services Medical Research Centre (DSMRC) was founded which is first of its kind in Myanmar. DSMRC became operational in the following year with the facilities including certified Biosafety Level 3 (BSL 3) and next generation genome sequencing. Recognising the military importance of diseases, Melioidosis was categorised in the higher priority group for strategic research plan. In the process of implementing the research, capacity building on theoretical foundation, clinical practice, epidemiology, and collaborative partnership were developed tactically. Among the international partners, there are top notch research scientists from Mahidol University, Mahidol Oxford Research Unit and University of South Alabama, Mobile (later with University of Nevada, Reno).

Conclusions: Afterwards, research on Melioidosis is being carried out not only at DSMRC, but it has extended to involveclinicians and researchers at Defence Services General Hospital (DSGH), Defence Services Medical Academy (DSMA) and Military Institute of Nursing and Paramedical Sciences. At this moment, research works on Melioidosis in the Military Medical Corps cover from simple research to advanced molecular studies.

Title: Meliodosis in the Lao PDR

Author: Andrew Simpson (Presenter), DSMA, Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Vientiane, Lao PDR

Background: Laos shares a long border with north-east Thailand, where melioidosis is endemic, as well as with Vietnam, Myanmar, Cambodia and China. However, the first case of melioidosis in Laos was not diagnosed until 1999 (by the Microbiology Laboratory at Mahosot Hospital). The number of cases diagnosed has subsequently increased yearly. A large prospective study of melioidosis, involving more than 1000 patients, has been conducted since the first case description. I will describe some of the clinical and epidemiological findings.

Title: “India is the Hotspot for Melioidosis!” - Are you serious?

Author: Chiranjay Mukhopadhyay (Presenter), Manipal Academy of Higher Education, India

Background: India is recently predicted as the ‘hotspot’ for Melioidosis in the global perspective. Number of cases is increasing by leaps and bounds every year in India, even from corners of the country where it was never suspected.

Study Design & Methods: If we look back at the laboratory up-gradation and detection rate of melioidosis cases in last 14 years, we can find a significant increase in numbers from 2 cases in 2006 to more than 300 in 2020 from our hospitals and other states of India. This talk will brief the current status of melioidosis in India highlighting the rationality for the prediction and the awareness to detect more number of cases for better prevention.

Results: The clinical presentation, mortality, bacterial virulence and environmental factors seem to be different as compared to other endemic countries. The patients range from infant to elderly with the disease affecting almost all organs of the body, including nervous system. Being a killer disease, the mortality hovers around 12-20%, which seems to be under-estimated though. Various uncommon virulence traits like LPS B genotype (74%) and Bim ABM, commonly affecting nervous system, were identified from native strains. The molecular epidemiology of the Indian strains and nutritionally depleted soil with different physio-chemical nature are unique as compared to other endemic countries.

Conclusions: Though unique in many aspects and having increasing trend in case detection, it may need more time and evidence to prove India as the hotspot. IMRF (https://www.melioidosisindia.com/) and Center for Emerging and Tropical Diseases in Manipal are working with National Center for Disease Control (NCDC), India hand in hand to find the true scenario.

Tuesday 15 December 2020

S26: Social dimensions of antimicrobial resistance

17.10-18.40hr

Room E

Chairpersons:

1. Phaik Yeong Cheah
2. Christopher Pell

Invited Speakers

1. An introduction to the Sonar-Global network and its ongoing efforts in AMR and infectious diseases
   Tamara Giles-Vernick
   Institut Pasteur, France

2. Capacity building efforts on the social dimensions of AMR
   Danny de Vries
   Amsterdam Institute for Global Health and Development (AIGHD)

3. AMR in Vietnam – a one health perspective
   Sonia Odette Lewycka
   Oxford Clinical Research Unit, Hanoi, Vietnam

4. Why do people purchase antibiotics over-the-counter? A qualitative study with patients, medical practitioners and dispensers in central, eastern and western Nepal
   Bipin Adhikari
   Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Title: An introduction to the Sonar-Global network and its ongoing efforts in AMR and infectious diseases

Author: Tamara Giles-Vernick (Presenter), Institut Pasteur, France

Background: The social sciences reveal linkages between infectious threats and political, social, economic, and ecological conditions, but are fragmented and poorly integrated into preparedness and response. SoNAR-Global is a global consortium funded by the European Commission and led by social scientists specializing in emerging infectious diseases and antimicrobial resistance. The project is tasked with developing a global network among social scientists for preparedness and response to infectious threats.

Study Design & Methods: The project includes work packages focusing on development of the network, vulnerability assessment tools, engagement models, and social sciences curricula. All follow a map-share-act format: we map existing stakeholders, tools, models, and curricula; share findings through dialogues with stakeholders; and act through implementation, scale up and evaluation.

Results: We have created a network of 526 individual members and 15 networks. Our platform includes a searchable directory and resources, including publications, blogs, research mapping for epidemics, podcasts, and webinars on COVID-19. Regional hubs are in southeast Asian (Bangkok), eastern Europe (Kiev), and West Africa (Dakar). We have created accessible tools to identify hidden forms of vulnerability and will propose policy recommendations for effective engagement of marginalized populations. Our Kampala (Uganda) vulnerability assessment accumulated systematic social sciences data of vulnerabilities on the eve of the COVID-19 pandemic. We have created two curricula to train social scientists in the social, political, and economic dimensions of preparedness and response to infectious threats.

Conclusions: SoNAR-Global has developed a dynamic network to strengthen social sciences capacity, implement tools and models, and catalyze new collaborations.

Title: Capacity building efforts on the social dimensions of AMR

Author: Danny de Vries (Presenter), University of Amsterdam, Netherlands
Co-authors: Vera Spaan, Karlijn Hoftstraat

Background: SoNAR-Global is a global consortium led by social scientists specializing in emerging infectious diseases (EID) and antimicrobial resistance (AMR). As part of strengthening the capacity for social science-informed interventions, the project has been mapping existing teaching materials on AMR and developing teaching materials for Sonar-Global. The objective of this study was to identify the current available trainings on the social dimensions of AMR and determine the training needs of non-social scientists.

Study Design & Methods: Quantitative analysis was conducted on a mapping of existing training infrastructures, needs and resources regarding social aspects of infectious threats. For the in-depth analysis eleven semi-structured interviews were conducted with non-social scientists and one social scientist.

Results: The mapping provided data on 27 trainings on AMR. Most of the trainings were Massive Open Online Courses (MOOC) which were openly available on online learning platforms (e.g. Coursera or Future Learn) and in English (24). Eleven trainings were focussed on the medical disciplines, eight were multi- or interdisciplinary, six were focussed on global/international public health and only two on the social sciences. The proportion of social AMR objectives of all objectives had a median of only 1%. The depth of the social domains covered was low in more than 80% of the trainings. Interview results with non-social scientists show that a training on the social dimensions of AMR for non-social scientists should provide a clear basis on the social sciences, what it is, what it does and what the main theories, frameworks and concepts are. Furthermore, it should make clear what the implications are of interdisciplinary collaboration, how the social sciences can contribute to the research and work of non-social scientists, social science tools and skills that non-social scientists can integrate into their own practice. It was noted that the course should be more practical, with case-studies, exercises, videos, webinars or group work through breakout rooms in live sessions to discuss AMR in different contexts.

Conclusions: There is a severe lack of relevant trainings that provide enough in-depth knowledge on the social dimensions of AMR. Further, to increase the participation of the social sciences in AMR research, it is needed to educate non-social scientists on the social aspects of AMR and how the social sciences can contribute to the response against AMR.

Title: AMR in Vietnam – a one health perspective

Author: Sonia Odette Lewycka (Presenter) Oxford Clinical Research Unit, Hanoi, Vietnam

Background: Antimicrobial resistance is globally recognised as an important and growing threat to health, and levels of antimicrobial resistance in Vietnam are amongst the highest in the world. The Vietnam National Action Plan on Combatting Drug Resistance includes aims to promote proper antibiotic use among health workers, the community and farmers, yet most antimicrobial stewardship research has focused on hospital settings, and little data is available about use in other settings. Few population-level interventions aiming to reduce antibiotic use have been evaluated, particularly in low- and middle-income countries with higher burdens of infectious disease, poor regulation, and high non-prescription antibiotic use.

Most interventions aiming to reduce antibiotic consumption at population level used a traditional education and training approach in healthcare settings, and conventional public campaigns through mass media, leaflets and websites. However, active engagement of participants may provide a more powerful way to change behaviour, especially where there is a complex interplay of social, cultural and economic factors.

We will implement interventions at three levels: hospitals, primary healthcare and communities. We will test a participatory quality improvement approach in hospitals, and three successively more active approaches to reduce inappropriate antibiotic use for humans and animals in communities. Here we describe formative research findings from the intervention development phase, identifying gaps in knowledge and understanding and insights to improve practice.

Title: Why do people purchase antibiotics over-the-counter? A qualitative study with patients, medical practitioners and dispensers in central, eastern and western Nepal

Author: Bipin Adhikari (Presenter), Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Co-authors: Sunil Pokharel, Shristi Raut, Janak Adhikari, Suman Thapa, Kumar Paudel, Narayan GC, Sandesh Neupane, Sanjeev Raj Neupane, Rakesh Yadav, Sirapa Shrestha, Komal Raj Rijal, Sujan Marahatta, Phaik Yeong Cheah, Christopher Pell

Background: Over-the-counter (OTC) use of antibiotics makes a major contribution to the burgeoning rise in antimicrobial resistance (AMR). Although recognized as a major problem in Nepal, inadequate attention has been paid towards the contributing factors and consequences. Drawing on qualitative research methods, this article explores the characteristics of OTC in Nepal, factors affecting it, and implications for policy.

Study Design & Methods: Data were collected in and around three tertiary hospitals from three provinces in eastern, western and central Nepal. Twelve semi-structured interviews (SSIs) were conducted with dispensers; eight focus group discussions (FGDs) and five SSIs were conducted with patients attending the hospitals; and six FGDs and eleven SSIs were conducted with clinicians. A pre-defined guide was used for all interviews. Interviews were audio-recorded, translated and transcribed into English and coded using a combination of an inductive and deductive approach.

Results: Drug shops were the primary location where patients engaged with health services. Interactions were brief and transactional: symptoms were described or explicit requests for specific medicine made, and money was exchanged. There were economic incentives for clients and drug stores: with patients able to save money by bypassing the formal health care services. Respondents described antibiotics as easily available OTC at drug shops. Dispensing included the empirical use of broad-spectrum antibiotics, often combining multiple antibiotics, without laboratory diagnostic and drug susceptibility testing. Inappropriate doses for a brief period (2-3 days) were also offered without a follow up. Respondents viewed OTC antibiotic as a convenient alternative to formal health care, the access to which was influenced by distance, time and money. Respondents also described the complexities of navigating through various departments in hospitals and little confidence in the quality of formal health care. Physicians and a few dispensers expressed concerns about AMR and referred to evadable policies around antibiotics use and poor regulation.

Conclusions: The findings point to the need for clear policy guidance and rigorous implementation for prescription-only antibiotics. The poor access and perceived quality of health care highlight the need for greater laboratory-based diagnosis with health system strengthening. Pharmacovigilance with private and public partnership, and community engagement are potential interventions.

Wednesday 16 December 2020

S27: Gut microbiota functions and natural products: to fight against COVID-19

8.30-10.00hr

Room A

Chairpersons:

1. Narisara Chantratita
2. Pornrutsami Jintaridth

Invited speakers:

1. Phytochemicals and the human microbiome: from epigenetic regulation to drug discovery
   Amandio Vieira
   Simon Fraser University, Canada

2. Short chain fatty acid from natural microbiome in fermented soybean food: inhibition of histone deacetylase activity against COVID-19
   Pornrutsami Jintaridth
   Department of Tropical Nutrition and Food Science, Mahidol University, Thailand

3. Seaweed components influence gut microbiota and short chain fatty acid production
   Suvimol Charoensiddhi
   Department of Food Science and Technology, Faculty of Agro-Industry, Kasetsart University, Thailand

4. Natural products and derivatives against SARS-CoV-2
   Prasat Kittakoop
   Chulabhorn Graduate Institute, Thailand

Title: Phytochemicals and the human microbiome: from epigenetic regulation to drug discovery

Author: Amandio Vieira (Presenter), Simon Fraser University, Canada

Background: Nutrients, phytochemicals, and other dietary components can influence epigenetic regulation in cells, and thereby influence the risk of various chronic diseases including cancer, type 2 diabetes, and cardiovascular diseases. Metabolites of dietary components, including those produced by the gut microbiome, can influence a range of chromatin modifications, e.g., histone and DNA methylation, histone acetylation, as well as expression of non-coding RNAs and other processes that affect chromatin structure, and thereby influence epigenetic regulation over cell growth, death, and differentiation. A diet rich in plant products (also rich in dietary fibre), leads to increased production in the gut of low molecular weight substances that are epigenetically active, e.g., butyrate and other short-chain fatty acids, as well as vitamin such as biotin and folate.

Study Design & Methods: none

Results: none

Conclusions: In this presentation, select nutrients including biotin and other vitamins and minerals, as well as phytochemicals such as flavonoids and microbiome metabolites including butyrate, will be discussed in an epigenetic context. The possibility of epigenetic reprogramming to lower risk of some chronic diseases will also be presented.

Title: Short chain fatty acid from natural microbiome in fermented soybean food: inhibition of histone deacetylase activity

Author: Pornrutsami Jintaridth (Presenter), Mahidol University, Thailand

Co-authors: Amandio Vieira, Suvimol Charoensiddhi, Chantira Sutthikornchai, Supachai Topanurak, Narisara Chantratid

Background: Tua Nao (fermented soybean cakes) is northern Thai food and northern local wisdom. It is mostly used as an ingredient in the northern recipe for "Namngiao" (spicy noodle soup with pork) and Nam phrik ong (chili sauce) etc. It is made from soybean with high nutritional values. For the production processes of some localities, soybean is boiled, after that, the process of fermentation is undertaken for 3 days and then it is dried by sun exposure. Boiling not only gets rid of germs but also destroys bacteria which cannot resist heat; therefore, there are remaining bacteria which have heat-resistant having properties of producing spores and enzymes which can digest proteins, fat and water insoluble fibers. The fermentation process with the characteristic of microbiome can result in helping one another in producing important substances in terms of nutrition and health such as peptide, fatty acids and SCFAs. The digestion of the microbiome creates SCFAs, namely acetate, propionate and butyrate having the property of controlling sugar levels, metabolism and cholesterol levels and enhancing feeling full, including strengthening cells in the digestive system, preventing intoxication in cells and functioning as energy sources for cells in the digestive system. Moreover, SCFAs also function as histone deacetylase inhibitors (HDAC inhibitors) with the properties of curing non-contagious chronic diseases, anti-aging, controlling cell division and immunity cells functions. Due to the fact that microbes in Tua Nao have not been studied systematically, they are not utilized fully. The research team will be conducted metagenomic of the microbiome and SCFA analysis in "Tua-Nao".

Study Design & Methods: "Tua-Nao" samples with the production source in the northern region of Thailand, namely Chiang Rai, Mae Hong Son, Chiang Mai, Lampoon, Lamphang, Pha-Yao will be collected whereby 30 samples in form of dried and wet samples depending on the production source and the source of soybean cultivation. They will be analyzed short chain fatty acid (SCFA) by gas-liquid-chromatography (GLC). DNA from "Tua-Nao" samples will be extracted for metagenomic analysis. HDAC inhibitor assay will be also studied.

Results: Study on metagenomic analysis of the microbiome and SCFA analysis by GLC in "Tua-Nao" revealed that the most microbiome were firmicutes (bacillales, lactobacillales, Clostridiales) and the rest was proteobacteria (enterobacterales). Total SCFAs were 100-700 µmol/ml and had high acetate depending production source and the source of soybean cultivation.

Conclusions: In any case, Tua Nao is prebiotic with fibers helping for functions of the gut microbiome in intestines and probiotic with living microorganisms that provide health benefits and produce SCFAs involved in the control of aging and longevity leading to delay age-associated functional declines. As part of this study to develop a production process by utilization of fermented soybean, we will determine SCFAs and identify microbiome from "Tua-Nao" produced in different places in northern of Thailand. Lastly, HDAC inhibitor activity assay will also studied. The study will bring about developing Tua-Nao from being only local wisdom to be Tua-Nao with high SCFAs as supplementary food rich in benefits favorable for well-being of the elderly and underprivileged children.

Title: Seaweed components influence gut microbiota and short-chain fatty acid production

Author: Suvimol Charoensiddhi (Presenter), Department of Food Science and Technology, Faculty of Agro-Industry, Kasetsart University, Thailand
Co-authors: Parichat Hongsprabhas, Wei Zhang, Michael Conlon

Background: Seaweeds are important sources of bioactive compounds with diverse structures and functionalities. Dietary fibre, a common main component of seaweeds, can benefit health through impacts on gut microbiota profiles and production of microbial metabolites, including the formation of short-chain fatty acids (SCFA). High fibre diet (complex plant polysaccharides) intake positively affects the gut microbiota compositions, which leads to more production of immunomodulatory products, particularly SCFA.

Study Design & Methods: This study aimed to understand the prebiotic potential and contribution of different seaweed fractions from green and red seaweed cultivated in Thailand. The digestibility of seaweed fractions was determined using an in vitro human digestion model in order to understand the likelihood of components reaching the large bowel and the resident microbiota. The health benefits of seaweed fractions were assessed by including them in an in vitro anaerobic batch fermentation system containing human fecal inocula that mimic the environment of the human large bowel.

Results: Seaweed polysaccharide-enriched fraction was not digested; sugar released during oral, gastric, and intestine phases were not different from those compared to the undigested sample ($p>0.05$). However, polysaccharide conformation may change during passing through the gastrointestinal tract model. After 24 h fermentation, seaweed fractions induced significantly higher production of SCFA, and increased the growth of some bacteria linked to immune benefits compared to the negative control ($p<0.05$).

Conclusions: These findings further demonstrate that seaweed-derived polysaccharides have the potential to be used as dietary supplements with gut and immune health benefits.

Title: Natural products and derivatives against SARS-CoV-2

Author: Prasat Kittakoop (Presenter), Chulabhorn Graduate Institute, Thailand

Background: Patients with SARS-CoV-2 infections (COVID-19) were first reported in Wuhan, China, in December 2019; the epidemic of this viral disease has been continued worldwide and causes many negative impacts on both public health and economics globally. A search for drugs for the treatment of COVID-19 has been intensively studied, however, effective drugs or vaccine to cure or prevent COVID-19 have not been successfully discovered. Chloroquine, a derivative of a natural alkaloid, quinine, is active against SARS-CoV-2 virus *in vitro*, but fails to be drug for the treatment of COVID-19. Hydroxychloroquine, a less toxic derivative of chloroquine, does not benefit patients hospitalized with COVID-19. Ivermectin, a drug for the treatment of many types of parasite infestations, has antiviral activity towards SARS-CoV-2 virus in vitro. Drug repurposing or drug repositioning, aiming to use the existing drugs for new therapeutic purposes, is one of the strategies for research on drug discovery for COVID-19. This lecture covers recent research on natural products and derivatives which have antiviral activity against SARS-CoV-2.

Wednesday 16 December 2020

S28: Malaria transmission: contribution of asymptomatic

population 08.30-10.00hr

Room B

Chairperson: Wang Nguitragool

Invited speakers:

1. Mosquito infectivity of *Plasmodium vivax*
   Wang Nguitragool
   Faculty of Tropical Medicine, Mahidol University, Thailand

2. Investigating the asymptomatic infectious reservoir in coastal Tanzania using skin feeding assays
   Jessica Lin
   University of North Carolina, United States

3. Contribution of asymptomatic *Plasmodium* infections to the transmission of malaria in Kayin State, Myanmar
   Victor Chaumeau
   Shoklo Malaria Research Unit, Thailand

Title: Mosquito infectivity of *Plasmodium vivax*

Author: Wang Nguitragool (Presenter), Faculty of Tropical Medicine, Mahidol University, Thailand

Background: The infectiousness of malaria parasites to mosquitoes is an important parameter that determines disease transmission. Previous research has indicated that the man-to-mosquito transmission depends on gametocyte density. But until recently,the knowledge about the relationship between gametocyte density and the mosquito infection rate had not been well defined. In recent years, there has been an increasing interest in quantifying mosquito infectivity to assess the contribution of asymptomatic carriers to malaria transmission.

Study Design & Methods: Recent data on mosquito infectivity of *Plasmodium vivax* were reviewed with the aim to identify key features of *P. vivax* mosquito infection that are common across different geographical settings. The literature was drawn from infection studies using membrane feeding assays and skin feeding assays, with blood sourced from both natural and induced infections.

Results: There is now indisputable evidence that *P. vivax* asymptomatic carriers can transmit malaria. Studies from different continents using different *Anopheles* mosquito species demonstrated infectivity of blood from asymptomatic carriers. The infectiousness of the parasite was found to depend on gametocyte density, with an asymptomatic *P. vivax* blood meal usually causing infection in a low percent (%) of fed mosquitoes. Recent studies, using both natural infections and the human challenge model, further demonstrated that only a few gametocytes in the blood meal are sufficient to cause mosquito infection. Interestingly, unlike *P. falciparum*, *P. vivax* gametocytemia is highly correlated with parasitemia. Thus mosquito infectivity can be reliably estimated from the total parasite density without gametocyte counting.

Conclusions: There has been a significant progress in defining *P. vivax* infectivity to mosquitoes. A few common characteristics have emerged across different settings and experimental models. However, there remains important information that is still missing for translating these findings to practice. In particular, there is still a need to quantify more precisely the contribution of asymptomatic carriers to onward transmission, which would be the necessary basis to justify and appropriate funds to actively remove these infections for malaria elimination.

Title: Investigating the asymptomatic infectious reservoir in coastal Tanzania using skin feeding assays

Author: Jessica Lin (Presenter), University of North Carolina, United States

Background: In an area of declining endemicity in Tanzania, we are investigating transmission of *Plasmodium falciparum* from asymptomatic individuals to *Anopheles gambiae* (IFAKARA strain) mosquitoes via direct skin feeding assays (DFAs).

Study Design & Methods: In Oct-Nov 2018 and Apr-Jul 2019, we used school- and clinic-based recruitment to screen 2,233 asymptomatic volunteers > 6 years of age. Participants were screened for gametocytes, the transmissible stage to mosquitoes, using two sex-specific RT-qPCR assays: PF3D7_0630000 (female target, limit of detection (LOD)=1 gametocyte/µL) and PfMGET (male target, LOD=0.1 gametocytes/µL).

Results: In the screened cohort, *P. falciparum* prevalences was 14% by rapid diagnostic test (RDT), 11% by microscopy, and 27% by 18s rRNA qPCR. We enrolled 206 participants, of which 67% were RDT-positive and 31% were positive only by qPCR. Adults were more likely to have low-density infections, with 81% of adults (>18yo) vs 55% of children (<18yo) harboring parasite densities <100 parasites/ul. Female gametocytes were detected in 37% (77/206) of participants, while male gametocytes were detected in 68% (141/206). There was no significant difference in gametocyte sex ratios for male and female participants, but younger participants were more likely to have female-biased gametocyte sex ratios (p=0.001). For the transmission studies, a total of 195 DFAs were completed, with 177 yielding at least 25 mosquitoes for midgut dissection and oocyst enumeration. In total, 53% (94/177) of participants were infectious to at least one mosquito. Of these, 4.3% were smear-positive for gametocytes of either sex, 40% were RT-qPCR positive for female gametocytes, and 67% were RT-qPCR positive for male gametocytes. Male gametocyte density (gametocytes/µL) was a significant predictor of the proportion of oocyst-positive mosquitoes (regr. coef.=0.0027, p=0.034), while the presenece of female gametocytes was associated with a higher number of oocyst-positive mosquitoes with (IRR=2.23, p=0.001).

Conclusions: Our ongoing study and analyses are expected to illustrate the pervasiveness of the asymptomatic infectious reservoir in coaastal Tanzania, as well as limitations in current molecular methods for capturing the totality of this reservoir and predicting the infectivity of parasite carriers.

Title: Contribution of asymptomatic *Plasmodium* infections to the transmission of malaria in Kayin state, Myanmar

Author: Victor Chaumeau (Presenter), Shoklo Malaria Research Unit, Thailand
Co-autohrs: Ladda Kajeechiwa, Jordi Landier, Mallika Imwong, Arjen Dondorp, Nicholas White, François Nosten

Background: The objective of mass antimalarial drug administration (MDA) is to eliminate the asymptomatic malaria parasite reservoirs rapidly to reduce transmission. In the Greater Mekong Subregion, where artemisinin-resistant *Plasmodium falciparum* is now widespread, MDA has been proposed as an elimination accelerator but the contribution of asymptomatic infections to malaria transmission has been questioned. The impact of MDA on entomological indices has not been characterized previously.

Study Design & Methods: MDA was conducted in 4 villages in Kayin State (Myanmar). Malaria mosquito vectors were captured 3 months before, during, and 3 months after MDA, and their *Plasmodium* infections were detected by polymerase chain reaction (PCR) analysis. The relationship between the entomological inoculation rate, the malaria prevalence in humans determined by ultrasensitive PCR, and MDA was characterized by generalized estimating equation regression.

Results: Asymptomatic *P. falciparum* and *P. vivax* infections were cleared by MDA. The *P. vivax* entomological inoculation rate was reduced by 12.5-fold (95% confidence interval [CI], 1.6–100-fold), but the reservoir of asymptomatic *P. vivax* infections was reconstituted within 3 months, presumably because of relapses. This was coincident with a 5.3-fold (95% CI, 4.8–6.0-fold) increase in the vector infection rate.

Conclusions: We conclude that asymptomatic infections are a major source of malaria transmission in Southeast Asia.

Wednesday 16 December 2020

S29: Scrub typhus animal models and vaccine development

08.30-10.00hr

Room C

Chairpersons:

1. Luis Lugo
2. Piyanate Sunyakumthorn

Invited speakers:

1. Why is the development of a long-lasting and broadly protective scrub typhus vaccine so elusive?
   Allen Richards
   Uniformed Services University of the Health Sciences, United States

2. A nonhuman primate model for scrub typhus
   Piyanate Sunyakumthorn
   Armed Forces Research Institute of Medical Sciences, Thailand

3. Development of scrub typhus vaccine
   Nam-Hyuk Cho
   Seoul National University, Republic of Korea

Title: Why is the development of a broadly protective and long lasting scrub typhus vaccine so elusive?

Author: Allen Richards (Presenter), Uniformed Services University of the Health Sciences, United States

Background: Development of a broadly protective and long lasting vaccine against scrub typhus has been underway since the 1930s without significant success, both in animal and human trials.

Study Design & Methods: Vaccine candidates have been developed utilizing attenuated, killed and live *Orientia tsutsugamushi* without a favorable outcome. More recently, subunit vaccines based upon well known antigens and combination of antigens using recombinant technology to produce protein and DNA vaccine candidates have been developed and assessed. In addition, enhancement of the host immune response, both humoral and cellular, to the vaccine candidates has been employed utilizing various adjuvants and different inoculation schemes.

Results: Unfortunately, these new materials and methods have yet to produce the long lasting broadly protective vaccines necessary to stimulate the appropriate immune response in laboratory animals and humans necessary to protect them from natural and laboratory exposure to heterologous challenges.

Conclusions: In conclusion, this presentation will discuss these previous vaccine studies and trials to impart upon you the difficulties encountered in the development of an efficacious, long lasting and broadly protective scrub typhus vaccine.

Title: A nonhuman primate model for scrub typhus

Author: Piyanate Sunyakumthorn (Presenter), AFRIMS, Thailand
Co-authors: James Jones, Carl Mason, Manutsanun Sumonwiriya, Matthew Reed, Susanna Dunachie, Eric Lombardini, Rawiwan Im-erbsin, Allen Richards, Kesara Chumpolkulwong, Luis Lugo-Roman, Nam-Hyuk Cho, Daniel Paris, Nicholas Day

Background: Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi*, an obligate intracellular bacterium, which can be transmitted to vertebrate hosts by the bite of larval *Leptotrombidium* mites (chiggers). The most common signs and symptoms of human scrub typhus are fever, headache, myalgia, lymphadenopathy, eschars, and sometimes rash. Many species of animals were utilized as animal models for scrub typhus studies including rodents (rats, mice, guinea pigs), nonhuman primates (NHP). NHP models demonstrated clinical signs and disease progression similar to those of human scrub typhus human scrub typhus patients.

Study Design & Methods: We have developed a rhesus macaque model for scrub typhus using an intradermal inoculation of *Orientia tsutsugamushi*. This rhesus scrub typhus model was challenged with different strains of *O. tsutsugamushi* including Karp, Gilliam, Kato, Boryong, and TA763.

Results: All macaques developed classic eschars with necrotic crust at the injection sites where upon the bacteria propagated and disseminated to other tissues. Elevation of body temperature and bacteremia were observed in the same time periods. The immunological assays demonstrated anti-*O. tsutsugamushi* specific antibody response and cell-mediated immune response in all inoculated macaques.

Conclusions: The surrogate endpoints from these studies are currently being used to perfect a disease severity grading system in order to facilitate the model use in the evaluation of novel scrub typhus vaccines and therapeutics.

Title: Development of scrub typhus vaccine

Author: Nam-Hyuk Cho (Presenter), Seoul National University, Republic of Korea

Background: Scrub typhus is an acute febrile disease caused by *Orientia tsutsugamushi* infection. Despite the wide range of approaches explored during the last seventy years, an effective prophylactic vaccine is not yet available.

Study Design & Methods: Here, we developed a novel recombinant antigen derived from conserved regions of 56 kDa type-specific antigen (TSA56), a major outer membrane protein responsible for genetic heterogeneity and antigenicity, and evaluated it as a protective vaccine antigen.

Results: Our findings demonstrate that immunization with conserved blocks of TSA56 (cTSA56) not only provides protective immunity against lethal challenges with the homologous genotype, but also confers significantly better protection against heterologous genotypes than TSA56. Adoptive transfer of CD4+ or CD8+ T cells from immunized mice provided significantly enhanced protection against lethal challenge, whereas immune B cells failed to do so, indicating that cellular immunity against the conserved epitopes plays a protective role. Moreover, immunization with a 10-mer peptide mixture, screened from CD8+ T cell epitopes within the conserved region of TSA56, provided enhanced protection against lethal challenge with *O. tsutsugamushi.*

Conclusions: Therefore, this novel recombinant antigen is a promising candidate for scrub typhus vaccine against a wide range of *O. tsutsugamushi* genotypes.

Wednesday 16 December 2020

S30: Antibiotic resistance: an overlooked pandemic

08.30-10.00hr

Room D

Chairperson: Samandra Demons

Invited Speakers:

1. Antimicrobial-resistant *Campylobacter* and its ecological fitness
   Taradon Luangtongkum
   Chulalongkorn University, Thailand

2. A looming threat: colistin resistance in *Acinetobacter baumannii*
   Iyarit Thaipisutikul
   Mahidol University, Thailand

3. The growing threat of multi-drug resistant gonorrhea
   Kelly Hourihan
   Walter Reed Army Institute of Research, Georgia

4. Development of fixed phage cocktails in the fight against multidrug-resistant organisms
   Damon Ellison
   Walter Reed Army Institute of Research, United States

Title: Antimicrobial-resistant *Campylobacter* and its ecological fitness

Author: Taradon Luangtongkum (Presenter), Chulalongkorn University, Thailand

Background: This presentation is a summary of research findings on the fitness cost of antimicrobial-resistant *Campylobacter* in poultry, a natural reservoir of this food-borne bacterial pathogen. *Campylobacter* is one of the most important causes of food-borne disease especially in industrialized countries.Approximately 400 – 500 million cases of diarrhea due to *Campylobacter* infection have been reported each year. Additionally, a large number of *Campylobacter* isolates from both humans and animals in Southeast Asia, especially Thailand, are resistant to clinically important antimicrobial agents particularly to fluoroquinolones (FQs).

Study Design & Methods: To determine whether antimicrobial-resistant *Campylobacter* is ecologically fit in antibiotic-free environment and whether it can persist after antibiotic withdrawal or not, pairwise competition experiments were conducted by inoculating a mixture of antimicrobial-resistant and antimicrobial-susceptible *C. jejuni* into chickens. The number of antimicrobial-resistant and antimicrobial-susceptible isolates was examined at 3, 6 and 10 days after inoculation (DAI) and the competition index was calculated at each DAI.

Results: The results showed that FQ-resistant *C. jejuni* was ecologically fit in antibiotic-free environment, while macrolide-resistant *C. jejuni* was not ecologically fit and could not persist in the absence of antibiotic selection pressure.

Conclusions: Although a withdrawal of FQs will unlikely reduce the prevalence of FQ-resistant *Campylobacter* in animals and animal products in the near future, a withdrawal or reduction of macrolide usage in animal production should be able to help reduce the prevalence of macrolide-resistant *Campylobacter* significantly.

Title: A looming threat, colistin resistance in *Acinetobacter baumannii*

Author: Iyarit Thaipisuttikul (Presenter), Mahidol University, Thailand

Background: Currently, extensively-resistant (XDR) *Acinetobacter baumannii* is arguably the most concerned bacterial pathogen due to its resistance to virtually all clinically available antibiotics. Colistin is practically a last resort for *A. baumannii* antimicrobial therapy. Although rare, colistin-resistant *A. baumannii* has been continuously reported. In most cases, mutations in pmrCAB lead to the modification of lipid A, the binding target of colistin in bacterial outer membrane. However, colistin-susceptible *A. baumannii* also exhibits some degrees of tolerance to colistin.

Study Design & Methods: Several approaches including gene sequencing, MLST, MALDI-TOF and in vitro fitness assays were employed for investigating the colistin-resistant *A. baumannii* isolated in Siriraj Hospital. Additionally, RNA-Seq was also performed to investigate the expressed genes during sub-lethal colistin exposure of a reference and a clinical *A. baumannii* strains.

Results: Two colistin-resistant clones with different degrees of colistin resistance and pmrCAB mutational profiles were identified. In contrast to previous reports, all clones exhibited no fitness loss. Additionally, resistance to colistin could also be induced upon exposure to sub-lethal dosage of colistin in susceptible strain with neither pmrCAB overexpression nor lipid A modification. RNA-Seq showed multiple overexpressed genes during the exposure, which required further investigation.

Conclusions: The mechanisms of colistin resistance in *A. baumannii* are complex involving the balance between resistance and fitness. Colistin tolerance during sub-lethal exposure to colistin could be significant clinically if colistin dosages in patients are inappropriate. The identification of isolates with no fitness loss raises the concern of possible stable resistance clone which could be a serious future threat.

Title: THE growing threat of multi-drug resistant gonorrhea

Author: M. Kelly Hourihan (Presenter), Walter Reed Army Institute of Research, Georgia
Co-authors: Nithinart Chaitaveep, Shannon Walls, Nino Mitaishvili, Matthew Scherer, Anna Navana, Woradee Lurchachaiwong

Background: Emerging antimicrobial resistance (AMR) to the gonococcal (GC) bacteria, *Neisseria gonorrhoeae*, is a global public health and Force Health Protection concern due to increased discovery of strains resistant to most available therapies. According to the World Health Organization, extended-spectrum cephalosporins are the only viable treatment for this common sexually-transmitted infection (STIs) in many countries. These alarming findings underscore the need for comprehensive, worldwide surveillance of AMR in GC infections to inform therapy decisions.

Study Design & Methods: The Walter Reed Army Institute of Research (WRAIR) is poised for global surveillance of GC resistance patterns through collaborations with WRAIR overseas laboratories and host nation stakeholders, including the countries of Georgia and Thailand. Both conventional microbiological assays and advanced multiplex molecular platforms are used to characterize trends in AMR of GC isolates, as well as co-infections with other STIs.

Results: AMR patterns from GC isolates collected by the Thai Royal Army military (2014-2016) were characterized via minimal inhibitory dilution. Susceptibility results demonstrated resistance to tetracycline, penicillin, and ciprofloxacin. Surveillance-studies performed on 142 urine samples collected from Georgian civilian and military were conducted using the Fast Track Diagnostics STD09 multiplex molecular assay. GC infection was identified in 58.5% of cases and co-infection with 2 or more STI pathogens was detected in 43.0% of cases.

Conclusions: These data indicate that GC infections are a continued global threat and that comprehensive surveillance of emerging AMR patterns in *N. gonorrhoeae* and of prevalence of co-infections with other bacteria are necessary to inform regional stake holders in proper antimicrobial therapies.

Title: Development of fixed phage cocktails in the fight against multidrug-resistant organisms

Author: Damon Ellison (Presenter), Walter Reed Army Institute of Research, United States
Co-authors: Amanda Ward, Andrey Filippov, Brett Swierczewski, Derese Getnet, Helen Freyberger, Mikeljon Nikolich, Yunxiu He

Background: Wound infections caused by multidrug resistant (MDR) Gram-negative bacterial pathogens present a persistent challenge for the United States Department of Defense Military Health System (MHS). Antibiotic treatment options are becoming more limited with the proliferation of multidrug resistance and the lack of new antibiotic development. *Pseudomonas aeruginosa* is an important Gram-negative pathogen that causes millions of serious infections globally every year and is a major cause of wound infections, including those seen in complicated combat-related wounds, burns and fractures. The rapid increase in infections with MDR *P. aeruginosa* is of particular concern as variants have emerged with resistance to carbapenems often used as last line therapeutics and are prevalent in military wounds and burns. *P. aeruginosa* also forms robust biofilms during infection that are associated with increased antimicrobial tolerance and wound infection persistence.

Study Design & Methods: The overarching goal of the US Army Bacteriophage Therapeutics (BT) program in the Walter Reed Army Institute of Research Wound Infections Department is to develop durable, off-the-shelf bacteriophage products for the treatment and potential prophylaxis of Gram-negative MDR infections.

Results: BT has developed and characterized a panel of therapeutic candidate lytic *P. aeruginosa* phages and employed a rational design approach to create a durable fixed cocktail formulation with lytic activity against 78% of strains in a panel of 100 genomically diverse MDR clinical isolates collected throughout the MHS.

Conclusions: The recent success of WRAIR therapeutic phages as treatments in expanded access cases of MDR *P. aeruginosa* infections indicates their potential for combating MDR organisms.

Wednesday 16 December 2020

S31: Risk communication (Thai/Eng session)

08.30-10.00hr

Room E

Chairpersons:

1. Khanchit Limpakarnjanarat
2. Pahurat Kongmuang Taisuwan

Invited speakers:

1. CCSA spokesperson sharing experience: building trust and telling truth (no abstract)
   Taweesilp Visanuyothin and Natapanu Nopakun
   Bureau of Risk Communciation and Health Behavior Development, Department of Disease Control; Department of Information, Ministry of Foreign Affairs

2. How to manage infodemic regarding COVID-19 outbreak in SEARO? (no abstract)
   Supriya Bezbaruah
   World Health Organization Regional Office for South-East Asia

3. COVID-19 response of governments in journalist view (no abstract)
   Jason Gale
   Bloomberg News

4. How to achieve million followers and make them stunning in social platforms concerning COVID-19 (no abstract)
   Pahurat Kongmuang Taisuwan
   Bureau of Risk Communication and Health Behavior Development, Department of Disease Control

Wednesday 16 December 2020

Sponsored session: Introducing the Royal Society of Tropical Medicine and Hygiene

10.00-10.15hr

Speaker: Tamar Ghosh
Chief Executive, Royal Society of Tropical Medicine and Hygiene, United Kingdom

The Royal Society of Tropical Medicine and Hygiene is a global charity and membership society that has been dedicated to improving tropical medicine and global health since 1907. Our activities include funding and disseminating multidisciplinary research through peer-reviewed journals and a calendar of meetings and events. We provide grants for UK and international research, and award medals for excellence in practice, and to recognise emerging talent. Hear more about the society and our grant programme with Chief Executive Tamar Ghosh.

Wednesday 16 December 2020

S32: Clinical management of COVID-19

10.15-11.45hr

Room A

Chairperson: Usa Thisyakorn

Invited speakers:

1. Pandemic and prevention of COVID-19 (no abstract)
   Terapong Tantawichien
   Faculty of Medicine Chulalongkorn University

2. Clinical manifestations and antiviral treatment
   Viravarn Luvira
   Faculty of Tropical Medicine, Mahidol University

3. Respiratory management of COVID-19
   Chaisith Sivakorn
   Faculty of Tropical Medicine, Mahidol University

4. Hemodynamic and critical care support in severe COVID-19
   Nattachai Srisawat
   Faculty of Medicine Chulalongkorn University

5. ICU management of COVID-19 patients: experience at Siriraj Hospital
   Ranistha Ratanarat
   Faculty of Medicine Siriraj Hospital, Mahidol University

Title: Clinical manifestations and antiviral treatment

Author: Viravarn Luvira (Presenter) Faculty of Tropical Medicine, Mahidol University

Background: COVID-19 has a broad range of clinical manifestations varying from asymptomatic conditions (40-45% of cases), mild upper respiratory symptoms to severe respiratory failure. Additionally, extrapulmonary manifestations can present in all systems. Symptoms generally appear 2-14 days after exposure to the virus. However, in children with COVID-19, the hyperinflammatory shock called “Multisystem Inflammatory Syndrome in Children (MIS-C)” occurs later between 1-6 weeks after infection. Recently, this syndrome was reported in adults and termed MIS-A.

Multiple drugs with *in vitro* antiretroviral effects have been used in clinical practices and trials with varying results. Among large-scale uncertainty in this field, to date, Remdesivir is recommended from panels for the treatment of only severe COVID-19 patients.
As the outbreak has progressed, so has the availability of cumulated data and knowledge regarding COVID-19. Clinicians and researchers are strongly advised to access latest relevant repositories in order to retrieve updates on latest clinical presentations and effective treatments.

Title: Respiratory management of COVID-19

Author: Chaisith Sivakorn (Presenter) Faculty of Tropical Medicine, Mahidol University

Almost half of patients with COVID-19 have abnormal chest x-ray findings with peripheral GGO affecting the lower lobes being the most common finding. Chest x-ray can be used in diagnosis and follow up in patients with COVID-19 pneumonia. Lung ultrasound (LUS) is useful in place where computed tomography is not available. LUS can clearly detect sub-pleural interstitial and consolidation. Furthermore, Point-of-care LUS is a noninvasive, rapid, repeatable, and sensitive bedside method. LUS score strongly correlates with the eventual need for invasive mechanical ventilation and is a strong predictor of mortality. Routine use of LUS may guide patients' management strategies, as well as resource allocation in case of surge capacity.

The phenomenon of 'silent' or 'happy' hypoxemia in COVID-19 patients is due to leftward shift of the oxyhemoglobin dissociation curve induced by hypoxemia-driven hyperventilation as well as possible direct viral interactions with hemoglobin. This pathophysiology causes preserved oxygen saturation despite low partial pressure of oxygen in arterial blood samples. Ventilation-perfusion mismatch, ranging from shunts to alveolar dead space ventilation, is the COVID-19 specific respiratory phenotypes which offers various therapeutic targets according to the stage of disease.

Conversely to other respiratory viral infections, systemic corticosteroid therapy had no observable impact on time to COVID-19 clearance from pharyngeal PCR. A prospective meta-analysis of clinical trials of critically ill patients with COVID-19 showed that administration of systemic corticosteroids was associated with lower 28-day all-cause mortality compared with usual care or placebo with number needed to treat 12.5.

In small cohort, Awake prone positioning (awake-PP) appears to be safe and may slow the respiratory deterioration in select patients with COVID-19, who require oxygen supplementation or NIV/CPAP. Recent data revealed significant improvement of oxygen saturation and respiratory rate of awake-PP. Conversely, a prospective, multicenter, adjusted observational cohort showed no reduction in intubation need or mortality when use awake-PP combined high flow nasal oxygen (HFNO) in COVID-19 patients with acute respiratory failure. High-quality studies are required to assess the degree to which awake prone positioning may be beneficial, as well as select those who may benefit from it the most. With such an easy intervention, there may be a temptation to intervene based on compassionate grounds—however, without evidence, it will be difficult to assess the true value of prone positioning for future pandemics.

HFNO and non-invasive ventilation (NIV) are both feasible in COID-19 patients, but come at additional costs for the machines and interfaces, have technical challenges, practical concerns, demand close monitoring and depend on a stable electrical and oxygen supply. Good interface fitting NIV and HFNO limits exhaled air dispersion. Nebulization should be avoided or, if being necessary, required adequately naturally-ventilated areas.

Ventilatory management in COVID-19 is like general viral pneumonia. Use low tidal volume, monitor driving pressure, use high positive end expiratory pressure only as a rescue therapy, applying early awake prone and considering lung morphology and thrombosis were key strategies for success.

Title: Hemodyanamic and critical care support in severe COVID-19

Author: Nattachai Srisawat (Presenter), Chulalongkorn University, Thailand

Background: While most cases coronavirus disease 2019 (COVID-19) are mild, severe COVID-19 pneumonia can occur with a mortality rate as high as 50%. It is unclear why some patients develop clinical features of sepsis/septic shock with multiple organ dysfunction. The majority of bacterial cultures from severe COVID-19 patients are negative, and although empiric antibiotics are commonly used, they are not recommended. However, while the respiratory tract is the principle site of infection for COVID-19, the disease has been shown to involve the GI tract as well and symptoms such as diarrhea are reported in about a third of cases]. Enterocytes in ileum and colon express the ACE2 receptor and virus has been detected in stool. Thus, there is a possibility that bacterial translocation from the GI tract might complicate severe COVID-19 disease.Endotoxin, a part of the cell wall of Gram-negative bacteria, has been extensively investigated and acknowledged as one of the key triggers of lethal shock during severe sepsis and also one of the primary drivers of the cytokine storm. Serum (1□3)-b-D-glucan (BG) has been evaluated as a potential marker of intestinal barrier dysfunction. Serum BG was tested in several mouse models of gut leakage, including dextran sulfate solution administration, endotoxin injection, and cecal ligation and puncture sepsis. However, the presence of endotoxemia and serum BG in severe COVID-19 have never been examined. Not only bacterial toxin but also direct bacterial invasion might play role in severe COVID-19. Exploring circulating bacteriome in severe COVID-19 may allow us to test the presence of any bacterial invasion during critical illness.

Title: ICU management of COVID-19 patients: Experience at Siriraj Hospital

Author: Ranistha Ratanarat (Presenter), Faculty of Medicine Siriraj Hospital, Mahidol University

Since late December 2019, there has been an outbreak of a novel enveloped RNA betacoronavirus called severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus causes coronavirus disease 2019 (COVID-19), which has become an ongoing pandemic. Up to one-quarter of COVID-19 patient required intensive care unit and global mortality rate is 3% which more severe in older age group and the presence of co-morbidities such as obesity, diabetes mellitus, immunocompromised, chronic pulmonary disease and chronic renal or liver disease.

In Thailand, approximately four thousand confirmed COVID-19 cases with 1.5% death rate has been reported. Thailand is an upper middle-income country which limited in infrastructure and human resources. Early stratification for high risk of severe disease and early treatment with good supportive care is the key massage. Critical care management of COVID-19, one of the most important components of the management will be discussed.

Wednesday 16 December 2020

S33: Human challenge for drug and vaccine development

10.15-11.45hr

Room B

Chairpersons:

1. Norman Waters
2. Michele Spring

Invited speakers:

1. *Plasmodium vivax* CHMI
   Anjali Yadava
   Walter Reed Army Institute of Research **(**WRAIR**)**, United States

2. *Plasmodium vivax* biomarker study in Thailand
   Michele Spring
   Armed Forces Research Institute of Medical Sciences, Thailand

3. Strategy to define and develop the appropriate challenge of *Plasmodium falciparum*
   Kirsten Lyke and Joana Da Silva
   University of Maryland, Center for Vaccine Development and Global Health, United States

4. Understanding the social and ethical implications of controlled human malaria infection study in Kenya: an embedded empirical ethics study
   Primus Che Chi
   KEMRI-Wellcome Trust Research Programme, Kenya

Title: *Plasmodium vivax* CHMI

Author: Anjali Yadava (Presenter), Walter Reed Army Institute of Research (WRAIR), United States

Background: *Plasmodium vivax* controlled human malaria infection is an important component for the evaluation of drugs, vaccines and pathologies associated with this parasite. However, very few PvCHMI have been performed to date. We conducted a PvCHMI in malaria-naïve subjects using infected *Anopheles dirus* mosquitoes to evaluate the safety and efficacy of a malaria vaccine candidate. This study was conducted in the United States using infected mosquitoes from Thailand. As part of that study, we collected safety data related to PvCHMI. Clinical and laboratory data collected, to include adverse events (AEs), following mosquito bite induced *P. vivax* infection in malaria-naïve subjects, who participated in a clinical trial to evaluate a malaria vaccine (NCT01157897), was retrospectively analyzed. Malaria diagnosis was based on microscopic analysis of Giemsa-stained slides. Exploratory molecular assays were used to detect parasites using real time PCR. Adverse events (AEs) were mild to moderate and no study-related serious AEs were observed in any of the subjects. A majority the symptoms resolved within a couple of days. Using molecular diagnostic methods, almost all the symptoms appeared after the initiation of treatment. Controlled human malaria challenge with *P. vivax* is safe with majority of the infections being detected prior to the appearance of clinical symptoms. Sensitive molecular diagnostic methods of detection alleviate most symptoms even further. We will discuss the challenges involved in the execution of the CHMI, and the outcome of the study.

Title: The search for a *Plasmodium vivax* hypnozoite biomarker

Author: Michele Spring (Presenter) AFRIMS, Thailand

Co-authors: Jessica Lin, Rhoel Dinglasan, Timothy Garrett, Sabaithip Sriwichai, Phimphan Pisutsan, Worachet Kuntawunginn, Pattaraporn. Vanachayangkul, Paphavee Lertsethtakarn, Krisada Jongsakul, Sathit Pichyangkul, Brian Vesely, Mariusz Wojnarski, Norman Waters

Background: Novel diagnostics of the hypnozoite stage would allow for targeted primaquine treatment for both those who have with *P. vivax* and for individuals returning from *P. vivax* endemic areas who require presumptive anti-relapse treatment (PART). Since hypnozoites remain clinically silent, activation and development of hypnozoites into schizonts remains a black box.

Study Design & Methods: Different methods are currently being employed to attempt to identify a hypnozoite diagnostic. Human liver-chimeric mouse (FRG KO huHep) models can take advantage of direct biopsy of liver tissue as well as peripherally released extracellular vesicles. Non-human primates and the relapsing *P. cynomolgi* model can serve as a surrogate *P. vivax* model. Human studies in individuals infected with *P. vivax* can be carefully designed to allow for relapse with prospectively sampling in a study environment where the re-infection risk to the subject has been minimized. System biology tools can evaluate key metabolites, proteins and transcripts, all which could signify new signaling avenues within the liver.

Results: We are leveraging this rapidly relapsing vivax phenotype in an ongoing clinical study in Thailand giving short acting artesunate and delaying primaquine until 6 weeks later, expecting 50% of subjects to relapse during that time. By collecting peripheral blood, urine and saliva samples at regular intervals prior to primaquine, we hope to maximize the opportunity to detect unique pathways inherent to hypnozoites.

Conclusions: Careful interrogation of pre-relapse biomarker signals could then be transitioned into a diagnostic product for improved radical cure individual treatment algorithms and interruption of community transmission.

Title: Strategy to define and develop the appropriate challenge of *Plasmodium falciparum*

Author: Kirsten Lyke and Joana Da Silva (Presenters), University of Maryland, Center for Vaccine Development and Global Health, United States

Background: *P. falciparum* is characterized by considerable strain diversity in the field. Most malaria vaccines are based upon a single, culture-adapted strain termed NF54, from West Africa, or its clone 3D7. Optimizing appropriate heterologous strains for Controlled Human Malaria Infection (CHMI) representative of field strain diversity has proved critical, but challenging.

Study Design & Methods: Using 'omics approaches, we describe properties characteristic of existing laboratory-adapted heterologous strains may be robust predictors of field efficacy, and how *Pf* isolates collected in ongoing attenuated *Pf* sporozoite (PFSPZ) Vaccine field trials may identify targets of vaccine-induced protection, which in turn can be used to prioritize strains to use in malaria vaccinology, including challenge studies.

Results: The results of genomics, proteomics and genome-wide epitome analyses and clone properties of a Brazilian strain, Pf7G8, show this strain to be a stringent predictor of PfSPZ Vaccine efficacy in CHMI and in the field, specifically in Africa. Results of concurrent heterologous strains will be discussed.

Conclusions: Existing heterologous strains utilized in CHMI are predictive of field results in Africa. Future analyses will strive to utilize similar methods to expand the repertoire of challenge strains and to predict correlates of immunity in vaccine trials.

Title: Understanding the social and ethical implications of controlled human malaria infection study in Kenya: An embedded empirical ethics study

Author: Primus Che Chi (Presenter), KEMRI-Wellcome Trust Research Programme, Kenya
Co-authors: Esther Owino, Irene Jao, Melissa Kapulu, Dorcas Kamuya, Maureen Njue, Vicki Marsh

Background: Controlled human malaria infection (CHMI) studies that involve deliberate infection of healthy adult volunteers with a specific strain of the malaria parasite under controlled conditions have been undertaken at the KEMRI-Wellcome Trust Research Programme KWTRP in Kenya since January 2017. A series of social science/empirical ethics studies have been embedded within the CHMI studies to explore emerging social and ethical issues within a low- and middle-income setting.

Study Design & Methods: Four rounds of embedded social science/empirical ethics research exploring participants understanding, perceptions, and experience of CHMI study participation were undertaken from 2017 to 2019. Data was collected through interviews, focus group discussions and non-participation observations. Participants included CHMI study volunteers, CHMI study staff, community representatives, fieldworkers and community engagement staff.

Results: One hundred and forty-nine people participated in the study. The major themes that emerged from the data analysis included motivation for study participation, deciding to participate, role of trust, perception of deliberate infection and experienced study benefits and burdens. Study compensation and free comprehensive health assessment during study screening were important motivations for participation. Although CHMI study volunteers had good understanding of key elements about the study, they expressed fluctuating fears and anxieties around the concept of deliberate infection. Volunteers reported many unanticipated psychological and emotional burdens. Most volunteers expressed no regrets in participating in the study and were willing to participate in similar studies in the future. Overall, the concept of deliberate infection was new to all participants.

Conclusions: CHMI studies in low- and middle-income settings raise important social and ethical issues that should be considered in the planning and conduct of such studies.

Wednesday 16 December 2020

S34: Dengue and other arboviral diseases

10.15-11.45hr

Room C

Chairperson: Stefan Fernandez

Invited speakers:

1. Evidence of stable endemicity of chikungunya virus in Southern Thailand
   Stefan Fernandez
   Armed Forces Research Institute of Medical Science, Thailand

2. Familial dengue transmission from the prospective family cohort study in Kamphaeng Phet, Thailand; Case studies in household transmission
   Darunee Buddhari
   USAMD-AFRIMS, Thailand

3. Mast cell tryptase as a predictive biomarker for developing severe dengue
   Robert Hontz
   NAMRU-2, Singapore

4. *In vitro* evidence of ivermectin as a inhibitory of arbovirus replication
   Taweewun Hunsawong
   USAMD-AFRIMS, Thailand

Title: Evidence of stable endemicity of chikungunya virus in Southern Thailand

Author: Stefan Fernandez (Presenter), AFRIMS, Thailand
Co-authors: Kathryn Anderson, Chonticha Klungthong, Taweewun Hunsawong, Sarunyou Chusri

Background: Chikungunya fever is caused by the alphavirus chikungunya virus (CHIKV) and is most commonly characterized by fever, headaches, muscle pain, retro-orbital pain and, frequently, by arthralgia. Disease symptoms may last a few days and it is seldom fatal. Outbreaks of the disease are thought to be sporadic, unpredictable and without a clear endemic pattern. Since 2012 AFRIMS has conducted a hospital-based arbovirus surveillance study in Southern Thailand in collaboration with Prince of Songkla University, PSU. The objective of this study is to monitor the circulation of important arboviruses in the region, including dengue virus, zika virus and CHIKV. The study enrolls subjects of all ages seeking clinical care at PSU hospital and various other clinics in the Province of Songkla. The study collects blood samples during the acute phase of the fever and once more during the convalescent period, 14 days later. Serum samples are used to determine the presence of circulating arboviruses in the region.

Study Design & Methods: Subjects are enrolled into the surveillance study when they present at PSU Hospital and other clinics in the province. Enrollment criteria includes fever and symptoms commonly associated with arbovirus infections. Medical history, clinical and demographic data are collected during enrolment, as well as a blood sample. A convalescent sample is also collected two weeks afterwards. Acute serum samples are tested by RT-PCR for the presence of dengue virus, zika virus and CHIKV virus. Some positive samples are further processed for virus isolation, sequencing and phylogenetic analyses. Paired acute and convalescent serum samples are tested for the presence of IgM/IgG or presence of neutralizing antibodies.

Results: CHIKV RT-PCR of acute serum samples shows a wide variation of CHIKV positive cases in our study, ranging from less than 1% in 2014 and 2015 to 16% of all fever cases captured in 2018 and 10% in 2019. The large percentage of positive cases in 2018/19 coincided with several localized outbreaks in Thailand. However, hemagglutination inhibition (HAI) assays using paired samples shows that the rate of seroconversion is significantly higher, ranging from 2.5% in 2017 to 19.2% (2018) and over 40% in 2019, of all fever cases. Phylogenetic analyses of the sequences obtained revealed that there may have been at least two independent introductions of the virus in the region.

Conclusions: Data suggest that CHIKV virus may circulate, endemically, in some areas of Southern Thailand, unlike other areas where CHIKV short-lived outbreaks are more common. While it is not clear why this is the case, our phylogenetic data point to multiple introductions of the virus in the region. Our study does not provide rates of the disease incidence, but identifies a region unique in the distribution of CHIKV and provides an avenue to test the efficacy of vaccine candidates.

Title: Familial dengue transmission from the prospective family cohort study in Kamphaeng Phet, Thailand; Case studies in household transmission

Author: Darunee Buddhari (Presenter), USAMD-AFRIMS, Thailand

Background: Dengue is a re-emerging global public health problem and the most common arbovirus causing human disease in the world. The previous studies point to the household of a dengue viremic individual as a source of DENV transmission, what remains less clear about DENV epidemiology is the effect of DENV infection on the entire family unit across all age groups including infants and the dynamics of transmission within the household.

Study Design & Methods: A prospective longitudinal cohort study designed to follow 500 multigenerational family units comprising approximately 2500 subjects of all ages is being conducted in Kamphaeng Phet province, Thailand. The study began in 2015 and is ongoing. Active surveillance is accomplished by contacting cohort subjects at least once per week and routine follow-up is performed annually. An episode of reported or documented fever in a cohort subject triggers an acute fever investigation in which acute and convalescent blood samples are obtained and tested for evidence of DENV infection. In addition, other cohort subjects who are in the same family unit as an infected cohort subject are evaluated in household contact investigations to determine patterns of household transmission.

Results: In this analysis, we provide case studies of 4 family units from the family cohort study, providing insights into features of household transmission during the study years 2015-2016.

Conclusions: Our preliminary data indicate that seroconversions to DENV occurred across all age groups, underscoring an urgent need to study the clinical spectrum of DENV-related disease in middle-aged and elderly persons, in particular. This study will gather detailed information on immunological profiles and comorbidities in these groups to better understand risk factors for dengue illness and potential differences in clinical manifestations in these groups.

Title: Mast cell tryptase as a predictive biomarker for developing severe dengue

Author: Robert Hontz (Presenter), NAMRU-2, Singapore
Co-authors: Ashley St. John, Chinmay Mantri, Diego Galan, Jenny Low, Tyler Warkentien

Background: Dengue is endemic to most tropical and sub-tropical countries, impacting hundreds of millions annually. Dengue disease progresses from mild symptoms "with or without warning signs" (dengue fever (DF) to life threatening "dengue hemorrhagic fever" (DHF). Data from Duke-National University of Singapore among Bangladeshi patients indicated that elevated chymase, a mast cell (MC) protease, predicted late onset DHF in children and adults. In this study, another MC protease, tryptase, a regulator of vascular leakage, was investigated to determine the extent of its association with dengue hemorrhagic complications.

Study Design & Methods: Here, we assessed the correlation between tryptase levels and signs of vascular leakage in prospectively recruited patients in Singaporean hospitals and clinics. Patients were sub-divided into groups based on outward signs at initial presentation: "bleeding" and "non-bleeding."

Results: The "bleeding" group showed average plasma tryptase concentrations of 385.31 pg/mL, compared to 326.61 pg/mL for the "non-bleeding" group (t-value=1.86; p=0.035); demonstrating statistically significant associations between elevated tryptase and vascular complications of dengue. Secondarily, immune cell counts were measured between both groups, showing that basophils were the only immune cell-type significantly higher (by t-test) in patients that experienced bleeding. Regression analysis detailed no significant correlation between basophil counts and serum tryptase levels.

Conclusions: Results indicate a correlation between higher serum tryptase levels and bleeding symptoms, making tryptase a promising biomarker for early detection of severe dengue disease. Such a target would be extremely promising for future development into an easy-to-use handheld or diagnostic device for early detection of dengue in resource-poor settings or remote environments.

Title: *In vitro* evidence of Ivermectin as an inhibitor of arboviruses replication

Author: Taweewun Hunsawong (Presenter), USAMD-AFRIMS, Thailand

Background: Arboviruses are RNA viruses transmitted to humans through the bites of infected arthropods like mosquito. Dengue virus (DENV), zika virus (ZIKV) and chikungunya virus (CHIKV) are the causative agents of three important human arboviral diseases. These viruses are often circulating in tropical and sub-tropical areas. At present, there is no specific FDA-approved drug or vaccine available to treat or prevent these arboviral diseases. Ivermectin is approved to use in human as an anti-parasitic drug. Due to its activity as a protease/helicase inhibitors, ivermectin has the potential to inhibit the replication cycle of arboviruses. Current literature suggests that ivermectin acts as an inhibitor of arboviruses replication by directly inhibiting the helicase activity of flaviviruses NS3 protein of at least yellow fever virus (YFV), DENV and West Nile virus (WNV). During DENV replication cycle, ivermectin interferes with importin α/β function by inhibiting import of viral proteins into the nucleus. In CHIKV replicon studies, ivermectin inhibits CHIKV replication in a dose dependent manner.

Study Design & Methods: We focused on various approaches and cell types to demonstrate the inhibitory effects of ivermectin. In our anti-viral experiments, we explored the ability of ivermectin to inhibit CHIKV (181 clone 25, live-attenuated vaccine strain) and ZIKV infections using two different cell lines, LLC-MK2 (mammalian cell line) and C6/36 (mosquito cell line).

Results: In our in-vitro studies we found that ivermectin has the ability to inhibit both CHIKV and ZIKV replication at 18h post infection. The half maximal inhibitory concentration (IC50) of ivermectin for CHIKV (7.9 µM) and ZIKV infections (4.3 µM) in LLC-MK2 cells was lower than that in C6/36 cell (8.4 µM and 10.8 µM for CHIKV and ZIKV, respectively). Our data suggest that ivermectin inhibits viral entry and replication in cells, rather than attachment.

Conclusions: Ivermectin directly effects the function of viral proteins essential to the virus replication cycle. *In vitro* evidence supports the use of ivermectin as treatment for pre- or post-exposure of arbovirus infections. In vivo studies are still required to demonstrate its efficacy.

Wednesday 16 December 2020

S35: Research work in Lao PDR under Her Royal Highness Princess Maha Chakri Sirindhorn Project (Thai session)

10.15-11.45hr

Room D

Chairpersons**:**

1. Prawat Nitiyanant
2. Teera Kusolsuk

Invited speakers**:**

1. Factors associated with diarrhea in children age 1-5 years old in Long Hospital, Long District, Luang Namtha Province, Lao PDR
   Souphasay Singngam
   Long Hospital, Luang Namtha Province, Lao PDR

2. Incidences of sarcocystis in market beef and Pork in Vientiane, Lao PDR (no abstract)
   Nalita Xaysanasy
   Mittaphab Hospital, Ministry of Health, Vientiane, Lao PDR

3. Quantity and quality of breast milk of Laotian lactating women
   Kitti Sranacharoenpong
   Institute of Nutrition, Mahidol University, Thailand

Title: Factors associated with diarrhea in children age 1-5 years old in Long Hospital, Long District, Luang Namtha Province, Lao PDR

Author: Souphasay Singngam (Presenter), Long Hospital, Luang Namtha Province, Lao PDR

Background: Diarrhea kills more children than malaria, measles, and AIDS combined. Proportional distribution of cause-specific deaths among children under five years of age, 2012 (excluding neonatal deaths). In Lao PDR, diarrhea is also classified as a leading cause of morbidity and death in children. According to the annual report of the maternal and child health centers for diarrhea (2008), 241 children died from acute diarrhea. The prevalence of pediatric (1-5 years-old) diarrhea in Long District, Luangnamtha Province in 2017 was 38.7%, 2018 was 39.4%, 2019 was 33.25 %. This study had shown the result of the Factors associated with diarrhea in children age 1-5 years-old in Long hospital, Long District, Luangnamtha Province, Lao PDR.

Objective: Factors associated with diarrhea in children age 1-5 years-old in Long District Hospital.

Method: A cross-sectional descriptive study was conducted with a total of 367 cases in Long District Hospital, Luangnamtha Province from June to September 2020. Using questionnaire.

Results: A total 367 cases were studied in long district hospital. Most cases were ethnic tribe called Akhar tribe (60.2%), more than a half of cases didn't know Lao language (73%), did not use toilet (25.3%), did not wash hand after used toilet (80.7%), used water from the mountain (90%), less information about diarrhea (27.2%)
Conclusion: The Factors associated with diarrhea in children age 1-5 years-old was poor hygiene.

Title: Quantity and quality of breast milk of Laotian lactating women

Author: Kitti Sranacharoenpong (Presenter), Institute of Nutrition, Mahidol University, Thailand
Co-authors: Punnee Ponprachanuvut, Sengchan Kounnavong, Nuttarat Srisangwan, Arisa Keeratichamroen, Kantanit Chammari, Piyanit Churak, Panrawee Praditsorn

Background: Lao PDR shows that there are limitations in the research on food consumption patterns of Lao lactating women. It is an urgent need to understand about the situation of lactating women affecting to qualitative and quantitative of breast milk and further impacts of their infants.

Study Design & Methods: The research was a cross-section study. We collected breast milk with the Laotian lactating women in rural areas in wet and dry seasons in Luang Pra Bang. The data collection consisted of 2 parts; quantity of breast milk using stable isotope technique, based on IAEA method and quality of breast milk to analyze nutrients relating to child growth. The semi-food frequency questionnaire was developed based on the Lao consumption data, also the survey in August, 2019. All questionnaire will be tested content validity index by 3 experts.

Results: The preliminary data showed the results in dry season. The total lactating women were 34 cases. Seventy percent (n=24) of lactating women were exclusive breastfeeding. The average quantity of daily breast milk intake was 730 g (SD=136 g). The average nutrient contents of hind-milk per 100 mL were 74 Kcal for total energy, 1.3 g for protein, 4.0 g for fat, 8.4 g for carbohydrate, 57.9 mcg for vitamin A, 31.9 mg for calcium, and 24.1 mg for phosphorus. Food pattern of lactating women consumed glutinous rice mainly (750g per day). Some ate instant noodles 2 packs per day in average. The using of cooking oil was limit to 2-3 teaspoons per day. Food taboos were still restriction for lactating women.

Conclusions: These results are useful for Lao PDR to develop the policy and guideline promoting food based approach for the lactating women.

Wednesday 16 December 2020

S36: Emergency Operation Center and function in the national response to COVID-19 (Thai/Eng session)

10.15-11.45hr

Room E

Chairperson: Pornpitak Panlar

Invited speakers:

1. Emergency Operation Center and function in the national response to COVID-19 (no abstract)
   Jessada Thanakitjaroenkul
   Ministry of Public Health, Thailand

2. National response plan and measure for COVID-19 (no abstract)
   Darin Areechokchai
   Ministry of Public Health, Thailand

3. Logistics and stockpile management in comprehensive COVID-19 program (no abstract)
   Apichai Pojlertaroon
   Ministry of Public Health, Thailand

4. Digital engagement to caption and control COVID-19 (no abstract)
   Yongjua Laosiritaworn
   Ministry of Public Health, Thailand

5. Legal aspect in the management of national COVID-19 response (no abstract)
   Suthinee Manosamoot
   Ministry of Public Health, Thailand

6. Mitigation program for affected COVID-19 (no abstract)
   Chakrarat Pittayawonganon
   Ministry of Public Health, Thailand

Wednesday 16 December 2020

Free paper IV: Zoonosis

11.50-12.50hr

Room A

Chairpersons:

1. Aongart Mahittikorn
2. Supaluk Popruk

Speakers:

1. The potential involvement of bats (Chiroptera) in enzootic transmission of Japanese encephalitis virus in West Kalimantan, Indonesia
   Ajib Diptyanusa
   Universitas Gadjah Mada, School of Medicine, Indonesia

2. Risk factors for zoonotic helminths among domestic animals in Agusan del Sur and Surigao del Norte: implications for public health
   Sheina Macy Manalo
   Department of Veterinary Paraclinical Sciences, College of Veterinary Medicine, University of the Philippines, Philippines

3. Impacts of farming practices on food safety: parasite contamination of vegetable farms
   Constance Aurelle Ramirez
   University of the Philippines Los Banos, Philippines

4. *Paragonimus westermani* infection of freshwater crab *Sundathelphusa philippina* and *melaniid* snails in cadacan river in Irosin, Sorsogon, Philippines
   Jasmin Ayyah Samudio
   Parasitology Research Laboratory, Animal Biology Division, Institute of Biological Sciences, College of Arts and Sciences, University of the Philippines Los Baños, Philipines

5. Incidence and risk factors associated with parasite soil contamination in selected rural communities in Caraga Region, Philippines
   Kim Louisse Patagnan
   UPLB-IBS, Philippines

6. Socio-economic determinants of intestinal helminth infections in selected rural communities of Mindanao, Philippines
   Anna Monica B. Dancel
   Animal Biology Division, Institute of Biological Sciences, University of the Philippines Los Banos, Philippines

7. Remaining pockets of high endemicity of schistosomiasis and and soil-transmitted helminthiasis in selected communities in Agusan del Sur and Surigao del Norte, the Philippines

Vicente Belizario Jr
Department of Parasitology, College of Public Health, University of the Philippines Manila, Philippines

8. ColoSSoS project- Detecting SARS-CoV-2 in Victoria wastewater under the COVID pandemic response
   Aaron Jex
   Walter and Eliza Hall Institute, Australia

Title: The potential involvement of bats (Chiroptera) in enzootic transmission of Japanese encephalitis virus in West Kalimantan, Indonesia

Author: Ajib Diptyanusa (Presenter), Universitas Gadjah Mada, School of Medicine, Indonesia

Background: The West Kalimantan province in Borneo island, Indonesia belongs to endemic area of Japanese encephalitis (JE) that accounts for approximately 80% of total cases yearly. As the presence of both small- and large-scale pig farming is uncommon in West Kalimantan, especially in the residential area of positive cases, another reservoir host might have played a role in the local transmission of JE virus in West Kalimantan, Indonesia. Current study aimed to identify the potential role of bats (Chiroptera) in the local transmission of JE.

Study Design & Methods: The cross sectional study was performed in 3 districts in West Kalimantan, covering 3 different ecosystems: woodland, coastal, and residential areas. Bat collection was performed using mist net and harp net, while mosquito collection was carried out using animal-baited trap and human landing collection. Molecular detection of JEV in bats and vector mosquitoes was performed using RT-PCR.

Results: A total of 80 bat serum samples were tested for JEV, among which 21 samples (26.2%) showed positive results, mainly from *Cynopterus brachyotis* (lesser short-nosed fruit bat) found in proximity of human dwellings. Additionally, 3 out of 103 mosquito pools showed JEV-positive, particularly from pools of *Culex vishnui* and *Cx. tritaeniorhynchus* collected at the same location as JE-positive bats.

Conclusions: Current study results demonstrated the possible role of bats in local transmission of JE in West Kalimantan. More aggressive measures are required in addressing the issue, particularly in initiating JE vaccination campaign and averting disruption of bats' natural habitats by human actions.

Title: Risk factors for zoonotic helminths among domestic animals in Caraga Region, Philippines: implications for public health

Author: Sheina Macy Manalo (Presenter), Department of Veterinary Paraclinical Sciences, College of Veterinary Medicine, University of the Philippines Los Baños, Philippines
Co-authors: Vachel Gay Paller, Martha Betson, Anna Monica Bordado, Billy Divina, Modesto Bandal, Rico Ancog, Vicente Jr. Belizario

Background: Domestic animals are sources of livelihood, food, companionship, and security for humans. However, this close association with animals allows for the transmission of zoonotic helminths that negatively impact human health. In many areas in the Philippines, very little is known about zoonotic parasites in domestic animals.

Study Design & Methods: In this study, fecal samples from 91 dog, 27 cat, 136 pig, 146 water buffalo, and 18 cattle in selected rural communities of two provinces in Caraga Region Mindanao in the Philippines were examined using standard parasitological techniques. Furthermore, 173 animal owners were interviewed regarding animal management practices and awareness of zoonotic helminth exposure. An additional 100 water buffalo owners were included in the survey of management practices.

Results: Sixteen species of zoonotic helminths were identified, with an overall prevalence of 52.8%. Hookworms and *Toxocara spp*. were most prevalent in companion animals while Fasciola spp. and strongyles in farm animals. Several factors such as animal age, sex, location, housing, and feeding practices were identified as significant risk factors for infections.

Conclusions: The high prevalence of zoonotic infections in domestic animals poses health threats to the community. The results highlight the importance of a One Health approach in addressing concerns about helminth zoonoses.

Title: Impacts of farming practices on food safety: parasite contamination of vegetable farms

Author: Constance Aurelle Ramirez (Presenter), University of the Philippines Los Banos, Philippines
Co-author: Vachel Gay Paller

Background: Fresh vegetables are an important part of a healthy diet and can be agent of transmission of intestinal parasites. This study aimed to assess the parasite incidence of contamination of freshly harvested vegetables and its possible source of contamination by assessing the soil and water samples from selected farms in Laguna, Philippines.

Study Design & Methods: A total of 168 vegetable, 55 soil, and 15 water samples collected from four selected farms and a reference farm were processed through various standard parasitological techniques.

Results: Of these, 17.3% of vegetables, 47.3% soil, and 73.3% water samples were found contaminated with parasites. Moreover, leafy vegetables, such as lettuce showed to be more contaminated. Results showed that strongylids/hookworms had the highest recovery from soil (38.2%) and vegetable (13.1%); other parasites were also recovered such as *Toxocara, Ascaris, Trichiuris, Trichostrongylu*s, and *Balantidium*. No helminth parasites were detected from water samples, however, *Cryptosporidium sp.* and *Giardia sp*. were observed in all samples. Remarkably, all parasites recovered in the farms were of animal in origin indicating open defecation of pets and farm animals as source of contamination. Furthermore, results revealed that some farming practices such as the use of animal manure as fertilizers, unhygienic practice of farmers, and sanitation issues were factors that contribute to parasite contamination in the farms.

Conclusions: These findings have implications on food safety that could pose risk to the farmers and consumers. Recommendations were discussed in the study for control and prevention of parasite contamination at the farm level.

Title: *Paragonimus westermani* infection of freshwater crab *Sundathelphusa philippina* and *melaniid* snails in Cadacan River in Irosin, Sorsogon, Philippines

Author: Author: Jasmin Ayyah Samudio (Presenter), Parasitology Research Laboratory, Animal Biology Division, Institute of Biological Sciences, College of Arts and Sciences, University of the Philippines Los Baños, Philipines
Co-author: Vachel Gay Paller

Background: Paragonimiasis, the disease caused by *Paragonimus westermani*, is transmitted primarily by freshwater crabs Sundathelphusa philippina in the Philippines. Human infection has been recorded, but there is a dearth of published information on the extent of infection in animal reservoirs, particularly in crabs and snails.

Study Design & Methods: This study aimed to investigate the infection status and risk factors of *P. westermani* in freshwater crabs and melaniid snails collected along Cadacan River in Irosin, Sorsogon, where human cases of paragonimiasis were previously reported.

Results: A total of 246 freshwater crabs (118 females, 128 males) were dissected, and the gills, muscles, gonads, and viscera were examined for the presence of metacercariae; of which, 41.87% were found infected. The metacercariae were recovered from the gills (100%) and muscle tissues (7.3%) of infected crabs. Male crabs were more likely to be infected (49.22%) than female crabs (33.90%) ($p < 0.05$). Moreover, 70.87% of crabs showed low parasite intensity level at ≤ 30 metacercariae/g tissue. A negative weak correlation was observed between parasite intensity and crab weight and carapace length. Meanwhile, only 12% of the 150 melaniid snails collected were positive with cercariae with *Tarebia granifera* and *Jagora asperata* as the most infected species. Household survey conducted revealed that some knowledge, attitudes, and practices of the locals contribute to the sustained transmission of the parasite in this endemic area

Conclusions: These findings revealed that *P. westermani* is still prevalent among intermediate hosts and that some social and environmental factors contributed to the sustained parasite transmission in this endemic community.

Title: Incidence and risk factors associated with parasite soil contamination in selected rural communities in Caraga Region, the Philippines

Author: Kim Louisse Patagnan (Presenter), UPLB-IBS, Philippines
Co-authors: Vachel Gay Paller, Angelou Marie Aquino, Billy Divina, Jasmine Rennete Jimenez, Martha Betson, Rico Ancog, Vicente, Jr. Belizario

Background: Soil-transmitted helminth (STH) infections remain a major public health concern in the Philippines. AS the name suggests, soil plays a significant role in the transmission of STH eggs. Soils from selected households in Region 13 were examined for parasite contamination.

Study Design & Methods: Soils samples from selected households in Region 13 were examined for parasite contamination. A total of 199 soil samples were processed through a modified sucrose flotation technique.

Results: Out of 199 samples, 83 (44.7%) were contaminated with parasite eggs namely *Ascaris sp*. (29.15%), *Trichuris sp*. (5.02%), *Toxocara sp*. (2.51%), *Capillaria sp*. (2.01%), strongyle/hookworm, and *Schistosoma sp.* (1.51%). Practices such as toilet sharing with neighbors ($p = 0.001$), cat's waste disposal ($p = 0.004$), and deworming of cats ($p = 0.003$) showed significant relationships with parasite soil contamination. The QGIS map also demonstrated the distribution of parasite soil contamination.

Conclusions: Practices such as toilet sharing with neighbors, animal waste disposal, and deworming practices showed significant associations with parasite soil contamination. The QGIS maps also demonstrated the distribution of parasite soil contamination.

Title: Socio-economic determinants of intestinal helminth infections in selected rural communities of Mindanao, Philippines

Author: Anna Monica B. Dancel (Presenter), Animal Biology Division, Institute of Biological Sciences, University of the Philippines Los Banos, Philippines
Co-authors: Vachel Gay Paller, Rico Ancog, Ma. Christina Corales, Jasmine Renette Jimenez, Billy Divina, Martha Betson, Vicente Belizario Jr.

Background: Emergence of intestinal helminth infection is linked to an array of socio-economic factors that manifests in the practices, exposure, and behavior of individuals toward the disease. Despite intervention efforts, these infections still prevail in poor communities, particularly in rural areas.

Study Design & Methods: This study sought to determine the status of intestinal helminth infections and its determinants in selected rural communities in Caraga Region, the Philippines. A total of 199 households were considered in the study covering four municipalities from two provinces.

Results: A relatively low socio-economic status was observed in all sites, with farming as the main livelihood source. Overall, similar patterns on access to resources, policies, and sanitation and hygiene practices were observed across the sites. The communities rely on local government regulations and oversight for guidance and protection. However, there has been complacency which could be due to lack of technological know-how for control strategies. This is also further aggravated by the complacency in standards and policies.

Conclusions: This study provides science-based evidence on the need to address issues that pose health threats to poor communities. Action involves reinforcement of the WASHED program and collaboration of local governments with relevant stakeholders and partners from the agriculture, education, and health sectors on education, training, monitoring, and treatment to help foster a more urgent, collaborative and action-oriented approach to control helminth infections in poor communities.

Title: Low schistosomiasis and moderate soil-transmitted helminthiasis prevalence in selected communities in Caraga Region, the Philippines: A state of controlled morbidity?

Author: Vicente Belizario Jr (Presenter), Department of Parasitology, College of Public Health, University of the Philippines Manila, Philippines
Co-authors: Allen Jethro Alonte, Lynell Alexie Ong, Anna Monica Bordado, Billy Divina, Rico Ancog, Martha Betson, Vachel Gay Paller

Background: Schistosomiasis and soil-transmitted helminthiasis (STH) remain major public health concerns in developing countries. In the Philippines, interventions recommended by the World Health Organization for schistosomiasis and STH control have been implemented through national control programs.

Study Design & Methods: This study aimed to determine the prevalence and intensity of schistosomiasis and STH in selected communities in co-endemic provinces of Agusan del Sur and Surigao del Norte, the Philippines, as part of Newton-funded project title ZooTrIP. Zoonotic Transmission of Intestinal Parasites: Implication for Control and Elimination. Stool samples, collected from 663 participants ages 10 to 60 years old, were processed by Kato-Katz technique and examined microscopically for the presence of intestinal helminth ova.

Results: Low schistosomiasis prevalence (8.3%) as well as moderate prevalence of heavy intensity (HI) schistosomiasis (1.8%), STH (22.8%), and HI STH (4.3%) were observed. After more than a decade of control program implementation, results showed a state of controlled morbidity for schistosomiasis which may be attributed to high mass drug administration (MDA) coverage rates, while STH remains a public health concern due to continuing challenges in water, sanitation, and hygiene (WASH).

Conclusions: Sustaining high MDA coverage rates along with an interdisciplinary approach involving human, animal, and environmental health are needed for transmission interruption of schistosomiasis, while addressing challenges in WASH are warranted to effectively control STH.

Wednesday 16 December 2020

Poster session 3: Malaria

11.50-12.50hr

Room B

1. Field evaluation of automatic new diagnostic CellCheck® in comparison to standard microscopy for detection of malaria from clinical suspected cases in Lampung Province, Indonesia
   Ayleen Kosasih
   University of Indonesia, Indonesia

2. Understanding heterogeneity of malaria infection at the village and household level in two serial cross-sectional surveys in Papua New Guinea
   Desmond Gul
   Burnet Institute, Australia

3. Molecular surveillance of dihydroartemisinin piperaquine resistance markers in Thailand
   Khine Nwe Win
   Mahidol University, Thailand

4. A first molecular evidence of *Plasmodium*-inhibiting *Wolbachia* strain in *Anopheles*
   Kasem Kulkaew
   Faculty of Medicine Siriraj Hospital Mahidol University, Thailand

5. Making malaria notifiable: testing and treating every case to eliminate the disease
   Marie Lamy
   Asia Pacific Leaders Malaria Alliance, Singapore

6. Genetic variations in histidine-rich protein 2 and histidine-rich protein 3 of Myanmar *Plasmodium falciparum* isolates
   Huong Giang Le
   Department of Parasitology and Tropical Medicine, and Institute of Health Sciences, Gyeongsang National University, Korea

7. Genetic polymorphism and natural selection of circumsporozoite surface protein in Vietnam
   Tuan Cuong Vo
   Department of Convergence Medical Science, Gyeongsang National University, Korea

8. Effects of KAE609 and KAF156 on cytoadhesion of *Plasmodium falciparum*
   Srisuda Keayarsa
   Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Thailand

9. Continued improvements in the accuracy of antimalarial drug level measurements: results from 10 years of proficiency testing conducted by WWARN
   Ranitha Vongpromek
   Infectious Diseases Data Observatory (IDDO) & Worldwide Antimalarial Resistance Network (WWARN), Thailand

10. Deforestation and malaria in Lao PDR: spatial epidemiology using earth observation satellite data
    Emilie Louise Akiko Matsumoto-Takahashi
    Department of Tropical Medicine and Malaria, Research Institute, National Center for Global Health and Medicine (NCGM), Tokyo, Japan

Title: Field evaluation of automatic new diagnostic CellCheck® in comparison to standard microscopy for detection of malaria from clinical suspected cases in Lampung Province, Indonesia.

Author: Ayleen Kosasih (Presenter), Faculty of Medicine, University of Indonesia, Indonesia
Co-authors: Ayu Nurdiantika, Endah Setyaningrum, Ayla Karius, Inge Sutanto, Harun Tri Djoko

Background: Direct visual finding of malarial parasites in the blood remains the most relevant detection method. However, microscopic examination with Giemsa staining is subjective and requires relatively long roundabout time. Digitalization of the parasite image or byproduct is developed to overcome this issue. CellsCheck® (Biosynex, France) deploys fluorescence-based principle for automated identification of parasites. This study aims to compare this novel technology with standard microscopy.

Study Design & Methods: Finger-pricked blood samples were collected from clinical suspected patients during September 2019-January 2020 in Lampung province, Indonesia. On-site testing was performed by CellsCheck®, whereas microscopic examination was done independently by expert in Jakarta. Real-Time PCR targeting 18S rRNA was performed for diagnostic verification of the discrepant results.

Results: 293 specimens were collected and examined by CellsCheck® and microscopy. CellsCheck® detected 40 (13.6%) malaria infections, compared to 38 (13.0%) by microscopy. 24 discordant results were found between CellsCheck and microscopy: *P. falciparum* vs. *P. vivax* (n=19), *P. falciparum* vs. negative (n=3), mixed infections vs. *P. vivax* (n=1), negative vs. *P. vivax* (n=1). After PCR verification, sensitivity, specificity, PPV, and NPV for malaria were 97.6%, 100%, 100%, and 99.6%, respectively. In terms of speciation, sensitivity for *P. vivax* was only 42%, but specificity, PPV, and NPV were 100%, 100%, and 92%. Evaluation could not be performed for *P. falciparum* as only one sample was positive.

Conclusions: Further improvement is required for speciation of CellsCheck although its performance to detect malaria positivity is comparable to the standard microscopic examination.

Title: Understanding heterogeneity of malaria infection at the village and household level in two serial cross-sectional surveys in Papua New Guinea

Author: Desmond Gul (Presenter), Burnet Institute, Australia
Co-authors: Elma Nate, Lina Lorry, Christian Koepfli, Alma Auwan, Moses Laman, Leanne Robinson, Daniela Rodriguez-Rodriguez, Stephan Karl, Archie Clements, Freya Fowkes, Javier Rosado, Ivo Mueller, Ingrid Felger, Mary Salib, Manuel Hetzel, Natalie Hofmann

Background: Malaria risk is highly heterogenous and localised hotspots within villages and households may be observed as transmission decreases. Understanding village and household-level spatial heterogeneity of malaria risk can support a transition to spatially targeted interventions in efforts towards malaria elimination.

Study Design & Methods: Data from two cross-sectional prevalence surveys conducted in 2014 and 2016 in two villages - Megiar and Mirap, in PNG were used. A semi-parametric regression model – generalised additive modelling, was used to characterise spatial heterogeneity of malaria risk and to investigate the contribution of individual and household-level risk factors.

Results: Hotspots for *P. falciparum* were more commonly observed than for *P. vivax*. The prevalence of both *P. falciparum* and *P. vivax* increased between 2014 and 2016, with hotspots more visible in 2016. Age was a consistent risk factor with *P. falciparum* peaking in 15 year old adolescents and *P. vivax* in 10 year old children. In Megiar, the observed spatial risk could be partially explained by household risk factors, in particular households that use outdoor surface water as their water source were at greater risk, likely through increased exposure to outdoor transmission. and households with thatched grass roofs were more protective than those with zinc roofs. In Mirap, increased spatial risk was correlated with proximity to densely vegetated areas of the village.

Conclusions: This analysis revealed within-village hotspots of malaria risk varied by *Plasmodium* species, across time and setting. Spatial and household risk factors were identified and may inform the development of tailored approaches to accelerate malaria control.

Title: Molecular surveillance of dihydroartemisinin-piperaquine resistance markers in Thailand

Author: Khine Nwe Win (Presenter), Mahidol University, Thailand
Co-author: Jetsumon Prachumsri, Wang Nguitragool

Background: Dihydroartemisinin-piperaquine (DHA-PPQ) is the current first-line treatment for *Plasmodium falciparum* malaria in Thailand. Declining efficacies of artemisinin-based combination therapies against *P. falciparum* have been widely documented in the Greater Mekong sub-region. Thus, monitoring of the resistance condition is important in preservation of DHA-PPQ efficacies. Our aim is to track the presence of *P. falciparum* DHA-PPQ resistance markers in northwestern Thailand.

Study Design & Methods: DNA was extracted from *P. falciparum*-infected archived blood samples from Tak province in 2013-2020, and subjected to molecular analysis to determine single nucleotide polymorphisms (SNP) on Kelch13 for artemisinin resistance and SNPs on Pfcrt gene or copy numbers of Plasmepsin-2 gene for piperaquine resistance. Pf3D7 was used as the reference strain.

Results: Preliminary results showed that approximately half of the samples has Kelch13 mutations. The most common SNP was G533S which has never been reported in Thailand. Other known resistance-associated SNPs including C580Y and G538V were also observed. Pfcrt SNPs and Plasmepsin-2 copy numbers are being analysed and the results will be presented.

Conclusions: A new SNP in Kelch13, G533S, was found in Tak province. Given the location of the study site and the timing of its emergence in 2014-2015, this finding is in good agreement with the presence of this SNP on China-Myanmar border around the same time (Zhang, et al. 2019). Because parasites carrying this mutation have recently been shown to have a significantly higher ring-stage survival than the wild-type (Zhang, et al. 2019), continued monitoring of Kelch13 markers and drug efficacy in northwestern Thailand will be important in the future.

Title: A first molecular evidence of *Plasmodium*-inhibiting *Wolbachia* strain in *Anopheles*

Author: Kasem Kulkeaw (Presenter), Faculty of Medicine Siriraj Hospital Mahidol University, Thailand
Co-authors: Nongnat Tongkrajang, Pichet Ruenchit, Chatchai Tananchai, Theeraphap Chareonviriyaphap

Background: 2222 Wolbachia, obligate intracellular bacteria, infect the majority of arthropods, including many mosquito species of medical importance. Some *Wolbachia* strains interfere with the development of *Plasmodium* parasites in female *Anopheles*, a major vector of malaria. The use of *Wolbachia* as a means to block malaria transmission is an emerging vector control strategy in highly endemic areas. Hence, identification of native *Wolbachia* strains in areas where malaria transmission is low may uncover a particular *Wolbachia* strain capable of *Plasmodium* interference. This study aims to identify native *Wolbachia* strains in female *Anopheles spp*. that are predominant in a low-malaria transmission area in mainland Southeast Asia.

Study Design & Methods: Following a two-year survey of malaria vectors in Umphang Valley of Tak Province, Thailand, DNA extracts of female *An. minimus*, *An. peditaeniatus*, and *An. maculatus* were subjected to amplification of the conserved region of the 16S rRNA-encoding gene. The DNA sequences of the amplicons were phylogenetically compared with those of known *Wolbachia* strains.

Results: Among three *Anopheles spp.,* amplification was detected in only the DNA samples from *An. minimus*. The DNA sequencing of amplicons revealed 100% similarity to *Wolbachia pipientis*, confirming the specificity of amplification. The *Wolbachia*-detected *An. minimus* samples were devoid of *Plasmodium* 18S rRNA amplification. The phylogenetic trees indicate a close relationship with *Wolbachia* strains in subgroup B.

Conclusions: To the best of our knowledge, the data presented herein provide the first molecular evidence of a *Wolbachia* strain in *An. minimus*, hereinafter named wAnmi, in a low-malaria transmission area in the Umphang Valley of western Thailand. Further biological characterization is required to examine its potential for malaria transmission control in the field.

Title: Making malaria notifiable: testing and treating every case to eliminate the disease

Author: Marie Lamy (Presenter), Asia Pacific Leaders Malaria Alliance, Singapore
Co-authors: Amita Chebbi, Gao Qi, Rittika Datta, Phone Si Hein, Chris Erwin G Mercado, Steve Mellor, Geoff Clark

Background: Resilient and responsive health systems are key to effectively preventing, detecting and responding to global health threats. This has been further demonstrated by the global efforts to tackle the COVID-19 pandemic and ongoing efforts to control and eliminate long existing infectious diseases, such as malaria. The 2018 Declaration of Astana emphasized the importance of improving access to primary health care by building an integrated health system where all sectors collaborate to address disease threats. The International Health Regulations (IHR) of 2005 provide a framework to promote global health security and limit the spread of health threats.

Study Design & Methods: The IHR stress the importance of notifying government authorities and the international community of all events that constitute a public health emergency of international concern. Using malaria in Asia Pacific as a case in point, we explored different policy considerations involved in making malaria a notifiable disease, with reference to specific experiences from China, Lao PDR, Nepal, the Philippines, and Vanuatu.

Results: The different policy considerations in making malaria a notifiable disease include the timing of legislative changes at different stages of elimination, investing in adequate infrastructure for a robust surveillance system that can support targeted interventions, and the importance of involving all sectors in the delivery of malaria services to detect, report and respond to every case.

Conclusions: An early warning function is a fundamental component of national, regional and global health security.

Title: Genetic variations in histidine-rich protein 2 and histidine-rich protein 3 of Myanmar *Plasmodium falciparum* isolates

Author: Hương Giang Lê (Presenter), Department of Parasitology and Tropical Medicine, and Institute of Health Sciences, Gyeongsang National University, Korea
Co-authors: Jung-Mi Kang, Jinyoung Lee, Khin Lin, Tong-Soo Kim, Won Gi Yoo, Moe Kyaw Myint, Byoung-Kuk Na

Background: Concern has been raised in recent years that deletion of *Plasmodium falciparum* histidine-rich protein 2 (pfhrp2) could affect the accuracy of PfHRP2-based rapid diagnostic tests (RDTs). In addition, genetic variation in pfhrp2 might influence the accuracy and sensitivity of RDTs. Here, the genetic variation in pfhrp2 and pfhrp3 in of Myanmar *Plasmodium falciparum* isolates was analyzed.

Study Design & Methods: Blood samples collected from *P. falciparum*-infected patients in Upper Myanmar in 2015 used in this study. The pfhrp2 and pfhrp3 were amplified by nested polymerase chain reaction, cloned, and sequenced. Genetic variation in Myanmar pfhrp2 and pfhrp3 was analyzed using the DNASTAR program. Comparative analysis of Myanmar and global pfhrp2 and pfhrp3 isolates was also performed.

Results: Myanmar pfhrp2 and pfhrp3 showed high levels of genetic variation with different arrangements of distinct repeat types. Novel amino acid changes were also found in Myanmar pfhrp2 and pfhrp3, but their frequencies were very low. Similar structural organization was shared by Myanmar and global pfhrp2 and pfhrp3, but differences in frequencies of repeat types and lengths were also observed between and among global isolates.

Conclusions: Length polymorphisms and amino acid substitutions generated extensive genetic variation in Myanmar pfhrp2 and pfhrp3. Comparative analysis revealed that global pfhrp2 and pfhrp3 share similar structural features, as well as extensive length polymorphisms and distinct organizations of repeat types. These results provide a better understanding of the genetic structure of pfhrp2 and pfhrp3 in global *P. falciparum* populations and suggest useful information to develop RDTs with improved quality.

Title: Genetic polymorphism and natural selection of circumsporozoite surface protein in Vietnam

Author: Tuấn Cường Võ (Presenter), Department of Convergence Medical Science, Gyeongsang National University, Korea
Co-authors: Haung Naw, Hương Giang Lê, Jung-Mi Kang, Hồng Quang Huỳnh, Byoung-Kuk Na

Background: *Plasmodium vivax* circumsporozoite surface protein (PvCSP) has been recognized as one of the leading vaccine candidates. However, the genetic diversity of pvcsp in the natural population is a major concern in the development of a PvCSP-based vaccine
.
Study Design & Methods: Sixty nine blood samples collected from *P. vivax*-infected Vietnamese patients were used. The pvcsp gene was amplified by polymerase chain reaction and sequenced. Polymorphic characteristics and natural selection in the Vietnam pvcsp population were analyzed. Polymorphic patterns of the global pvcsp were also comparatively investigated.

Results: A total of 117 pvcsp sequences were obtained. Vietnam pvcsp sequences were divided into two allele types, VK210 (n = 38) and VK247 (n = 79). The N-terminal and C-terminal regions of Vietnam pvcsp were under natural selection and displayed limited genetic variations. The N-terminal regions in both VK210 and VK247 alleles were highly conserved. The C-terminal region showed different patterns of insertions and repeat motifs in both allele types. Meanwhile, the central repeat region (CRR) was highly polymorphic with 25 and 44 haplotypes for VK210 and VK247, respectively. Genetic diversity in the CRR was mainly caused by the different numbers, types and combinations of peptide repeat motifs. Comparative analysis of the global pvcsp population suggested the complicated genetic nature of pvcsp in the global population.

Conclusions: Non-negligible genetic diversity was found in the Vietnam pvcsp population. These results widened understanding on the genetic makeup of pvcsp in the global *P. vivax* population and provided valuable information for development of vaccines based on PvCSP.

Title: Effects of KAE609 and KAF156 on Cytoadhesion of *Plasmodium falciparum*

Author: Srisuda Keayarsa (Presenter), Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Co-authors: Yutatirat Singhaboot, Arjen Dondorp, Nattaporn Piaraksa, Kesinee Chotivanich, Nicholas White

Background: The sequestration of trophozoite-infected red blood cells (IRBCs) in the microvasculature is central to the pathophysiology of severe and cerebral malaria. IRBC cytoadhesion is mediated mainly by *P. falciparum*- Erythrocyte Membrane Protein-1 (PfEMP-1) expressed on the surface of the IRBCs adhering to vascular endothelial cell receptors, including CD36, ICAM-1. In the context of increasing resistance to artemisinin and partner drugs in artemisinin-based combination therapy new antimalarial compounds have been developed, including the spiroindolone KAE609 (cipargamin) and the imidazolopiperazine KAF156 (ganaplacide).

Study Design & Methods: In this study, we assessed the effects of these two new antimalarial compounds on the cytoadhesion of *P.falciparum*-IRBCs to human dermal microvascular endothelial cells (HDMVECs). Using a standard static assay *in vitro* cytoadhesion was assessed after parasite exposure to KAE609, KAF156, artesunate, quinine or no drug. The numbers of adherent IRBCs before and after drug exposure were counted per 1000 HDVMECs and expressed as proportion of inhibition. 50% inhibition concentrations (IC50) were calculated from the response curve using ICEstimater V1.2.

Results: For the control (no drug), the mean (SD) of IRBCs adherent to 1000 HDVMECs was 1844.8 (±372.3) IRBCs/1000 HDMVECs. The mean (SD) of 50% inhibition concentration was 6.7 (±1.1) ng/mL for artesunate, 6.9 (±1.5) ng/mL for KAE609, and 10.7 (±3.5) ng/mL for KAF156. Quinine (up to 500 ng/ml) did not inhibit cytoadherence of *P. falciparum*.

Conclusions: Both cipargamin and ganaplacide are potent inhibitors of ring-stage *P.falciparum* development and thereby prevent cytoadhesion. This supports the development of these drugs as new treatments for uncomplicated and severe *falciparum* malaria.

Title: Continued improvements in the accuracy of antimalarial drug level measurements: results from 10 years of proficiency testing conducted by WWARN

Author: Mehul Dhorda (Presenter), Infectious Diseases Data Observatory (IDDO) WorldWide Antimalarial Resistance Network (WWARN), Thailand
Co-authors: Christiaan Lourens, Pak Sadomthian, Teeradet Khomvarn, Philippe Guérin, Joel Tarning, Ranitha Vongpromek

Background: Accurate drug level measurements are crucial for the optimization of antimalarials dosing and confirmation of emerging resistance. To demonstrate accuracy and comparability of such measurements between laboratories and over time, laboratory performance must be independently verified. We present results from 9 rounds of proficiency testing conducted over 10 years by the ISO17043-accredited WWARN Proficiency Testing (WWARN-PT) scheme for antimalarial drug level measurements.

Study Design & Methods: Each round of PT consisted of 2 cycles; laboratories received 12 human plasma samples per cycle, spiked with varying amounts of antimalarials, and measured levels of each drug using in-house validated methods. Their performance was evaluated by calculating and grading the Z-score, where |Z-score|<2 was considered 'satisfactory', 2≤|Z-score|<3 'questionable' and |Z-score|≥3 'unsatisfactory'. Z-scores were transformed to their natural logarithms to obtain a normal distribution and subsequently fitted with a log-linear model for analysis.

Results: From 2010-2019, 11 participating laboratories reported 6,315 results for 14 antimalarial drugs. Z-scores ranged from <0.001 to 210.72 of which 93.2% were graded 'satisfactory', 3.2% 'questionable' and 3.6% 'unsatisfactory'. In 7 laboratories which participated in ≥3 rounds of PT, the proportion of Z-scores <1 increased from 50.3% to 85.5% between the first and last year of participation. Ln(Z-scores) decreased in 5/7 of these laboratories with the reduction being statistically significant for 2 laboratories. The lowest mean Z-score and the highest proportion of satisfactory results were attained after a median of 6 rounds (range: 2-7) and 7 rounds (range: 1-8) of PT, respectively.

Conclusions: Laboratories participating in the WWARN-PT scheme showed sustained improvements in the accuracy of antimalarial drug level measurements. Participating in the WWARN-PT confirmed and/or helped to enhance the accuracy of participants' measurements, thus increasing the value and reliability of their results generated to support improvements in antimalarial treatments.

Title: Deforestation and malaria in Lao PDR: spatial epidemiology using earth observation satellite data

Author: Emilie Louise Akiko Matsumoto-Takahashi (Presenter), Department of Tropical Medicine and Malaria, Research Institute, National Center for Global Health and Medicine (NCGM), Tokyo, Japan
Co-authors: Moritoshi Iwagami, Kei Oyoshi, Yoshinobu Sasaki, Shigeyuki Kano

Background: Deforestation is considered to influence malaria incidence, as it affects the habitat of *Anopheles* mosquitoes. The aim of the present study is to analyze the impact of deforestation on the prevalence of malaria using environmental factors acquired by earth observation satellites (EOS).

Study Design & Methods: Annual Parasite Indices (API: number of patients per 1,000 population) were calculated from 2002 to 2015 using data obtained from the Ministry of Health, Lao PDR. Such EOS data as forested land area, ground surface temperature, precipitation, etc. were obtained from Japan Aerospace Exploration Agency (JAXA). Structured equation modeling (SEM) was conducted to determine the association between API and EOS data.

Results: From 2002 to 2015, the average ground surface temperature continued to rise every year, and forested land decreased year by year. The SEM identified 2 significant factors independently associated with the API, namely area and the proportion of forested land. Specifically, most malaria cases occurred in the southern regions of Lao PDR, and the API decreased as the proportion of the forested land decreased ($p<0.01$).

Conclusions: As the main vector in Lao PDR, *Anopheles dirus*, is the forest-living mosquito, the forested land is expected to play an important role in malaria incidence in the country. Moreover, deforested areas are being transformed into rubber plantation which will increase again the vector population and vector/human contact as well. It is important to grasp these areas using EOS data to monitor development and environmental factors which could hinder elimination of malaria.

Wednesday 16 December 2020

Poster session 4: Vector borne diseases

11.50-12.50hr

Room C

1. Causal relationship model of Zika prevention behavior among women of reproductive age in upper central region, Thailand
   Sawanya Siriphakhamongkhon
   Office of Disease Prevention and Control 3, Nakhon Sawan Province, Department of Disease Control, Thailand

2. Anti-dengue activity of *Dendrocalamus sericeus* ethanolic crude extract
   Jundee Rabablert
   Silpakorn University, Thailand

3. Coverage and utilization of bed nets among population at risk of malaria living along Thai-Myanmar border in Tak Province, Thailand
   Kasama Pooseesod
   Faculty of Tropical Medicine, Mahidol University, Thailand

4. Village-scale analysis of malaria dynamics in a malaria elimination program: identification of factors associated to local heterogeneity
   Eva Legendre
   Aix Marseille Univ, IRD, INSERM, SESSTIM, Marseille, France

5. Study on diversity and habitat preferences of Phlebotomine sand flies in Cambodia Nin Noch
   U.S. Naval Medical Research Unit TWO Cambodia

6. Overall prevalence and distribution of knockdown resistance (kdr) mutations in a natural population of *Aedes aegypti* in Mandalay region, Myanmar
   Haung Naw
   Gyeongsang National University College of Medicine. South Korea

7. A multiplex PCR based on mitochondrial COI sequence for identification three groups of *Anopheles subpictus* complex in Thailand
   Parinya Wilai
   Chiang Mai University, Thailand

8. Towards the development of bio-acoustic sensors for adult mosquito vector counts in Thailand: analysis of mosquito wingbeat audio signals
   Myat Su Yin
   Faculty of ICT, Mahidol University, Thailand

9. Health literacy and ika virus disease among the reproductive age women in upper central region of Thailand
   Samran Siriphakhamongkhon

Office of Disease Prevention and Control 3, Nakhon Sawan Province. Department of Disease Control Thailand

10. Point mutations in the voltage-gated sodium channel gene of pyrethroid -resistant *Aedes aegypti* mosquitoes and their insecticide susceptibility
    Jakkrawarn Chompoosri
    National Institute of Health, Department of Medical Sciences, Thailand

11. Chemical composition and mosquitocidal activity of *Cymbopogon citratus* essential oil against *Aedes aegypti* from dengue and chikungunya risk areas
    Chayada Khamsawas
    National Institute of Health, Department of Medical Sciences, Thailand

Title: Causal relationship model of Zika prevention behavior

Author: Sawanya Siriphakhamongkhon (Presenter), Office of Disease Prevention and Control 3, Nakhon Sawan Province. Department of Disease Control, Thailand
Co-authors: Samran Siriphakhamongkhon, Jirawan Thaweekhatgorn

Background: Due to contract the Zika virus during pregnancy, a baby has an increased risk of being born with microcephaly. The aim of this study was to analyze a causal relationship model of Zika prevention behaviors among women of reproductive age.

Study Design & Methods: The cross - sectional analytic study selected 778 female aged 18 - 49 years by simple random sampling. The data were collected by questionnaires. The latent variables consisted of 1) Economic and Social Status 2) Environmental Support and Perception of Information 3) Health Literacy and dependent variable was the Zika Prevention Behavior.

Results: The research findings can be summarized as follows: The model is congruent with the evidence-based practice. The consideration was based on chi-square=26.31, $\varkappa 2/df = 1.05$, p-value=0.39. Thus, it is evident that the chi-square value varied from zero with no statistical significance (GFI=0.99, AGFI=0.98, RMR = 0.11, RMSEA = 0.01). The weighted values of the factors were in the form of standard scores for the observed variables for the model for Zika Prevention Behavior. In total, the positive values ranged from 0.18 to 0.98 ($p<0.05$). There were variables placed in order from highest to lowest weighted values, Economic and Social Status (direct & indirect influenced=0.38, 0.89), Environmental Support and Perception of Information (direct & indirect influenced=0.12, 0.79) and Health Literacy (0.04). All variables could be used to explain on this model 22.0 percent.

Conclusions: It reveals that could be addressed via the results from this study that might improve prevention practices to help women protect themselves from Zika virus.

Title: Anti-dengue activity of *Dendrocalamus sericeus* ethanolic crude extract

Author: Author: Jundee Rabablert (Presenter), Silpakorn University, Thailand

Background: Dengue virus serotype 2 (DV2), genus Flavivirus, Family Flaviviridae causes dengue hemorrhagic fever/dengue shock syndrome. Dendrocalamus asper had antibacterial activity against E. coli strains, which cause diarrhea in poultry, piglets and humans. Pyroligneous acid from bamboo has antiviral activity against encephalomyocarditis virus (EMCV) which causes encephalomyocarditis. Up to date, there is still no vaccine and antiviral drugs.

Study Design & Methods: This study investigates the antiviral activity of Dendrocalamus sericeus
aqueous extract and D. sericeus ethanolic extract in DV2-infected Vero cells. MTT [3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide] assay was carried out to determine the maximum non-toxic dose (MNTD) of the aqueous and ethanolic crude extracts, followed by the anti-dengue activity of both extracts against DV2 by means of plaque assay at various times (pre-, simultaneous, post-treatment).

Results: The MNTD values of aqueous and ethanolic crude extract on Vero cells were 28.5µg/ml. Plaque assay revealed the MNTD of D. sericeus ethanolic extract inhibited DV2 100% (pre-treatment), 100% (simultaneous treatment), 58% (post-treatment). Conversely, D. sericeus aqueous extract had no anti-dengue activity.

Conclusions: It was concluded that D. sericeus ethanolic extract inhibited dengue entry and dengue replication directly.

Title: Coverage and utilization of bed nets among population at risk of malaria living along Thai-Myanmar border in Tak Province, Thailand

Author: Kasama Pooseesod (Presenter), Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Suparat Phuanukoonnon, Saranath Lawpoolsri Niyom, Pratap Singhasivanon, Nattanee Meemon, Jetsumon Sattabongkot Prachumsri, Liwang Cui

Background: Malaria is still endemic in some parts of Thailand. Increased coverage and utilization of bed net, especially insecticide-treated net (ITN) or long-lasting insecticidal net (LLIN) was a key national malaria control program. Bed net ownership and utilization is necessary information for planning effective malaria control program; however, this information has not been available in particular to the population at risk of malaria living along Thai-Myanmar border in Tak province.

Study Design & Methods: The cross-sectional study was conducted using questionnaire and bed net inspection. The study setting was in ICEMR villages. A generalize linear model (GLM) was performed to explore the sociodemographic factors associated with bed net utilization.

Results: The survey covered 331 households from 5 hamlets (subsets of 2 villages). Almost (98.5%) households had at least one bed net per household and, 74.3% had at least one ITN/LLIN. However, only 30.8% of households had reached standard policy as one ITN/ LLINs per two persons. Most of residents used bed net (92.1% used last night and 80.9% used every day), of those using bed net, however, 61.9% used ITNs or LLINs last night and 53.1% used every day. Nonetheless, the usage rates of bed nets (any type) last night were high, among children, and pregnant women (95.3% and 90.0%, respectively). Bed net was rarely used when staying overnight in the forest or the farm plots. The other reasons for not sleeping under bed net every day were dissatisfaction toward quality of free bed net (unsuitable size and rough texture of material), and insufficient number of bed net to cover all sleeping spaces.

Conclusions: The coverage and usage rates of bed nets were high, however, only one third reached the standard per policy. Overnight in the forest or the farm plots, dissatisfactory of quality of free bed net, and insufficient bed net were factors influencing everyday use of bed net. Maintaining high coverage and utility rate of bed nets should be a priority for this high-risk population.

Title: Village-scale analysis of malaria dynamics in a malaria elimination program: identification of factors associated to local heterogeneity

Author: Eva Legendre (Presenter), Aix Marseille Univ, IRD, INSERM, SESSTIM, Marseille, France
Co-authors: Sokhna Dieng, Laurent Lehot, Aung Myint Thu, Florian Girond, Gilles Delmas, Jade D Rae, Vincent Herbreteau, Jean Gaudart, Jordi Landier, François Nosten

Background: The Malaria Elimination Task Force (METF) was launched in 2014 in Karen/Kayin state, Myanmar to reduce *P. falciparum (PF*) transmission before artemisin resistance could spread beyond the Greater Mekong Subregion. This program relies on early diagnostic and treatment at community-based Malaria Posts (MPs) and targeted mass drug administration on high prevalence villages. Our objective was to identify the different local PF dynamics and associated factors at village-scale.

Study Design & Methods: From May 2014 to February 2020, 1,205 malaria posts were set up and reported weekly malaria incident cases. A PAM (Partitioning Around Medoids) clustering associated with dynamic time warping metric is used to separate villages into groups sharing similar malaria dynamics (seasonality, peaks of incidence…). Classification and regression tree methods identified factors associated with each profile.

Results: Respecting functional frame, *PF* incident case series from 657 villages were transformed into functional data and classified into 8 incidence-dynamic profiles. Two low incidence profiles corresponded to villages with only residual malaria transmission or sporadic cases. Four medium incidence profiles corresponded to 56 villages and displayed rainy season-, cold season-, or outbreak-related peaks. Two high incidence profiles corresponded to 9 persistent foci of high transmission. Environmental factors (landscape) and occurrence of mass interventions were associated to specific profiles.

Conclusions: This study, by modelling simultaneously numerous longitudinal village data as functions, highlights the local heterogeneity of dynamics and contribute to the identification of conditions favourable to persistence or resurgence of malaria transmission.

Title: Study on diversity and habitat preferences of Phlebotomine sand flies in Cambodia

Author: Nin Noch (Presenter), U.S. Naval Medical Resarch Unit TWO, Cambodia
Co-authors: Boren Huot, Didot Budi Prasetyo, Jodi M. Fiorenzano, Sochantha Tho, Sokly Mom, Sokny Mao

Background: Phlebotomine sand flies are hematophagous insects with the potential to transmit Leishmania parasites and pathogenic Phleboviruses. There is limited information available regarding Phlebotomine sand fly diversity or on their associated pathogens in Cambodia. Historically, only 10 Phlebotomine species have previously been recorded in Cambodia, three species of Phlebotomous and seven species of Sergentomyia. This study aimed to update the distribution record, measure diversity, habitats preferences, and prevalence of Leishmania parasite in Phlebotomine sand flies collected across ten provinces of Cambodia.

Study Design & Methods: Sand flies were collected using CO2-baited CDC light traps deployed in a variety of habitats from 6:00 PM to 6:00 AM. Head and posterior abdomen of the specimens were separated and slide-mounted in Berlese fluid for morphological identification, while the thoraxes were stored at -80° C for pathogen screening.

Results: A total of 6,505 sand flies were collected; with the majority (45.9%) collected from caves. At least 1 species from genus *Chinius*, 9 species of *Phlebotomus*, and 17 species of *Sergentomyia* were morphologically identified, including 13 new distribution records. Both *Phlebotomus* and Sergentomyia were abundant in caves compared to other habitats. Pathogen screening is still underway, with no specimens currently positive for *Leishmania* parasite.

Conclusions: The findings suggest there is much to be learned about sand fly fauna of Cambodia and the potential health risks they pose due to their associated pathogens.

Title: Overall prevalence and distribution of knockdown resistance (kdr) mutations in a natural population of *Aedes aegypti* in Mandalay region, Myanmar

Author: Haung Naw (Presenter), Department of Convergence Medical Science, Gyeongsang National University College of Medicine, Korea
Co-authors: Moe Kyaw Myint, Jung-Mi Kang, Yi Yi Mya, Tuấn Cường Võ, Hương Giang Lê, Mya Nilar Chaw Su, Tong-Soo Kim, Jinyoung Lee, Byoung-Kuk Na

Background: Knockdown resistance (kdr) mutations in voltage-gated sodium channel (VGSC) of the mosquitoes confer resistance to insecticides. Although insecticide resistance has been suspected to be widespread in the natural population of *Aedes aegypti* in Myanmar, only limited information is currently available.

Study Design & Methods: A total of 1,040 *A. aegypti* mosquitoes were collected in four townships, Aung Myae Thar San, Chanmya Thar Se, Amarapura, and Pyaw Bwe, Mandalay region, Myanmar during 2016 to 2017. Genomic DNA was extracted from the mosquitoes and the segment 6 region flanking domains II and III of VGSC were amplified by polymerase chain reaction and sequenced.

Results: Sequence analysis of VGSC in *A. aegypti* of Myanmar revealed amino acid mutations at 13 and 11 positions in domains II and III of VGSC, respectively. High frequencies of S989P (68.6%), V1016G (73.5%), and F1534C (40.1%) were found in domains II and III. T1520I was also found, but the frequency was low (8.1%). The frequency of S989P/V1016G was high (55.0%), and the frequencies of V1016G/F1534C and S989P/V1016G/F1534C were also high at 30.1% and 23.5%, respectively. Novel mutations in domain II (L963Q, M976I, V977A, M994T, L995F, V996M/A, D998N, V999A, N1013D, and F1020S) and domain III (K1514R, Y1523H, V1529A, F1534L, F1537S, V1546A, F1551S, G1581D, and K1584R) were also identified.

Conclusions: These results suggest that high frequencies of kdr mutations are identified in Myanmar *A. aegypti* population, indicating a high level of insecticide resistance. Current insecticide application program in Myanmar should be carefully reconsidered to develop alternative controlling methods for *A. aegypti* population.

Title: A multiplex PCR based on mitochondrial COI sequence for identification three groups of *Anopheles subpictus* complex in Thailand

Author: Parinya Wilai (Presenter), Center of Insect Vector Study, Department of Parasitology, Faculty of Medicine, Chiang Mai University, Thailand
Co-authors: Thanari Phanitchakun, Anuluck Junkum, Pradya Somboon, Jassada Saingamsook, Atiporn Saeung

Background: Knowledge on the *Anopheles subpictus* complex is not completely known. Our recent study revealed that *An. subpictus* in Thailand is distinct from those reported as species A, B, C and D in India and Sri Lanka. In Thailand, three distinct groups based on COI gene have been detected, but their ITS2 sequences were similar. As recently diverged species may show little or no divergence at this marker, more information regarding the three groups is necessary.

Study Design & Methods: In this study, a multiplex PCR was designed to differentiate the three groups of *An. subpictus* in Thailand.

Results: The assay provided products of 627 bp, 357 bp and 187 bp for groups 1, 2 and 3, respectively. The results from the multiplex PCR were in agreement with DNA sequencing.

Conclusions: Since this method is simple, fast, cheap and reliable, it will be useful for studying this mosquito complex in the future.

Title: Towards the development of bio-acoustic sensors for adult mosquito vector counts in Thailand: analysis of mosquito wingbeat audio signals

Author: Myat Su Yin (Presenter), Faculty of ICT, Mahidol University, Thailand
Co-authors: Peter Haddawy, Chaitawat Sa-ngamuang, Tup Kongthaworn, Patchara Sriwichai, Borvorntat Nirandmongkol, Chanaporn Chaisumritchoke, Patiwat Sa-angchai

Background: Adult mosquito vector abundance is one of important parameters to evaluate the risk of transmission in vector borne diseases such as malaria and dengue. Recent work has explored using audio sensors to identify species and count adult mosquito numbers based on characteristics of wingbeat sounds. This study takes first steps to produce audio feature data to distinguish the mosquito vectors in Thailand.

Study Design & Methods: We collected wingbeat audio recordings of adult males and females of the mosquito vectors in Thailand (*Anopheles dirus, An. minimus, Aedes aegypti, Ae. albopictus,* and *Cx.quinquefasciatus*). After removing noise and artifacts from the audio recordings, we gathered the frequency ranges and nine audio signal features.

Results: Males have higher frequency ranges than females in all five species, with well-separated frequency ranges within each species. Males among the five species have overlapping frequency ranges (664 - 956 Hz). The female mosquito frequencies form two groups: a group of *Ae. albopictus* and *An. dirus* in the range 563 - 609 Hz, and a group of *Ae. aegypti, An. minimus,* and *Cx. quinquefasciatus* in the range 333 - 536 Hz. Ranking of the nine features using ANOVA, Chi-square, and information gain tests shows that Spectral Centroid, Mel-Frequency Cepstral Coefficients, Spectral Bandwidth, and Spectral Flatness best discriminate between the species.

Conclusions: Mosquito wingbeat audio frequency ranges can be used to identify the gender of five species relevant to Thailand and four features are promising for use in classification models to distinguish between species, providing a basis for the development of bio-acoustic sensors.

Title: Health literacy and Zika virus disease among the reproductive age women in upper central region of Thailand

Author: Samran Siriphakhamongkhon (Presenter), Office of Disease Prevention and Control 3, Nakhon Sawan Province. Department of Disease Control, Thailand
Co-authors: Jirawan Thaweekhatgorn, Sawanya Siriphakhamongkhon

Background: Health literacy is thought to impact women's Zika prevention behavior, yet no tool has been conducted on the topic. The aim of this study was; to create a self-assessment Zika health literacy scale in women of the reproductive age of the upper central region of Thailand.

Study Design & Methods: This survey research was collected 778 samples from women reproductive-aged 18-49 in Upper Central Region Thailand by multi-stage sampling. The data were collected by questionnaires.

Results: The research findings can be summarized as follows: The self-assessment Zika health literacy scale consisted of 25 items in which the reliability in the whole paper was equal to 0.96 and the weighted values of the factors ranged from 0.63 to 0.85. The result of the testing model of the self-assessment Zika health literacy scale in women of reproductive age by confirming factor analysis. The model is congruent with evidence-based practice. The consideration was based on chi-square = 400.004, p = 0.001, GFI =.961, AGFI = 0.93 RMR =.015.

Conclusions: Public health officers should adopt the result from this study, in order to solving the problem of prevention and improving health literacy among the reproductive-age women in the upper central region of Thailand.

Title: Point mutations in the voltage-gated sodium channel gene of pyrethroid-resistant *Aedes aegypti* mosquitoes and their insecticide susceptibility

Author: Jakkrawarn Chompoosri (Presenter), National Institute of Health, Department of Medical Sciences, Thailand
Co-authors: Chayada Khamsawas, Ballang Uppapong

Background: In Thailand, intensive and long-term use of pyrethroid insecticides to control *Aedes aegypti* mosquitoes results in the development of resistance mechanisms, such as knockdown resistance (kdr). The objective of this study was to assess the presence of kdr mutations in the Voltage-gated sodium channel (VGSC) gene in field-caught *Ae. aegypti* mosquitoes from Chanthaburi and to determine the effective insecticide for the control of the pyrethroid-resistant mosquitoes.

Study Design & Methods: Genomic DNA extracted from individual field-caught *Ae. aegypti* males was PCR amplified and then subjected to DNA sequencing. The F1 progeny females were tested with 10 insecticides from organophosphates, carbamates and pyrethroids by WHO susceptibility test.

Results: Based on the analysis of 72 sequences of the VGSC gene, two kdr mutations (Ser989Pro and Val1016Gly) were detected in Ae. aegypti. The frequency of kdr mutations in the evaluated samples of *Ae. aegypti* was 66.7%. For insecticide susceptibility test, the phenotypic and genotypic pyrethroid-resistant mosquitoes were susceptible to both 1.0% fenitrothion (organophosphates) and 0.336% fenobucarb (carbamates) with a mortality rate of 100%.

Conclusions: At present, the insecticide resistance in *Ae. aegypti* is a growing concern in Thailand. This study provides the evidence of phenotypic and genotypic pyrethroid resistance in *Ae. aegypti* from Chanthaburi. In general terms, high frequency of kdr mutations and phenotypic pyretroid resistance in Ae. aegypti populations that are detected timely, will be relevant to the Mosquito Control Programme. The data on insecticide susceptibility test were reported to Tambon Health Promoting Hospital in the study area for the control of pyrethroid-resistant mosquitoes.

Title: Chemical composition and mosquitocidal activity of *Cymbopogon citratus* essential oil against *Aedes aegypti* from dengue and chikungunya risk areas

Author: Chayada Khamsawas (Presenter), National Institute of Health, Department of Medical Sciences, Thailand
Co-authors: Jakkrawarn Chompoosri, Ballang Uppapong

Background: Dengue and chikungunya remain major public health problems in Thailand. In an effort to find effective and safe insecticides to control *Aedes aegypti* mosquitoes, plant-derived essential oil may serve as an alternative compound to commercially available mosquito insecticides. In this study, the efficacy of *Cymbopogon citratus* essential oil was investigated against *Ae. aegypti* from areas where their parent mosquitoes were infected with dengue and chikungunya viruses.

Study Design & Methods: Three field strains of *Ae. aegypti* from Chiang Mai, Tak and Phitsanulok were detected for dengue and chikungunya viruses by One-step qRT-PCR. Essential oil from *C. citratus* was extracted by hydodistillation and its chemical compositions were identified by GC-MS. This oil was tested on susceptible strain of *Ae. aegypti* to establish discriminating concentration against F1 progeny from field-caught *Ae. aegypti*.

Results: The mosquitoes from all three provinces were positive for both dengue and chikungunya viruses. Dengue infection rates in *Ae. aegypti* ranged from 0.74% to 2.28% with DENV 1, DENV 2 and DENV 3 serotypes, whereas chikungunya infection rates in the mosquitoes ranged from 1.97% to 4.80%. The major constituents of essential oil identified were geranial (28.77%) and neral (22.74%). Discriminating concentration of the essential oil was set at 0.814%. Using the established concentration, all three field strains of F1 female *Ae. aegypti* were found completely susceptible to the essential oil.

Conclusions: The efficacy of *C. citratus* essential oil is possibly based on its major chemical composition. *C. citratus* is promising plant source for the control of *Ae. aegypti* in dengue and chikungunya-risk areas.

Wednesday 16 December 2020

Poster session 5: Bacterial related diseases

11.50-12.50hr

Room D

1. Distribution of *Burkholderia pseudomallei* sequence types (ST) in Malaysia (1964-2019) and the emergence of ST1342
   Polly Soo Xi Yap
   University of Malaya, Malaysia

2. Typing and molecular characterization of carbapenem-resistant *Acinetobacter baumannii* isolates from a nosocomial outbreak in a tertiary teaching hospital
   Jia Jie Woon
   University of Malaya, Malaysia

3. Prevalence of carbapenemase-producing *Pseudomonas aeruginosa* strains from a Malaysian tertiary hospital
   Kalaivani Kalai Chelvam
   University Malaya, Malaysia

4. Molecular epidemiology of non-carbapenemase-producing carbapenem-resistant *Klebsiella pneumoniae* isolated in Malaysia
   Yee Qing Lee
   University of Malaya, Malaysia

5. VtrN suppresses expression of type III secretion system 2 in *Vibrio parahaemolyticus*
   Sarunporn Tandhavanant
   Faculty of Tropical Medicine, Mahidol University, Thailand

6. Association of phylogroups with resistance profiles of *Escherichia coli* isolates from asymptomatic bacteriuria in pregnant women
   Lalitha Maniam
   University of Malaya, Malaysia

7. Molecular investigation of carbapenem-resistant Enterobacteriaceae isolated from a tertiary teaching hospital in Malaysia
   Zhi Xian Kong
   University of Malaya, Malaysia

8. Projecting impacts of short course multidrug-resistant tuberculosis in South-East Asia Region using a mathematical model
   Win Min Han
   Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Title: Distribution of *Burkholderia pseudomallei* sequence types (ST) in Malaysia (1964-2019) and the emergence of ST1342

Author: Polly Soo Xi Yap (Presenter), University of Malaya, Malaysia
Co-authors: Cindy Shuan Ju Teh, Kumutha Malar Vellasamy, Noorfatin Jihan Zulkefli, Zhi Xian Kong, Jamuna Vadivelu, Vanitha Mariappan

Background: *Burkholderia pseudomallei*, a Gram-negative bacterial pathogen that causes melioidosis, is of public health importance in endemic areas including Malaysia. An investigation of the molecular epidemiology links of *B. pseudomallei* would contribute to better understanding of the clonal relationships, transmission dynamics and evolutionary change.

Study Design & Methods: Multi-locus sequence typing (MLST) of 45 clinical *B. pseudomallei* isolates collected from sporadic meliodosis cases in Malaysia was performed. In addition, a total of 449 *B. pseudomallei* Malaysian strains submitted to the MLST database from 1964 until 2019 were included in the time analysis and distribution study using e-BURST tool. A timeline analysis was also conducted to determine the endemic STs, emergence and re-emergence of ST(s).

Results: Genotyping of 45 clinical strains were resolved into 12 sequence types (STs), while majority were ST46 (n=11) and ST1342 (n=7). Concomitantly, ST46 was the most prevalent ST in Malaysia which occurred since 1964. All the Malaysian *B. pseudomallei* strains were resolved into 77 different STs with 29 of them uniquely present only in Malaysia. ST1342 was most closely related to ST1034, in which both STs were unique to Malaysia and first isolated from soil samples in Pahang, a state in Malaysia.

Conclusions: The present study revealed high diversity of *B. pseudomallei* in Malaysia. Localised evolution giving rise to the emergence of new STs was observed, suggesting that host and environmental factors play crucial role in the evolutionary changes of B. pseudomallei.

Title: Typing and molecular characterization of carbapenem-resistant *Acinetobacter baumannii* isolates from a nosocomial outbreak in a tertiary teaching hospital

Author: Jia Jie Woon (Presenter), University of Malaya, Malaysia
Co-authors: Cindy Shuan Ju Teh, Nuryana Idris, Sasheela Ponnampalavanar

Background: The emergence of carbapenem-resistant *Acinetobacter baumannii* (CRAB) has been responsible for an increasing number of nosocomial infection and colonization, posing unnecessary and detrimental effects to hospitalized patients. In this study, we investigated 33 CRAB isolates obtained from an outbreak in a hospital in terms of their antimicrobial susceptibility, resistance determinants, genetic relatedness and the possible causal factor of the outbreak.

Study Design & Methods: Thirty-three clinical isolates were obtained from the outbreak occurred in November and December 2019. Antimicrobial susceptibility profiles of each isolates was determined using VITEK 2 system. Their clonal relationships were examined using pulsed field gel electrophoresis (PFGE). Polymerase chain reaction (PCR) and DNA sequencing were employed to characterize the carbapenem resistance genetic determinants.

Results: Antimicrobial susceptibility testing indicated that 94% (n=31) of the isolates possessed extensive drug resistance phenotype, whereby only 45% and 9% of them showed susceptible to trimethoprim-sulfamethoxazole and aminoglycoside, respectively. All isolates remained susceptible to colistin. PFGE further subtyped the isolates into 14 pulsotypes, with pulsotype F as the predominant pulsotype, consisting of isolates which were mainly from ICU. PCR analysis revealed that all isolates harboured blaOXA-23-like and blaOXA-51-like carbapenemase gene. Metallo-β-lactamase gene including blaVIM, blaIMP and blaNDM were absent in all isolates.

Conclusions: The occurrence of outbreak, together with the increase incidence of A. baumannii showing resistance to critically important antibiotic underlines the importance of continuous clinical and microbiological surveillance as well as the prompt implementation of infection control measures and antibiotic stewardship program to minimize the spread of this pathogen and prevent the emergence of resistance in the clinical setting.

Title: Prevalence of carbapenemase-producing Pseudomonas aeruginosa strains from a Malaysian tertiary hospital

Author: Kalaivani Kalai Chelvam (Presenter), University Malaya, Malaysia
Co-authors: Cindy Teh Shuan Ju, Kumutha Malar Vellasamy, Jamunarani Vadivelu

Background: *Pseudomonas aeruginosa* is an opportunistic pathogen associated with a range of nosocomial infections. Increasing resistance toward β-lactams, especially carbapenems, poses a serious therapeutic challenge. This study aimed to determine the antibiotic susceptibility profiles of the clinical isolates of *P. aeruginosa* from a Malaysian tertiary hospital, in correlation with the phenotypic characteristics and biofilm formation.

Study Design & Methods: A total of 250 non-replicate clinical strains isolated from University Malaya Medical Centre (UMMC) were collected. The antimicrobial susceptibility of the strains to different antimicrobial agents were determined using automated Viteks 2 system. Pyocyanin, siderophore, protease and biofilm assays were performed in order to determine the phenotypic characteristics and biofilm formation.

Results: The resistance of the strains toward the carbapenems and ceftazidime was the highest (≥90%). *P. aeruginosa* strains displayed high level resistance to imipenem and meropenem which showed association with strong biofilm producers (OD570nm 3 and above). Majority of the strains were high to moderate pyocyanin producers (82%), high siderophore producers (85%) and able to secrete protease (80%).

Conclusions: The isolation of carbapenem resistant strains is alarming as carbapenems with antipseudomonal activity are important therapeutic agents for *P. aeruginosa* infections. Thus, implementation of strict infection control measures are essential. This may also help to reduce spread of carbapenemase encoding genes among strains or bacterial species.

Title: Molecular epidemiology of non-carbapenemase-producing carbapenem-resistant *Klebsiella pneumoniae* isolated in Malaysia

Author: Yee Qing Lee (Presenter), University of Malaya, Malaysia
Co-authors: Cindy Shuan Ju Teh, Chun Wie Chong, Min Yi Lau, Sasheela Sri La Sri Ponnampalavanar, Zhi Xian Kong, Yit Yin Kam

Background: Carbapenem-resistant *Klebsiella pneumoniae* has been an emerging global threat. More recently, the isolation of non-carbapenemase-producing (NC-CRKP) strains has been increasingly observed. NC-CRKP confers carbapenem resistance via the production of extended-spectrum β-lactamase (ESBL) or plasmid-mediated AmpC cephalosporinase combined with a structural mutation. In this study, we sought to determine the presence of NC-CRKP in UMMC with their resistance profile and strain clonality.

Study Design & Methods: A retrospective study of NC-CRKP in a Malaysia tertiary teaching hospital from 2013 to October 2019 was conducted. Carbapenemase genes and porin-associated genes were determined by polymerase chain reaction (PCR). The sensitivity towards antibiotics was detected via the Vitek® 2 system. The minimum inhibitory concentration (MIC) for imipenem, meropenem and colistin was determined via the broth microdilution method. The strains relatedness was determined via pulsed-field gel electrophoresis (PFGE).

Results: A total of 66 NC-CRKP strains were isolated from the hospital. Loss of ompK35 and ompK36 genes were detected in 4.5 % and 37.9 % of the strains respectively. All 66 strains were resistant to amoxicillin/clavulanate, ampicillin and cefuroxime. 43.9 % of the strains were monoresistant to carbapenem antibiotics (imipenem, n=1; meropenem, n=5; and ertapenem, n=23). According to the broth microdilution method, 4.5 % of the strains were colistin-resistant. Among the isolates, 26 were closely related (> 80% similarity) based on PFGE analysis.

Conclusions: All NC-CRKP strains collected were ESBL-producers. The increase of NC-CRKP is worrying as different mechanisms are utilized by NC-CRKP to develop resistance and cause infections since only 40.9 % of them showed porin loss.

Title: Hemolysin co-regulated protein 1 (Hcp1) variant is associated with decreased virulence and low antigenicity in *Burkholderia pseudomallei*

Author: Sarunporn Tandhavanant (Presenter), Mahidol University, Thailand
Co-authors: Rungnapa Phunpang, Peeraya Ekchariyawat, Claire Chewapreecha, Natnaree Saiprom, Thatcha Yimthin, Sineenart Sengyee, Rathanin Seng, Adul Dulsuk, Ganjana Lertmemongkolchai, T. Eoin West, Narisara Chantratita

Background: Hemolysin co-regulated protein 1 (Hcp1) is a virulence factor of *Burkholderia pseudomallei*. hcp1, located within T6SS-1, plays an essential role in the *B. pseudomallei* intercellular spread. Hcp1 is a potential diagnostic target and vaccine candidate. We hypothesized that *B. pseudomallei* population may have variation in hcp1 and affect their virulence and antigenicity.

Study Design & Methods: Whole genome sequencing (WGS) analysis was used to examine the variation of hcp1 in 699 clinical isolates in Thailand. To assess the Hcp1 specific antibodies, we performed ELISA using two recombinant Hcp1 proteins from wild-type strain K96243 (WT) and variant strain DR90076A as target antigens. 33 plasma samples from melioidosis patients infected with WT (N=19) and variant (N=14) strains were used. To determine pathogenicity, we compared multinucleated giant cell (MNGC) formation efficiency in a human lung epithelial cell line after 10-h infection.

Results: By mapping WGS data against K96243 reference genome, we observed two Hcp1 types consisting of WT (N=684, 97.9%) and variant (N=14, 2.0%) in clinical isolates. 87% nucleotides and 81% amino acids of variant Hcp1 were identical to WT. The median levels of IgG against WT-Hcp1 from patients infected with WT strains was significantly higher than patients infected with variant strains. In contrast, low IgG levels against variant-Hcp1 was detected from both patient groups. MNGC formation analysis demonstrated that the variants induced less MNGC than the WT strains.

Conclusions: We have identified hcp1 variants in clinical *B. pseudomallei* isolates. Our data suggest that Hcp1 variation may influence the pathogenicity and immunogenicity of *B. pseudomallei.*

Title: Association of phylogroups with resistance profiles of *Escherichia coli* isolates from asymptomatic bacteriuria in pregnant women

Author: Lalitha Maniam (Presenter), Department of Medical Microbiology, Faculty of Medicine, University of Malaya, 50603 Kuala Lumpur, Malaysia
Co-authors: Kumutha Malar Vellasamy, Hassan Mahmood Jindal, Vallikannu Narayanan, Mahmoud Danaee, Jamuna Vadivelu, Vinod Pallath

Background: Asymptomatic bacteriuria (ASB) during pregnancy, could predispose symptomatic urinary tract infection (UTI) and warrants treatment. The predominant pathogen of urinary tract *E.coli* is shown to develop multidrug resistance (MDR). This study aimed to identify the association of *E. coli* phylogroups with their antibiotic resistance patterns in an attempt to profile the nature of organisms developing MDR. The data could aid in mitigating the development of MDR through initiating the refinement of diagnostic and management algorithm for ASB and UTI.

Study Design & Methods: 160 E. coli isolated from 1315 midstream urine sample of pregnant women without symptomatic UTI were subjected to phylogrouping and antibiotic sensitivity test against 14 antibiotics using Kirby Bauer disc diffusion method according to the CLSI guideline.

Results: Majority of the *E. coli* isolates in this study belonged to phylogenetic group B2 (41.3%) followed by group A (25.0%), Group B1 (16.9%) and group D (16.3%). Generally, resistance to ampicillin (77.5%) was the highest among all the antibiotics tested, followed by amoxicillin-clavulanate (54.4%), amikacin (43.8%), cefuroxime (33.8) and ampicillin-sulbactam (32.5). 58.7% (77) isolates were with MDR of which 29 belonged to phylogroup B2, 19 to A, 15 to B1 and 14 to D.
Conclusions: Antibiotic resistance among phylogroup B2 (extra intestinal pathogenic phenotype) was higher for all antibiotics tested, demonstrating the need for a refined approach to diagnosis and management to prevent the development of symptomatic UTI in these patients with similar MDR strains.

Title: Molecular investigation of carbapenem-resistant Enterobacteriaceae isolated from a tertiary teaching hospital in Malaysia

Author: Zhi Xian Kong (Presenter), University of Malaya, Malaysia
Co-authors: Kartini Abdul Jabar, Sasheela Ponnampalavanar, Rina N. Karunakaran, Chun Wie Chong, Cindy Shuang Ju The

Background: Carbapenem-resistant Enterobacteriaceae (CRE) has rapidly disseminated worldwide and compromising our ability to treat infectious diseases. This study aimed to investigate the prevalence of CRE and the associated carbapenemase resistance mechanism as well as the risk factors associated with in-hospital mortality.

Study Design & Methods: A total of 168 CRE strains from 2014-2015 isolated from a tertiary teaching hospital were included in this study. The presence of carbapenemase genes were determined using PCR. Minimum inhibitory concentration of imipenem, meropenem and colistin were investigated through broth-microdilution method. The genotypic relatedness of carbapenem-resistant *K. pneumoniae* (CRKp) strains were determined by PFGE. The risk factors of patients infected by CRE associated with in-hospital mortality were investigated.

Results: *K. pneumoniae* was the most common CRE isolated. The carbapenemase genes detected were OXA-48, OXA-232 and NDM in which OXA-48 was the predominant carbapenemase gene. A total of 40 CRE strains harboured two different carbapenemase genes. A total of 30 pulsotypes were identified among 140 CRKp strains. The predominant pulsotype were found to circulate among 2014 and 2015. Both the period between CRE isolation and start of therapy is found to be statistically associated with in-hospital mortality.

Conclusions: The CRE that resistant to multiple antimicrobial agents has gained notoriety as one of the public health concerns. In this study, we have identified the predominant carbapenemase gene and the genotype that circulating in the hospital. The rate of in-hospital mortality could be reduced with rapid diagnosis that can prompt the appropriate treatment.

Title: Projecting impacts of short course multidrug-resistant tuberculosis in South-East Asia Region using a mathematical model

Author: Win Min Han (Presenter), Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Co-authors: Wiriya Mahikul, Thomas Pouplin, Saranath Lawpoolsri, Lisa White, Wirichada Pan-Ngum

Background: This study aimed to predict the impacts of shorter duration MDR-TB treatment regimens on both MDR-TB percentage among new cases and overall MDR-TB cases in the Southeast Asia Region.

Study Design & Methods: A deterministic compartmental model was constructed to describe transmission of MDTB. The population-level impacts of short-course treatment regimens were compared with the conventional regimens.

Results: The model predicted that overall TB incidence in 2035 will be reduced from 216 (95% credible interval [CI], 203-227) per 100,000 population in 2020 to 187 (95% CI, 172-201) per 100,000 population in 2035, with a reduction of 13.4% (95% CI: 11.4-15.3). Despite reduction in TB infections, the model also predicted that percentage of MDR-TB in newly diagnosed TB infections will be increased from 3.4% (95% CI, 3.2-3.5) in 2020 to 5.8% (95% CI, 5.4-6.2) by 2035 i.e. an increment of 70.6% (95% CI, 68.7-77.1). With the introduction of short-course regimen, MDR-TB transmission can be slowed down by approximately 10% over this period. The multi-way analysis showed that higher eligibility to short-course treatment and earlier treatment initiation resulted in the greater the reduction of MDR-TB cases and percentage of resistance among new infections, compared to the baseline scenario which was set as no introduction of short-course regimen. The effect of varying the DST coverage seems to be minimal on both outcomes.

Conclusions: Policies which promote the expansion of short-course regimen and early MDR-TB treatment initiation should be considered along with other interventions to tackle antimicrobial resistance in the region.

Wednesday 16 December 2020

Free paper V: Parasitic infection and others

11.50-12.50hr

Room E

Chairpersons:

1. Dorn Wattanakulpanich
2. Urusa Thaenkham

Speakers:

1. Epidemiological surveillance and holistic intervention targeting intestinal parasitic infection in the endemic area
   Aulia Rahmi Pawestri
   Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Thailand

2. Epidemiology, clinical presentations and treatment outcome of *Strongyloides stercoralis* infection in a tertiary care hospital, Kuala Lumpur Malaysia
   Azlin Muhammad
   Universiti Kebangsaan Malaysia, Malaysia

3. Coverage evaluation of mass drug administration for elimination of schistosomiasis in Sigi and Poso District, Indonesia
   Helena Ullyartha Pangaribuan
   National Institute of Health Research and Development, MoH RI, Indonesia

4. Knowledge and prevalence of helminthiasis in expectant mothers in Malang Indonesia
   Yulia Dwi Setia
   Parasitology Department Faculty of Medicine Universitas Brawijaya, Indonesia

5. Real-world long-term human papillomavirus vaccine effectiveness in Thai adult women
   Ga Young Lee
   Faculty of Tropical Medicine, Mahidol University, Thailand

6. Will citizen science change human behavior towards infectious disease control?
   Mika Saito
   Graduate School of Medicine, University of the Ryukyus, Japan

7. The effects of valproic acid on the biosynthesis of fatty acids and polyketides in microorganisms
   Prapassorn Poolchanuan
   Chulabhorn Research Institute, Thailand

Title: Epidemiological surveillance and holistic intervention targeting intestinal parasitic infection in the endemic area

Author: Aulia Rahmi Pawestri (Presenter), Department of Protozoology, Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Chamnan Pinna, Kanthinich Thima, Pannamas Maneekan, Saengduen Moonsom*, Somphob Leetachewa, Tawatchai Yingtaweesak

Background: Intestinal parasitic infection (IPI), including diarrhea is a global health issue in developing countries. In Thailand, it ranked third of all food-and-waterborne diseases, with the highest prevalence in the Northern-Western region. Tha Song Yang District in Tak Province has the second highest cases of bloody diarrhea. Due to mild symptoms, it lacks of epidemiological features and specific preventive measure of the disease. This study aimed to determine prevalence of symptomatic and symptomatic IPI cases and explored disease-associated risk factors in this endemic area.

Study Design & Methods: We collected samples from human individuals, animals and water sources during the rainy and dry seasons and retrieved symptomatic case data from Tha Song Yang hospital records. For the holistic intervention, we provided health education, facilitated group discussions and active brainstorming on participatory prevention and control of the IPI to stakeholders from involved sectors. We also trained laboratory technicians and physicians on gold standard diagnosis of the IPI by microscopy. We evaluated disease-associated knowledge, attitude and practice (KAP) and symptomatic cases from hospital records before and after the intervention.

Results: The prevalence of asymptomatic cases was much higher than the reported cases. We discovered infective stage of the intestinal parasites in animal stool and water sources, indicating possible transmission routes of the IPI. After the intervention, the number of symptomatic cases was reduced significantly. KAP regarding water and waste management was also significantly improved.

Conclusions: This study highlighted the impact of a holistic intervention to address gaps in disease surveillance and formulation of IPI-specific prevention.

Title: Epidemiology, clinical presentations and treatment outcome of *Strongyloides stercoralis* infection in a tertiary care hospital, Kuala Lumpur, Malaysia

Author: Azlin Muhammad (Presenter), Universiti Kebangsaan Malaysia, Malaysia

Background: The threadworm, *Strongyloides stercoralis* is a soil-transmitted helminth (STH) causing the disease strongyloidiasis. It is an opportunistic infection that can cause severe clinical manifestations when disseminated, with more than 80% mortality rate. However, due to the difficulty in the diagnosis, it is often lead to underreporting of its true prevalence rate thus became the most neglected helminthes infection in the world. Currently the epidemiological data were very lacking in Malaysia and studies were done exclusively amongst the aborigine populations.

Study Design & Methods: A cross-sectional study was carried out to determine the prevalence of Strongyloides stercoralis infection among 150 patients in Hospital Cancelor Tunku Mukhriz (HCTM). Multiple stool samples were collected from consenting participants and subjected to larval cultivation using modified Harada Mori technique. Results were noted after 7 days by directly viewing the parasites under microscope. Patients demographic data and clinical details were collected via patients record and questionnaires.

Results: 8 out of 150 samples (5.3%) was found to be positive with *Strongyloides stercoralis* infection. Four patients presented with hyperinfection during admission. Univariate analysis revealed age more than 40 years old, working with soil, on corticosteroid and having malignancies had significantly higher prevalence than others. Multiple logistic regression analysis confirmed taking corticosteroid ($P < 0.001$) and having haematologic malignancy ($P = 0.003$) are significant risk factors for this infection. The commonest presenting symptoms were acute severe diarrhoea (100%), acute dermatitis (90%) and dyspnea (87%). Albendazole 400mg twice a day for 3 days was added to their medication during hospital stay. Six patients died within 60 days due to sepsis and organ failure.

Conclusions: The prevalence of strongyloidiasis in this hospital is higher than other studies in Malaysia. It can be due to the pool of immunosuppressed patients and the culture method used for the diagnosis. Clinicians should have a high index of suspicion of this infection in high risk patients and be aware of the best management. The aim is to prevent hyperinfection and dissemination of the parasites which will reduce the mortality rates.

Title: Coverage evaluation of mass drug administration for elimination of schistosomiasis in Sigi and Poso District, Indonesia

Author: Helena Ullyartha pangaribuan (Presenter), National Institute of Health Research and Development, MoH RI, Indonesia

Background: Mass drug administration (MDA) of schistosomiasis with praziquantel has been implemented in Indonesia for elimination.

Study Design & Methods: This study objective was to validate the reported coverage, investigate additional issues for improving programme and explore reason for non-compliance. A cross-sectional study was conducted among 3 randomly – selected enumeration Areas (EA) using Probability Sampling with Segmentation and is derived from the modified segment design. The sites study are Napu, Lindu, and Bada Valley. This study was conducted a month after MDA.

Results: Total of 1080 peoples were interviewed with structured questionnaire. The compliance with drug ingestion was vary from 74-91%. About 84,5% inhabitants admitted to consuming praziquantel. Ranging between 40-52 % of people experienced side effects. The side effect were dizziness, headache, vomiting. Overall, the side-effects of praziquantel were mild and transient, and did not require serious intervention. Coverage within these areas (Napu, Bada, Lindu) was respectively 91%, 86% and 74% according to the treatment registers; it was 91%, 83% and 74%, according to survey responses. The rate of compliance was 82% for Napu, 73% for Bada and just 57% for Lindu. Meanwhile, the primary explanation for non-compliance was away when MDA (40 %), not aware of MDA (20 %) and the refusal (18%).

Conclusions: This result showed that a repeat visit is beneficial for dose completeness and adherence rates. These findings are very useful for schistosomiasis programs, especially in assessing the primary coverage evaluation and validation of reported coverage

Title: Knowledge and prevalence of helminthiasis in expectant mothers in Malang Indonesia

Author: Yulia Dwi Setia (Presenter), Parasitology Department Faculty of Medicine Universitas Brawijaya, Indonesia
Co-authors: Aulia Rahmi Pawestri, Dearikha Karina Mayashinta, Nadya Ratu Chesty Maharani Saleh, Rivo Yudhinata Brian Nugraha, Sri Poeranto, Wike Astrid Cahayani

Background: Helminthiasis in pregnant women, leading to anemia, low birth weight and stunting, is a major health concern in Indonesia, including in urban settings. Despite being the second largest city in East Java, Malang still has a high number of helminthiasis. This study aimed to determine the prevalence of helminthiasis in expectant mothers and explore their knowledge regarding disease-related risk factors.

Study Design & Methods: Forty-three expectant mothers from three districts were enrolled. They were given questionnaires assessing the level of knowledge regarding risk factors, transmission, and prevention of helminthiasis. Stool samples were also collected and microscopically examined for helminthiasis.

Results: Almost half (47%) of participants had experienced anemia before. Yet, 42% of participants did not have knowledge on risk factors and symptoms of helminthiasis. One third had no knowledge on the transmission route and prevention. Only three samples were positive for helminths (6.9%). Chi-square analysis did not show a correlation between the prevalence and knowledge level.

Conclusions: In summary, in this study, there was no significant correlation between the knowledge level and prevalence of helminthiasis in expectant mothers. The low prevalence could be attributed to the technical limitation of a single stool sample collection. Nevertheless, since many study participants showed moderate-to-poor knowledge regarding helminthic infection, an integrated health education is required, especially in expectant mothers.

Title: Real-world long-term human papillomavirus vaccine effectiveness in Thai adult women

Author: Ga young Lee (Presenter), Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Supitcha Kamolratanakul, Nimit Taechakraichana, Piyawat Laowahutanont, Palita Lungchukiet, Perapong Inthasorn, Rasik Rangsiprakarn, Punnee Pitisuttithum, Wichai Termrungruanglert, Saranath Lawpoolsri

Background: Since 2007, a substantial number of Thai adult women received human papillomavirus (HPV) vaccine yet its effectiveness remained unknown. This study aimed to determine the real-world effectiveness of bi- or quadrivalent HPV vaccines in Thai adult women at ≥ 5 years post-vaccination in reduction of HPV 16/18 associated low-grade squamous intraepithelial lesion or worse (LSIL+), atypical squamous cells of undetermined significance or worse (ASC-US+), and HPV 16/18 positivity.

Study Design & Methods: Retrospective cohort study was conducted in Thai women aged 20-45 years in Bangkok. Vaccinated and unvaccinated group were matched by baseline years. HPV/Pap co-test results were collected from medical records and/or cervical sample collection at our study sites. Adjusted hazard ratio was measured by multivariable cox regression analysis.

Results: A total of 993 participants (493 vaccinated and 500 unvaccinated) were enrolled from 2018 to 2019. Median age at baseline was 34 years (IQR 29 - 38). Median follow up period was 7.3 years (IQR 6.0 - 8.7, range 5 - 16.7). More women in vaccinated group were single (29.2% vs. 13.2%, p<0.001), university graduates (83.2% vs. 75.4%, P=0.009), but vaccinated and unvaccinated had similar personal monthly income (>20,000 THB/month 63.9% vs 62.4% respectively, p=0.685). There were no cases of HPV 16/18 associated LSIL+ in vaccinated group, and 4 cases in unvaccinated group. For reduction of HPV 16/18 associated ASC-US+ and HPV 16/18 positivity, the vaccine effectiveness was 88.0% (95% CI 2.0 – 98.5) and 84.6% (95% CI 43.5 - 95.8) respectively.

Conclusions: HPV vaccine effectiveness was shown to be high in adult women for the first time in the real-world scenario in a developing country.

Title: Will citizen science change human behavior towards infectious disease control?

Author: Mika Saito (Presenter), Graduate School of Medicine, University of the Ryukyus, Japan

Background: “Citizen science” was defined as the participation of the community in scientific work, through collaboration between scientists and citizens. Challenges to solve problems in 21st Century, such as land use change due to disasters and wars, globalization, and global warming, increased the risk of emerging and re-emerging diseases. In the face of limited research resources and budgets, citizen participation has the potential to solve problems. We are currently implementing citizen science practices and action research in Okinawa to develop a model for citizen-participatory monitoring of mosquitoes for mosquito-borne disease control. In this presentation, I introduce this practice and discuss how to motivate citizens towards behavior change.

Study Design & Methods: In October 2018, the Matsuda Gajan Science Club (GSC, Gajan means mosquito in Okinawa) was established in Matsuda, Ginoza Village, Okinawa, mainly for school children. Actions are:<Research with citizen>Once a month, we monitored the habitat of mosquitoes and larvae.<Learning with citizen> Science Cafe, Gajan Festival, Gajan science camp<Communication and outgoing with citizen> Community - cleanup activities, Newspaper, local TV, Facebook Global exchange - TV conference with Hawaii Waimea Middle School, JICA infectious disease course Questionnaire about mosquito-borne diseases and the control was conducted to GSC participants and their family

Results: The eliability of monitoring data collected by citizens who are in frequent contact with the surrounding environment is high, and the resulting risk maps have the potential to serve as a model for participatory monitoring. Through this practice, the family increased the opportunity to talk about mosquitoes and the diseases and increased knowledge. Children increased mosquito monitoring practice, but families did not.

Conclusions: The practice of citizen science with children has improved citizens' infectious disease literacy, triggered dialogue and placemaking between children and parents, and changed children's behavioral patterns. It has shown the potential to contribute to community development and policy advocacy for the future, but there are hurdles in changing behavioral patterns from children to adults and to the community. However, there is hope that it can be done while having fun and fighting mosquito-borne diseases.

Title: The effects of valproic acid on the biosynthesis of fatty acids and polyketides in microorganisms

Author: Prapassorn Poolchanuan (Presenter) Chulabhorn Research Institute, Thailand
Co-authors: Panida Unagul, Sanit Thongnest, Suthep Wiyakrutta, Nattaya Ngamrojanavanich, Chulabhorn Mahidol, Somsak Ruchirawat, Prasat Kittakoop

Background: Valproic acid or valproate (VPA) is a drug for the treatment of epilepsy, bipolar disorder, migraine headaches and neuropathic pain. VPA is also an epigenetic modulator, known as a histone deacetylase inhibitor, and it has been subjected to clinical study for cancer treatment. In this work, microorganisms were cultivated in culture media containing 100 μM of VPA under shaking condition. Fatty acids were extracted using hexane, and fatty acid profiles were analyzed by gas chromatography. It was found that productions of some fatty acids were significantly affected by VPA. Further exploration of VPA on fatty acid production in microorganisms including fungi, yeast, and bacteria, as well as representative gut microbiome, showed that VPA could enhance, reduce or completely inhibit the production of some fatty acids. VPA could induce the production of trans-9-elaidic acid; this fatty acid was found to have cellular effects in human macrophages. Moreover, VPA was found to inhibit the production of some polyketides produced by a model fungus. The present work suggests that the induction or inhibition of fatty acid biosynthesis by VPA (100 μM) in gut microbiome could give effects to patients treated with VPA. Normally, oral administration of this drug used by patients is up to 600 to 900 mg; the concentration of VPA in the human gut may reach a concentration of 100 μM, which may give effects to fatty acid profiles in gut microorganisms.

Wednesday 16 December 2020

S37: New serological tools and approaches for malaria and COVID-19

13.00-14.30hr

Room A

Chairpersons:

1. Ivo Mueller
2. Chris Drakeley

Invited Speakers:

1. *P. vivax* serology: A tool to identify and target potential hypnozoite carriers
   Rhea Longley
   The Walter and Eliza Hall Institute of Medical Research, Australia

2. VAR2CSA serology to detect *P. falciparum* transmission patterns
   Alfredo Mayor
   Barcelona Institute for Global Health, Spain

3. Using health facility-based serological surveillance to predict receptive areas at risk of malaria outbreaks in elimination areas
   Henry Surendra
   Eijkman-Oxford Clinical Research Unit, Indonesia

4. Applying malaria serological surveillance techniques to COVID-19
   Michael White
   Institut Pasteur, France

Title: *P. vivax* serology: A tool to identify and target potential hypnozoite carriers

Author: Rhea Longley (Presenter), The Walter and Eliza Hall Institute of Medical Research, Australia

Background: Malaria infections due to *Plasmodium vivax* are a major challenge for elimination in the Asia-Pacific region. This is partly due to the lack of surveillance tools appropriate for use in low transmission settings, along with the absence of an effective vaccine. Improving our understanding of naturally acquired immune responses induced following *P. vivax* infections could enable novel strategies to be implemented for surveillance and vaccine design. In this study we aimed to characterise the *P. vivax*-specific antibody response in individuals from endemic areas by assessing the acquisition and decay of total IgG, IgG subclass, IgM and functional antibodies.

Study Design & Methods: We used a panel of 60 *P. vivax* proteins, and multiple cohorts from *P. vivax*-endemic areas to measure antibody responses and associate those with infection.

Results: We identified a bi-phasic pattern of IgG antibody decay following a peak 1-2 weeks after clinical *P. vivax* infection in Thai patients (n=34). In these individuals with limited past exposure, IgG1 was the dominant subclass and followed similar kinetics to total IgG. In contrast, in a pool of plasma from highly immune adults from Papua New Guinea, nearly all proteins induced both IgG1 and IgG3. By assessing responses every 2-4 weeks up until 9-months post *P. vivax* infection, we have shown that IgM responses can be long-lived in these Thai patients. To assess functional antibody responses, we have developed and validated a novel multiplexed assay to measure the interaction between *P. vivax*-specific IgG and complement (C1q). We are currently measuring the presence and decay of C1q-fixing antibodies in the same cohort of Thai patients.

Conclusions: We have tested the use of total IgG, IgG1, IgG3 and IgM antibody responses to all 60 proteins for classifying individuals as recently exposed to *P. vivax* infections or not. Using total IgG responses to a panel of 8 *P. vivax* proteins, we could accurately classify recent exposure with more than 80% sensitivity and specificity using large yearlong observational cohort studies in Thailand (n=829), Brazil (n=928) and the Solomon Islands (n=754). These novel serological markers of recent exposure have the potential to dramatically increase our ability to efficiently target limited resources for malaria elimination, and highlight the value in increasing our understanding of naturally acquired immune responses to malaria.

Title: VAR2CSA serology to detect *P. falciparum* transmission patterns

Author: Alfredo Mayor (Presenter), Barcelona Institute for Global Health, Spain

Background: Women attending antenatal care constitute an easy-access population for the surveillance of infectious disease. Pregnant women develop antibodies against VAR2CSA, the *P. falciparum* antigen that mediates sequestration in the placenta. Therefore, appropriately selected antibodies can provide information about a woman's history of exposure during a very specific window of exposure (ie., a pregnancy).

Study Design & Methods: We have developed a multiplex bead-based suspension array to test the presence of antibodies against VAR2CSA among pregnant women from Mozambique, Benin, Kenya, Gabon and Tanzania. We expanded this array to multiplex the determination of malaria antigens (PfHRP2 and pLDH) and antibodies against non-pregnancy-specific *P. falciparum* antigens, along with antigens against other infectious diseases.

Results: We selected two VAR2CSA peptides of limited polymorphism which are targeted by short-lived IgG responses readily boosted during *P. falciparum* infection. The presence of antibodies against these 2 peptides mirrored changes in malaria transmission in southern Mozambique and reductions in exposure associated with the use of intermittent preventive treatment in pregnancy, and allowed the identification of local clusters of transmission. A multiplex assay was further developed to multiplex Plasmodium bioproducts commonly targeted by rapid diagnostic tests, as well as serological markers of exposure to RSV, Pertussis, Tetanus and Hepatitis B.

Conclusions: These data suggest that the detection of antibodies against VAR2CSA can complement surveillance approaches to estimate the malaria burden among pregnant women and the underlying community over time and space. This serological approach has the potential to be multiplexed to assess markers of exposure to other pathogens.

Title: Using health facility-based serological surveillance to predict receptive areas at risk of malaria outbreaks in elimination areas

Author: Henry Surendra (Presenter), Eijkman-Oxford Clinical Research Unit, Indonesia
Co-authors: Chetan Chitnis, Chris Drakeley, Gillian Stresman, Jackie Cook, Kevin Tetteh, Riris Ahmad, Rizqiani Kusumasari, Siska Damayanti, Supargiyono Supargiyono, Theodola Rahayujati

Background: In order to improve malaria burden estimates in low transmission settings, more sensitive tools and efficient sampling strategies are required. This study evaluated the use of serological measures from repeated health facility-based cross-sectional surveys to investigate *Plasmodium falciparum* and *Plasmodium vivax* transmission dynamics in an area nearing elimination in Indonesia.

Study Design & Methods: Quarterly surveys were conducted in eight public health facilities in Kulon Progo District, Indonesia, from May 2017 to April 2018. Demographic data were collected from all clinic patients and their companions, with household coordinates collected using participatory mapping methods. In addition to standard microscopy tests, bead-based serological assays were performed on finger-prick bloodspot samples from 9453 people. Seroconversion rates (SCR, i.e. the proportion of people in the population who are expected to seroconvert per year) were estimated by fitting a simple reversible catalytic model to seroprevalence data. Mixed effects logistic regression was used to examine factors associated with malaria exposure, and spatial analysis was performed to identify areas with clustering of high antibody responses.

Results: Parasite prevalence by microscopy was extremely low (0.06% (95% confidence interval 0.03–0.14, n =6) and 0 for *P. vivax* and *P. falciparum*, respectively). However, spatial analysis of *P. vivax* antibody responses identified high-risk areas that were subsequently the site of a *P. vivax* outbreak in August 2017 (62 cases detected through passive and reactive detection systems). These areas overlapped with *P. falciparum* high-risk areas and were detected in each survey. General low transmission was confirmed by the SCR estimated from a pool of the four surveys in people aged 15 years old and under (0.020 (95% confidence interval 0.017–0.024) and 0.005 (95% confidence interval 0.003–0.008) for *P. vivax* and *P. falciparum*, respectively). The SCR estimates in those over 15 years old were 0.066 (95% confidence interval 0.041–0.105) and 0.032 (95% confidence interval 0.015–0.069) for *P. vivax* and *P. falciparum*, respectively

Conclusions: These findings demonstrate the potential use of health facility-based serological surveillance to better identify and target areas still receptive to malaria in an elimination setting. Further implementation research is needed to enable integration of these methods with existing surveillance systems.

Title: Applying malaria serological surveillance techniques to COVID19

Author: Michael White (Presenter), Institut Pasteur, France

Background: Infection with SARS-CoV-2 induces an antibody response targeting multiple antigens that changes over time. This study aims adapts methods originally developed for malaria serology to develop more accurate serological diagnostics.

Study Design & Methods: A multiplex serological assay was developed to measure IgG and IgM antibody responses to seven SARS-CoV-2 spike or nucleoprotein antigens, two antigens for the nucleoproteins of the 229E and NL63 seasonal coronaviruses, and three non-coronavirus antigens. Antibodies were measured in serum samples from individuals in French hospitals with RT-qPCR confirmed SARS-CoV-2 infection (n = 259), and negative control serum samples collected before the start of the SARS-CoV-2 epidemic (n = 335). Machine learning classifiers were trained with the multiplex data to classify individuals with previous SARS-CoV-2 infection. A mathematical model of antibody kinetics informed by prior information from other coronaviruses was used to estimate time-varying antibody responses and assess the sensitivity and classification performance of serological diagnostics during the first year following symptom onset.

Results: IgG antibody responses to trimeric Spike protein identified individuals with previous RT-qPCR confirmed SARS-CoV-2 infection with 91·6% sensitivity (95% confidence interval (CI); 87·5%, 94·5%) and 99·1% specificity (95% CI; 97·4%, 99·7%). Using a serological signature of IgG and IgM to multiple antigens, it was possible to identify infected individuals with 98·8% sensitivity (95% CI; 96·5%, 99·6%) and 99·3% specificity (95% CI; 97·6%, 99·8%). Informed by prior data from other coronaviruses, we estimate that one year following infection, a monoplex assay with optimal anti-Stri IgG cutoff has 88·7% sensitivity (95% CI: 63·4%, 97·4%), and that a multiplex assay can increase sensitivity to 96·4% (95% CI: 80·9%, 100·0%).

Conclusions: Serological signatures based on antibody responses to multiple antigens can provide accurate and robust serological classification of individuals with previous SARS-CoV-2 infection. This provides potential solutions to two pressing challenges for SARS-CoV-2 serological surveillance: classifying individuals who were infected greater than six months ago, and measuring seroprevalence in serological surveys in very low transmission settings.

Wednesday 16 December 2020

S38: Malaria animal models

13.00-14.30hr

Room B

Chairperson**:** Luis Lugo

Invited speakers

1. Aotus monkeys as a model for human malaria *(P. vivax, P. falciparum)* infections
   Fiona McCallum
   Australian Defence Force Malaria and Infectious Disease Institute, Australia

2. Rhesus monkey models for drug discovery in malaria at WRAIR
   Gregory Reichard
   Walter Reed Army Institute of Research, United States

3. Immune protection in a relapsing *P. cynomolgi* rhesus model
   Sathit Pichyangkul
   USAMD-AFRIMS, Thailand

4. A humanized mouse model for *Plasmodium vivax* to test interventions that block liver stage to blood stage transition and blood stage infection
   Carola Schaefer
   Seattle Children's Research Institute, United States

Title: Aotus monkeys as a model for human malaria (*P. falciparum, P. vivax*) for the evaluation of promising antimalarial drug candidates

Author: Fiona McCallum (Presenter), Australian Defence Force Malaria and Infectious Disease Institute, Australia
Co-author: Mike Edstein

Background: The Aotus monkey-malaria model is a well-established animal model for human malaria. The model is currently used at the Australian Defence Force Malaria and Infectious Disease Institute (ADFMIDI) to evaluate promising antimalarial drug candidates against human malaria.

Study Design & Methods: The Aotus monkey-malaria model is used to assess selected antimalarial candidates that have been shown to possess high in vivo efficacy and favourable pharmacokinetic profiles in the mouse-*Plasmodium berghei* model. The blood stage drug efficacy studies are evaluated using the chloroquine resistant *P. falciparum* (FVO) and *P. vivax* (AMRU1) lines. The efficacy studies are designed to determine the rate and extent of parasite clearance, prevention of recrudescence, assessment of drug disposition, and monitoring for animal health.

Results: The Aotus monkey-malaria model has proven valuable in predicting (i) the pharmacokinetic profile of candidate antimalarials, and (ii) the in vivo efficacy of promising antimalarial drug candidates. The model is advantageous in allowing investigations to evaluate drug efficacy against higher blood parasitaemia than can be ethically achieved using controlled human malaria infection models, for the assessment of drug-drug interaction and dose optimization. The primate model provides a clear prediction of human efficacy providing a logical transition to first-time in human studies.

Conclusions: This model is currently used in a restricted manner for highly promising drug candidates. Care and responsiveness must be exercised around the rapid, progressive development of alternative animal and human models.

Title: Rhesus monkey models for drug discovery in malaria at WRAIR

Author: Gregory Reichard (Presenter), WRAIR, United States
Co-authors: Alison Roth

Background: The primary focus of antimalarial drug discovery at WRAIR for several decades has been the discovery of candidate molecules which will serve as drugs for chemoprophylaxis of malaria. The approval of tafenoquine (TQ) in August 2018 since future candidates will need to have a biological profile that is as better than TQ. This translates into a requirement for a chemoprophylaxis drug candidate to have efficacy against all stages of the parasite, including the hypnozoite stage, which is responsible for relapsing malaria due to infections resulting parasites and *Plasmodium (P.) vivax* or *P. ovale*, endemic to Southeast Asia, and parts of Africa.

Study Design & Methods: The *P. cynomolgi* in vitro assay utilizes a 384-well in vitro culture system consisting of primary non-human primate hepatocytes (PNHPHs) to support the growth and development of both schizont and hypnozoite *P. cynomolgi* liver stage forms. Sporozoites are dissected from *Anopheles dirus* mosquitoes that have been infected with *P. cynomolgi bastianellii* (B strain) and maintained at AFRIMS then shipped to WRAIR. Compounds are evaluated in single-dose manner (5-10 mM) measuring the inhibitory response in both prophylactic and curative (radical) treatment mode The primary single-point screen will evaluate the selectivity of the compound for inhibiting parasite growth (hypnozoite and schizont) versus activity against NHP cells. Active compounds are evaluated in a 12- point dose-response starting at 10 mM and serial diluted (3-fold) using robotic transfer. The *P. cynomolgi in vivo* assayCausal prophylactic test evaluates the effectiveness of drugs to prevent malaria. Test compounds are given weekly on days -7, 0, 7, 14, 21, 28. Tafenoquine (1 mpk q.w) is used as a (+) controlRadical Curative test evaluates the antimalarial activity of the compound(s) against both blood stage (blood schizontocide), and/or liver stage (tissue schizontocide or anti-relapse) malaria. Test compounds are given daily for 7 days following parasitemia levels > 5000 count/uL. Tafenoquine (0.3 mpk q.d) is used as a (+) control.

Results: Compounds or combinations of compounds have been screened in the *p. cyno in vitro* assay resulting in the identification of active compounds that show activity against all stages of the parasite including the hypnozoite stage. Some of these compounds or combinations have been tested in-vivo in both prophylactic and radical cure mode showing a good correlation of activity when comparing the *p. cyno in vitro* and *in vivo* test systems.

Conclusions: The establishment of an *in vitro p. cynomolgi* liver stage assay is a significant breakthrough in the toolset for testing hypotheses and interrogating chemical collections with the objective of discovering new small molecule antihypnozoite therapeutics. A clear correlative relationship is observed for compounds and compound combinations that have been assessed in both the *in vitro p. cynomolgi* liver stage assay and the *in vivo p. cyno* NHP model.

Title: Protection in a relapsing *P. cynomolgi* rhesus model induced by a chemoprophylaxis with

Author: Sathit Pichyangkul (Presenter), USAMD-AFRIMS, Thailand
Co-authors: Amporn Limsalakpeth, Brian Vesely, Kosol Yongvanitchit, Luis Lugo, Michele Spring, Norman Waters, Ratawan Ubalee, Rawiwan Im-Erbsin, Utaiwan Srichairatanakool

Background: We examined if a chemoprophylaxis with sporozoite (CPS) immunization regimen could induce protection against primary *P. cynomolgi* infection and subsequent relapses in rhesus monkeys, a relevant model for *vivax* malaria.

Study Design & Methods: Rhesus monkeys received three CPS immunizations with *P. cynomolgi* sporozoites under 2 antimalarial drug regimens. Group 1 animals (n=6) received artesunate/chloroquine (AS/CQ) followed by a radical cure with CQ plus primaquine (PQ) and group 2 animals (n=6) received atovaquone-proguanil (AP) followed by PQ.

Results: Upon wild type *P. cynomologi* sporozoite challenge, all animals in a control group (n=6) developed primary infection and two relapses. The majority of group 1 animals (AS/CQ-CQ+PQ) did not show protection except one animal which developed primary infection, but had only one relapse. Four out of six of group 2 animals (AP-PQ) demonstrated some degree of protection. Two animals had complete protection, and the other two animals had partial protection: one did not develop primary infection but had 2 relapses and the other did not have a first relapse, but developed primary infection and second relapse. After challenge, high frequencies of sporozoite-specific memory CD8+ T cells in the liver (14-18%) were observed in two of the three animals that did not have primary infection.

Conclusions: The finding that that CPS immunization with AP-PQ can induce immune protection in relapsing *P.cynomolgi* rhesus monkeys provides a model to further study the mechanisms of protective immune responses which will guide the design of an effective pre-erythrocytic *P. vivax* vaccine.

Title: A humanized mouse model for *Plasmodium vivax* to test interventions that block liver stage to blood stage transition and blood stage infection

Author: Carola Schaefer (Presenter), Seattle Children's Research Institute, United States
Co-authors: Chaitra Parthiban, Debashree Goswami, Erika Flannery , Jetsumon Sattabongkot, Laura Reynolds, Martino Bardelli, Nicholas Dambrauskas, Niwat Kangwanrangsan, Noah Sather, Olesya Trakhimets, Sean Murphy, Sebastian Mikolajczak, Simon Draper, Spencer Kennedy , Stefan Kappe, Thomas Rawlinson, Wanlapa Roobsoong

Background: The human malaria parasite *Plasmodium vivax* is widely distributed and causes significant morbidity globally. Yet this parasite remains understudied and preclinical evaluation of novel interventions remains difficult, mainly due to the lack of suitable laboratory models.

Study Design & Methods: Here, we report the use of a humanized mouse model to test interventions that can block *P. vivax* parasite transition from asymptomatic liver stage infection to symptomatic blood stage infection. Human liver-chimeric FRGN KO huHep mice infected with *P. vivax* sporozoites were infused with human reticulocytes, allowing robust and reproducible liver infection, exo-erythrocytic schizont maturation, exo-erythrocytic merozoite formation and transition of these infectious forms to reticulocyte infection.

Results: Parasites developed into all asexual, erythrocytic forms within their physiological 48-hour life cycle in vivoand mature schizonts expressing merozoite surface protein 1 (MSP1) as well as free merozoites could be detected by immunofluorescence assays. Expression of the sexual stage marker Pvs16 was detected on a subset of exo-erythrocytic schizonts as well as on first generation erythrocytic stages, implying that this parasite can commit to sexual stage development as it emerges from the liver. In order to test the utility of this model for preclinical assessment of interventions, the invasion blocking potential of a monoclonal antibody targeting the essential interaction of the *P. vivax* Duffy Binding Protein (PvDBP) with the Duffy antigen receptor was tested by passive immunization. This antibody inhibited invasion by over 95% in this model.

Conclusions: The FRGN KO huHep/huRetic model is highly suitable to test blood stage interventions. Using this model, we provide unprecedented in vivo evidence that PvDBP constitutes a promising blood stage vaccine candidate that can block transition from liver to blood.

Wednesday 16 December 2020

S39: Management of severe dengue

13.00-14.30hr

Room C

Chairperson: Terapong Tantawichien

Invited speakers:

1. Overview and management of dengue infection (no abstract)
   Terapong Tantawichien
   Faculty of Medicine Chulalongkorn University

2. Pulmonary complication in Dengue patients
   Chaisith Sivakorn
   Faculty of Tropical Medicine, Mahidol University

3. Acute kidney injury and renal replacement therapy (no abstract)
   Weerapong Phumratanaprapin
   Faculty of Tropical Medicine, Mahidol University

4. Fluid management, hemodynamic, critical care and CRRT support
   Nattachai Srisawat
   Faculty of Medicine Chulalongkorn University

5. Severe dengue case demonstration
   Wiwat Chancharoenthana
   Faculty of Tropical Medicine, Mahidol University

Title: Pulmonary complication in Dengue patients

Author: Chaisith Sivakorn (Presenter) Faculty of Tropical Medicine, Mahidol University

Background: Thoracic manifestations of dengue are pleural effusion, pneumonia, pulmonary hemorrhage, hemoptysis and acute respiratory distress syndrome which occur most in severe dengue including Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). Dyspnea, cough and hemoptysis are the most common symptoms. Most of Dengue patients with ARDS has underlying diseases and co-infection with other bacterial infection. Major cause of ARDS in Dengue are usually not directly cause by Dengue infection.

Lung pathology of severe Dengue patient has significantly involved in alveoli and alveolar macrophages causing by antibody dependent enhancement. Pulmonary hemorrhage, hyper cellularity with septal necrosis and thickening has shown in lung pathology in severe dengue patient. In region of septal thickening presenting numerous alveolar macrophages (AM) with loss of membrane integrity, altered heterochromatin and loss of mitochondrial integrity. The cell membrane is disrupted at many points also showing bleb-like outward expansions.

Computed tomography in severe Dengue show bilateral multifocal areas of consolidation which is the sign of pulmonary edema or pulmonary hemorrhage. Ultrasound is the promising machine that is able to detect abnormalities in Dengue patient including fluid accumulation in Dengue with warning sign and severe plasma leakage, severe hemorrhage and severe organ impairment in severe Dengue. Major findings of lung ultrasound in Dengue are Interstitial separated or coalescent B-lines, lung consolidation and pleural effusion. The incidence of pulmonary manifestations is high among the complicated cases of dengue fever (DHF & DSS) and can be used as an indicator of serious presentation.

Title: Fluid management, hemodynamic, critical care and CRRT support

Author: Nattachai Srisawat (Presenter), Chulalongkorn University, Thailand

Background: Dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS) are among the most common causes of hospital admission, death, and disability in children in the Tropics. Recently, the age group of dengue infection has shifted to adolescents and adults. Data from Southeast Asia have shown that the mean age of reported dengue cases has increased from 5–9 years to older children and adults. In Thailand, affected adults over 15 years of age comprise 30–40% of dengue cases. Plasma leakage is the hallmark of severe dengue infection and leads to DSS. Until the present time, there has been no specific treatment for this condition. Hemodynamic optimization is the only mainstay treatment as supportive treatment during this critical period. The aim of this article is to review the most up-to-date knowledge of critical care management focusing on fluid management, choice of vasopressor, and target blood pressure in severe adult dengue infection.

Title: Severe dengue case demonstration

Author: Wiwat Chancharoenthana (Presenter) Faculty of Tropical Medicine, Mahidol University

Background: Although dengue infection with the dengue virus (DENV) causes a mild self-limiting illness in the majority of individuals, some cases develop severe dengue infection with manifestations of many organ failure such as cardiovascular system, the nervous system, the kidneys, the gut, and the hematological system. Furthermore, individuals with comorbid illnesses could be prone to more severe form due to the vulnerable organ function. Therefore, early recognition of signs and symptoms of severe dengue infection along with appropriate fluid resuscitation and supportive care are often an important part of treatment. This case study demonstrates that impact of close monitoring fluid intake and output, vital signs, and hematocrit levels in the critical periods are cornerstone. In addition, administration of colloids and early renal replacement therapy for refractory shock and severe metabolic acidosis should prompt to prescribe in case of severe dengue sequelae.

Wednesday 16 December 2020

S40: Healthcare and technology innovations

13.00-14.30hr

Room D

Chairpersons:

1. Santi Maneewatchararangsri
2. Supachai Topanurak

Invited speakers:

1. Innovation roadmap, ecosystem and management in Thailand (no abstract)
   Nathasit Gerdsri
   College of Management, Mahidol University

2. From natural product research to innovative medical devices (no abstract)
   Supayang Voravuthikunchai
   Natural Product Research Center of Excellence, Prince of Songkla University

3. Novel innovation in cancer immunotherapy (no abstract)
   Suradej Hongeng
   Faculty of Medicine Ramathibodi Hospital, Mahidol University

Wednesday 16 December 2020

S41: Field epidemiologists fighting against COVID-19 pandemic in Thailand

13.00-14.30hr

Room E

Chairperson: Chawetsan Namwat

Invited speakers:

1. Surveillance**:** process and data management from local to central level (no abstract)
   Walairat Chaifoo
   Ministry of Public Health, Thailand
2. Field epidemiologists' responses and capacities (no abstract)
   Phanthanee Thitichai
   Ministry of Public Health, Thailand
3. COVID-19 infection in pub bar cluster, Thailand (no abstract)
   Rapeepong Suphanchaimat
   Ministry of Public Health, Thailand
4. COVID-19 outbreak investigation at boxing stadium, Thailand (no abstract)
   Nichakul Pisitpayat
   Ministry of Public Health, Thailand
5. COVID-19 infection among Dawah group in Thailand (no abstract)
   Farooq Phiriyasart
   Ministry of Public Health, Thailand

Wednesday 16 December 2020

S42: Use of models for policy and decision support in emerging infection

14.40-16.10hr

Room A

Chairpersons:

1. Jodie McVernon
2. Wirichada Pan-ngum

Invited speakers:

1. Assessment of social distancing strategies against COVID-19 by mathematical modelling in Thai setting
   Wirichada Pan-ngum
   Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand

2. Modelling to support pandemic response in Australia
   Jodie Mc Vernon
   The Peter Doherty Institute for Infection and Immunity, Australia

3. Real-time modelling for pandemic control in Malaysia and the Philippines
   James Trauer
   Monash University, Australia

4. COVID-19 pandemic modelling in context: uniting people and technology across nations
   Lisa White
   University of Oxford, United Kingdom

Title: Assessment of social distancing strategies against COVID-19 by mathematical modelling in Thai setting

Author: Wirichada Pan-ngum (Presenter), Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand, Thailand
Co-author: Ainura Moldokmatova, Lisa White, Nantasit Luangasanatip, Parinda Wattanasri, Ricardo Aguas, Sompob Saralamba

Background: Mathematical modelling can play an important role in designing interventions strategies to control the disease pandemic on national and international scale. This approach is especially useful when several diease characteristics and the interactions with interventions are largely still unclear.

Study Design & Methods: Our research team is part of an international group of the COVID-19 Modelling (CoMo) Consortium. Participatory simulation modelling approach through the webtools (https://comomodel.net/) is well suited to high priority and complex topics. It provides policymakers with timely and dynamic support and enabling the modelling process to be built around the co-production of knowledge between modellers and policymakers.

Results: For Thai context, the model has been used to explore several health decisions to relax the government interventions along with how to improve the country economy after the first wave of COVID-19 while keeping the country safe from the return of infections. This will be the highlights of the talk.

Conclusions: Modelling community and simple communication tools are essential for successful usage of mathematical models to help with health decision making process.

Title: Modelling to support pandemic response in Australia

Author: Jodie McVernon (Presenter), The Peter Doherty Institute for Infection and Immunity, Australia

Background: Epidemiologic models provide useful frameworks for synthesis of emerging evidence in uncertain and rapidly evolving situations. Model-derived insights have supported Australia's response to COVID-19.

Study Design & Methods: Three models focused on distinct information needs are considered, with a focus on the participatory process underpinning their development and application to decision making:
1. A theoretical clinical pathways model was used to determine the need for combined public health and social measures to constrain case numbers within health sector capacity;
2. An agent-based model representing extended family group mixing structures in remote Aboriginal and Torres Strait Islander communities evaluated alternative initial outbreak response strategies;
3. A mathematical model explored different indications for SARS-CoV-2 testing relative to laboratory capacity and epidemic control objectives, optimising the value of testing to support public health response.

Results: These models were developed in response to specific questions initiated by decision makers, with objectives defined through consultation. Iterative feedback was obtained and incorporated during the development process, ensuring that input assumptions and interventions were reasonable and acceptable to end users. Findings were conveyed directly to key committees involved in decision making, and modellers were involved in preparation of materials for messaging to key stakeholders and the public.

Conclusions: Close engagement with decision makers supports appropriate development of 'fit for purpose' models as one of many sources of evidence to inform policy and practice. This process requires long term relationship building and mutual understanding of the benefits and limitations of modelling, and its application to real world problems.

Title: Real-time modelling for pandemic control in Malaysia and the Philippines

Author: James Trauer (Presenter), Monash University, Australia

Background: COVID-19 has fundamentally changed many aspects of health care, life, society and the economy across the world, and epidemiological modelling is no exception. We were commissioned by the World Health Organization Western Pacific Regional Office to undertake policy-relevant modelling for COVID-19 control to support Malaysia and the Philippines.

Study Design & Methods: The COVID-19 epidemic changed so rapidly in these countries that a modelling analysis undertaken one week would often be out of date by the next. We adapted our existing platform for TB control to allow for rapid adjustment of our model, frequent recalibration to surveillance data and interactive visualisation for communication with in-country staff.

Results: A major focus of our work has been identifying and managing points in our workflow that could lead to errors or inefficiencies, with the aim of creating an end-to-end pipeline that provides model outputs from calibration data. This has allowed us to rapidly integrate emerging evidence into our platform, including the incorporation of features such as testing-dependent case detection and heterogeneity in susceptibility. In the Philippines our results suggest that even the most strongly affected regions retain the potential remain at risk of major epidemics, while in Malaysia our results show a sustained effect of public health policies on the epidemic that is not captured with mobility data alone.

Conclusions: To produce robust, relevant, policy-relevant models to support countries to develop strategies to fight the current pandemic, modelling practices should markedly change from traditional cyclical approaches.

Title: COVID-19 pandemic modelling in context: uniting people and technology across nations

Author: Lisa White (Presenter), University of Oxford, United Kingdom

Background: Historically, the policymakers in low- and middle-income countries (LMIC) have used the services of modellers from high-income countries (HICs), which often caused an issue of relevancy of provided expertise to local contexts. To avoid such situation, the COVID-19 International Modelling Consortium (CoMo Consortium) has adopted a participatory approach to provide decision-making support to policymakers, using evidence from epidemiological and economic models adapted to each country's context.

Study Design & Methods: The CoMo Consortium has developed an age-structured, compartmental SEIRS (susceptible-exposed-infectious-recovered-susceptible) model to estimate the trajectory of COVID-19 based on different scenarios and to assess the potential impact of the various NPIs, as well as treatments and vaccines, when they become available. A user-friendly, web-based interface enables training on and use of the model by member modelling groups, while dashboards and visualisation tools allow policymakers to see the predicted impacts of different NPIs in real time.

Results: In March 2020, a small group of researchers at the University of Oxford together with academic colleagues at Cornell University have initiated a platform, focused on the epidemiological and economic modelling support to the countries with limited resources and research capacity. Within less than seven months this initiative has grown to a multinational consortium that brought together public health experts, clinicians and policy makers from more than 40 countries across Africa, Asia, and South and North America. One of the key features of the consortium is a close collaboration between CoMo consortium technical teams, country modelling groups and national ministries of health and other policymakers. This approach allows the consortium to tailor the modelling process and outputs to each particular country context. In addition to providing the modelling support, the consortium takes a special consideration to the capacity building of country modelling groups, allowing the country teams to get technical support from the consortium and share the knowledge and experience with other countries with similar issues or context.

Conclusions: As opposed to an on-line tool alone, this symbiosis of experts, both from LMICs and HICs, and technology has shown to be very effective in providing the modelling services to many countries. As a result, a number of country modelling groups have successfully collaborated with their governments and their proposed models were applied as one of the key tools supporting national policy decisions.

Wednesday 16 December 2020

S43: Residual malaria transmission in the Asia-Pacific: challenges and new opportunities

14.40-16.10hr

Room B

Chairpersons:

1. Ivo Mueller
2. Leanne Robinson

Invited Speakers:

1. Forest malaria in Cambodia: the occupational and spatial clustering of malaria infection risk in a cross-sectional survey in Mondulkiri, Cambodia
   Mirco Sandfort
   Institut Pasteur Paris, France

2. The epidemiology of declining and re-surging *P. falciparum* and *P. vivax* in Papua New Guinea
   Leanne Robinson
   Burnet Institute; WEHI & PNGIMR, Australia

3. Decreased bioefficacy of long-lasting insecticidal nets and the resurgence of malaria in Papua New Guinea
   Stephan Karl
   Australian Institute of Tropical Health and Medicine, James Cook University, Australia

4. Improving primaquine treatment for *P. vivax* malaria
   Kamala Ley-Thriemer
   Menzies School of Health Research, Australia

5. Tafenoquine: a silver bullet for *P. vivax* elimination? (no abstract)
   Narimane Nekkab
   Institut Pasteur, France

Title: Forest malaria in cambodia: the occupational and spatial clustering of malaria infection risk in a cross-sectional survey in Mondulkiri, Cambodia

Author: Mirco Sandfort (Presenter), Institut Pasteur Paris, France
Co-authors: Amélie Vantaux, Anaïs Pepey, Benoit Witkowski, Dysoley Lek, Ivo Mueller, Leanne J. Robinson, Michael White, Nimol Khim, Saorin Kim, Soazic Gardais, Thomas Obadia

Background: After a trough in annual malaria incidence in Cambodia in 2016, numbers were higher in 2017-2019. Given the goal of malaria elimination by 2025, the remaining risk needs to be targeted cost-effectively.

Study Design & Methods: In a cross-sectional survey in Mondulkiri province from December 2017 until April 2018, 4200 participants were PCR-tested for *Plasmodium spp.* infections. Antibody levels against *P. vivax* antigens were measured and used to estimate recent exposure to infection.

Results: *P. vivax* predominated over *P. falciparum* with a prevalence of 6.8% and 3.3% ($p<0.001$), respectively. Prevalence was highest in male, occupationally active age groups (max. 21.4% and 11.1% at 21-25 years for both species, $p<0.001$). Travels to forest sites (aOR 2.18, $p<0.001$) and forest work (aOR 2.89, $p<0.001$) increased risk for *Plasmodium spp.* infection. Residing in forest villages was a spatial risk factor (aOR 12.43, $p<0.001$). Antibody levels to RBP2b were increased in forest-goers (8-fold, $p<0.001$) but less strongly upon residence in the forest (8.5 vs. 2.5-fold if living outside or inside the forest, each $p<0.001$). Cases clustered significantly within 50m based on household locations. Prevalence of recent exposure to a *P. vivax* infection was 23.1% overall, peaking at 57.4% in 31-35 years old men ($p<0.001$) and in forest villages (max. 67.0%, $p<0.001$).

Conclusions: Forest-related activities increase malaria infection risk in high-burden pockets in Cambodia, with elevated baseline risk if residing in forested areas, potentially due to peri-domestic transmission. Undetected hypnozoite carriage and thus onward transmission might be substantial. Case clustering on household-level suggests their use for locally adapted radius-based reactive control interventions as cost-effective tools for malaria elimination.

Title: The epidemiology of declining and re-surging *P. falciparum* and *P. vivax* in Papua New Guinea

Author: Leanne J Robinson (Presenter), Burnet Institute; WEHI & PNGIMR, Australia
Co-authors: Maria Ome-Kaius, Dulcie Lautu-Gumal, Shazia Ruybal-Pesántez, Desmond Gul, Desmond Sui, Daisy Mantila, Daniela Rodriguez Rodriguez, Mary Salib, Johanna Kattenberg, Stephan Karl, James Kazura, Ivo Mueller, Moses Laman

Background: Over the past decade there has been a scale up of the malaria control program in Papua New Guinea, with 3-yearly nationwide distribution of long-lasting insecticide treated nets and a switch to artemisinin combination therapy for case management. Between 2008 and 2014, substantial reductions in the burden of clinical malaria and prevalence of infection were observed, followed by an increasing burden since 2015. An in-depth program of studies has been conducted over this time to understand the changing epidemiology of *P. falciparum* and *P. vivax* infections.

Study Design & Methods: Serial cross-sectional surveys and longitudinal cohort studies conducted in Madang and East Sepik Provinces combined sensitive molecular diagnosis of infections with demographic, clinical and spatial data. Individual and household-level risk factors and the spatial and temporal heterogeneity of infection risk were investigated, within studies and across sites and timepoints.

Results: Reductions in the burden of *P. falciparum* and *P. vivax* between 2005 and 2014 were greater in East Sepik than Madang and occurred more quickly for *P. falciparum* than *P. vivax*. The increasing prevalence of malaria since 2015 is dominated by *P. falciparum* and hotspots for *P. falciparum* are more commonly observed than for *P. vivax*. More than 80% of infections are asymptomatic and low-density escaping routine detection and treatment.

Conclusions: Understanding the dynamic, heterogenous and often differential epidemiology of *P. falciparum* and *P. vivax* in PNG communities is important in order to guide the targeted implementation of control strategies and ensure progress towards the regional goal of malaria elimination by 2030.

Title: Decreased bioefficacy of long-lasting insecticidal nets and the resurgence of malaria in Papua New Guinea

Author: Stephan Karl (Presenter), Australian Institute of Tropical Health and Medicine, James Cook University, Australia
Co-authors: Leanne Robinson, Lincoln Timinao, Peter Kaman, Nakei Bubun, Tim Freeman, Moses Laman, Leo Makita, William Pomat, Louis Schofield, Michelle Katusele, Ivo Mueller, Rebecca Vinit, Muker Sakur, Lisa Reimer

Background: Papua New Guinea (PNG) has the highest malaria transmission outside of Africa. Long-lasting insecticidal nets (LLINs) are believed to have helped to reduce average malaria prevalence in PNG from 16% in 2008 to 1% in 2014. Since 2015 malaria in PNG has resurged significantly. Here, we present observations documenting decreased bioefficacy of unused LLINs with manufacturing dates between 2013 and 2019 collected from villages and LLIN distributors in PNG.

Study Design & Methods: Overall, n = 192 unused LLINs with 78 different batch numbers were tested. These had been distributed to or were intended for distribution in 15 PNG Provinces. WHO cone bioassays were conducted on the LLINs according to WHO guidelines using 25 fully pyrethroid susceptible *An. farauti* mosquitoes per piece of net.All cone bioassays included positive and negative controls. We used LLINs manufactured in 2012 and with a known 100% 24 h mortality as positive controls and pieces of untreated netting as negative controls. Results were excluded if 24 h mortality in the negative control exceeded 10%. Test results were adjusted using 'Abbott's formula' when negative control 24 h mortality was >0% and ≤10%. Results were confirmed by independent tests using *An. gambiae* S3 and Kisumu strains, as well as *An. dirus.*

Results: Specifically, we show that of n = 167 tested LLINs manufactured after 2013, only 17% are fulfilling the required World Health Organisation bioefficacy standards of ≥ 80% 24 h mortality or ≥ 95% 60 min knockdown in bioassays with pyrethroid susceptible *Anopheles farauti* mosquitoes. In contrast, all (100%, n = 25) LLINs with manufacturing dates prior to 2013 are meeting these bioefficacy standards.
Conclusions: These results suggest that decreased bioefficacy of LLINs is contributing to the malaria resurgence in PNG and increased scrutiny of LLIN quality is warranted.

Title: Improving primaquine treatment for *P. vivax* malaria

Author: Kamala Thriemer (Presenter), Menzies School of Health Research, Australia

Background: Vivax malaria continues to exert a huge public health burden in the Asia-Pacific region, South America and the Horn of Africa with an estimated 14.3 million cases in 2017. Vivax malaria is associated with significant morbidity and mortality, and there is increasing recognition of the public health importance related to *P. vivax* control and elimination. The elimination of vivax malaria will require effective radical cure and its wider roll out has been hampered by low effectiveness of a prolonged 14-day course of primaquine and concern over safety in the absence of point of care tests to identify patients with G6PD deficiency.

Study Design & Methods:

Results: Two breakthroughs have increased the likelihood that radical cure will be rolled out in all vivax endemic regions. Novel radical cure treatment regimens, including shorter primaquine regimens as well as tafenoquine are available now and are expected to have improved effectiveness. Novel technologies allow point of care testing to identify patients with low G6PD enzyme activity at risk of haemolysis. Details on choice of treatment regimen in different scenarios and locations as well as effective ways of rolling those out remain to be determined.

Conclusions: The effective and safe deployment of those novel tools could have significant impact towards malaria elimination.

Wednesday 16 December 2020

S44: A view to a 'cure'

14.40-16.10hr

Room C

Chairpersons:

1. Yupaporn Wattanagoon
2. Wirongrong Chierakul

Invited speakers:

1. Viravarn Luvira (no abstract)
   Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

2. Chaisith Sivakorn (no abstract)
   Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

3. Jittima Dhitavat (no abstract)
   Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

4. Supitcha Kamolratanakul (no abstract)
   Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University

Wednesday 16 December 2020

S45: TB/MDR-TB is challenging

14.40-16.10hr

Room D

Chairperson: Francois Nosten

Invited speakers:

1. TB/DR-TB control activities during COVID-19 pandemic by National TB Programme, Myanmar
   Cho Cho San
   National Tuberculosis Programme, Myanmar

2. Childhood tuberculosis treatment outcomes and mortality risk factors within a migrant population at the Thailand-Myanmar border, 2013-2018
   Amy Carroll
   Barts Health NHS Trust, London, United Kingdom

3. Mortality in migrants with tuberculosis on the Thai-Myanmar border
   Banyar Maung Maung
   Shoklo Malaria Research Unit, Thailand

4. Tuberculosis in unregistered migrants from Myanmar
   Htet Ko Ko Aung
   Shoklo Malaria Research Unit, Thailand

Title: TB/DR-TB control activities during COVID-19 pandemic by National TB Programme, Myanmar

Author: Cho Cho San (Presenter), National Tuberculosis Programme, Myanmar

Background: Pandemic spread of COVID-19 infection is challenging globally as well as in country levels in all aspects which includes Tuberculosis control and provision of TB diagnosis and treatment interventions. In Myanmar, it affects 40-50% reduction of TB diagnosis and notification due to public fear to visit clinics, suspension of Active Case Finding (ACF) activities, closure of private GP clinics, limited sputum transportation and travel restriction orders, etc. and thereby limiting GeneXpert testing, passive and active case findings for TB control. Moreover, impact of COVID-19 pandemic can be seen in TB treatment as it hinders community DOT and clinic activities which include regular follow up appointments to provide direct support to patients. To mitigate these effects, NTP (Myanmar) has responded using TB contingency plans for sustainability of TB control activities. This includes segregation of work force, strengthening sputum transportation, plans to avoid interruption of anti-TB drugs, integrating TB screening in community fever clinics for COVID-19 screening, safety and infection control measures, procurement and supply chain management system for drugs and other commodities including PPE, and allocating resources (GeneXpert machines) for COVID-19 testing. Way forward plans have been developed with new normal approaches in resuming case finding, holding and program activities.

Title: Childhood tuberculosis treatment outcomes and mortality risk factors within a migrant population at the Thailand-Myanmar border, 2013-2018

Author: Amy Carroll (Presenter), Barts Health NHS Trust, London, United Kingdom
Co-authors: Win Pa Pa Htun, Banyar Maung Maung, Michele Vincenti-Delmas, Francois Nosten, Colette Smith, Pam Sonnenberg

Background: Tuberculosis (TB) is a leading cause of death in children but epidemiological data are scarce, particularly for hard-to-reach populations. We aimed to identify the risk factors for unsuccessful outcome and TB mortality in migrant children at a residential TB programme on the Thailand-Myanmar border.

Study Design & Methods: We conducted retrospective analysis of routine programmatic data for child TB cases diagnosed between 2013-2018. Treatment outcomes were described and risk factors for unsuccessful outcome and death were identified using multivariate logistic regression.

Results: Childhood TB accounted for 17.3% (n=399) of all patients with TB. Most children (n=367) were enrolled in treatment, with 90.5% of these completing treatment successfully. Among all diagnosed cases, unsuccessful treatment outcomes were experienced by 42/399 (10.5%) children, comprising 26 (6.5%) lost to follow-up, 15 (3.8%) deaths and one (0.2%) treatment failure. In multivariate analysis, extra-pulmonary TB (aOR 3.83; 95% CI 1.38-10.60) and bacteriologic TB confirmation (aOR 4.68; 95% CI 1.43-15.27) were independent risk factors for unsuccessful outcome, and HIV positivity (aOR 5.49; 95% CI 1.57-19.23) and bacteriological confirmation (aOR 10.09; 95% CI 2.23-45.54) were independently associated with death.

Conclusions: Children are hugely burdened by TB disease within this migrant population. This supportive residential TB programme achieved treatment success rates exceeding 90%. Efforts to identify and treat children with TB in in hard-to-reach populations need to be stepped up to reduce health disparities.

Title: Mortality in migrants with tuberculosis on the Thai-Myanmar border

Author: Banyar Maung Maung (Presenter) Shoklo Malaria Research Unit, Thailand

Background: Tuberculosis remains a major health concern and one of the top ten infectious causes of mortality around the world. An estimated 1.5 million people died from tuberculosis in 2018 worldwide. The aim of this study is to estimate the mortality and causes of deaths in migrants with tuberculosis along the Thai-Myanmar border.

Method: We reviewed the clinical data of confirmed tuberculosis cases between 2013 and 2018 at the Shoklo Malaria Research Unit. Case fatality rate (CFR) for all patients enrolled was estimated for patients with drug sensitive and multi-drug resistant TB as well as HIV co-infected patients. TB diagnosis is made by clinical signs and symptoms, chest-X rays, sputum microscopy, GeneXpert, and sputum culture.

Result: During study period, 1704 drug sensitive TB patients and 109 MDR-TB patients were identified. Case fatality rate is 8.8% for drug sensitive TB patients, 11.9% for MDR TB patients and 15% in HIV co-infected patients. Among the 178 drug sensitive patients who died, 33% (47) died of TB related causes such as pneumothorax, massive hemoptysis, severe lung destruction, TB meningitis, late presentation, disseminated TB (miliary TB), and 30% (44) died of systemic diseases. While 15% (22) died of AIDS and related opportunistic infections. CFR (21%) is highest in patients above 54 years old and 69% of all deaths occur in males. Among 109 MDR-TB patients, the causes of death are 46% (6) TB related, 46% (6) HIV/AIDS related and 7.7% (1) caused by a systemic disease. Risk factors of death are old age, HIV/AIDS and preexisting systemic diseases.

Conclusion: Approximately two thirds of drug sensitive TB deaths were due to non-TB related causes (systematic diseases and AIDS related opportunistic infection). Early diagnosis and treatment of TB, effective multidisciplinary approach, better cooperation from family, community and other hospitals are important factors to reduce TB mortality.

Title: Tuberculosis in unregistered migrants from Myanmar

Author: Htet Ko Ko Aung (Presenter), Shoklo Malaria Research Unit, Thailand
Co-authors: Francois Nosten, Win Pa Pa Htun, Banyar Maung Maung, December Chit Yi, Janurian Naw

Background: Since 2009, the Shoklo Malaria Research Unit (SMRU)'s Tuberculosis program has provided TB diagnosis and treatment services to migrants and cross-border local ethnic population living in Tak province in Thailand and Myawaddy district (Myanmar) in collaboration with Thai and Myanmar National TB Programs.

Study Design & Methods: This is a retrospective review of notified TB cases using routine programmatic data collected between March 2010 and June 2020 in the two SMRU TB clinics. This review describes the 10-year-long achievements of the SMRU TB program including trends in TB case detection, socio-demographic and clinical characteristics of TB patients detected and their treatment outcomes of TB.

Results: A total of 11,804 people with symptoms suggestive of TB had a sputum examination (83.3%) and/or, CXR (93.2%). Among TB patients taking 1st line anti TB treatment, 92.5% were identified as pulmonary TB in which half of them are bacteriologically confirmed and 7.5% as extra-pulmonary TB. 5532 out of 11,804 (59%) were tested by GeneXpert of which 1426 were found to be positive. Amongst these positive, 91.9% were rifampicin sensitive Mycobactrium tuberculosis (MTB) and 8.1% of rifampicin resistant MTB strain also defined as Multidrug resistant TB (MDR-TB). 126 out of 1198 (10.5%) bacteriologically confirmed TB cases were MDR-TB by culture and drug susceptibility testing (DST) and this proportion has been stable over the ten years. Overall a total of 2424 confirmed TB cases, male=1579(65%) and 147 drug resistant TB cases, male=95 (65%) in which the diagnosis for MDR-TB of 126 (85.7%) patients are confirmed with culture and DST and 134 (91.2%) patients with GeneXpert were enrolled in the SMRU TB centers. While 98.8% of these registered TB patients underwent HIV testing, 18.6% of patients were found to be TB-HIV co-infected. In the 2424 TB patients, 1678 (69.2%) received the standard anti TB initial regimen, 483 (19.9%) received the pediatric regimen, and 26.3 (10.9%) received the retreatment regimen. The overall treatment success rate (TSR) achieved was 81.9% and 18.1% of these patients were recorded as treatment failure (1.6%), death (8.1%), lost to follow up (4.1%) or were not evaluated after being transferred out to other treatment centers (4.3%). Among treated MDRTB patients in the program, successful outcome rate of 72.4% was achieved.

Conclusions: This review shows the high burden of tuberculosis in this marginalized population where the rates of MDR-TB infections and HIV co-infection are high and presentation is late. This explains the relatively high mortality and the below average TSR.

Wednesday 16 December 2020

S46: Capturing of COVID-19 cases travelling from high risk countries at port of entry, state and local quarantine, and development of national laboratory services (Thai/Eng session)

14.40-16.10hr

Room E

Chairperson: Suksont Jittimanee

Invite speakers:

1. Control measures of COVID-19 at international ports of Thailand
   Chollasap Sharma
   International Communicable Disease Control, Don Meang Airport, Division of Port Health

2. Arrangement of state quarantine best practice and experience from Thailand (no abstract)
   Suksont Jittimanee
   Institute for Urban Disease Control and Prevention

3. Development of national COVID-19 laboratory system (no abstract)
   Pilailuk Akkapaiboon Okada
   National Institute of Health, Department of Medical Sciences, Nonthaburi, Thailand

4. Prompt response from zero to hundred percentage to be national laboratory reference for COVID-19: an experience from Bangkok (no abstract)
   Kamolthip Atsawawaranunt
   Institute for Urban Disease Control and Prevention

Title: Control measures of COVID-19 at international point of entry – Thailand

Author: Chollasap Sharma (Presenter), Department of Disease Control, Thailand

Background: Airport, seaport and land-port are 3 types of point of entry screening discussed. In the session we will focus more on the airport as this is the major mode of human transport in modern day.

Study Design & Methods: This is a perspective from a front-liner screening and managing COVID-19 at the division of port health, Thailand. During the beginning first 3.5 months before the emergency decree was announce in Thailand, it was harder to control the novel virus. There were few stakeholders and regulators. There were need for more protocol as well as resources especially man-power, Personal Protective Equipment, thermoscan, container and translater.

Results: Despite our rapid response to contain the disease, by January it was declared as Public Health Emergency of International Concern. After Songkran festival Thailand step up the screening following announcement of Emergency decree

Conclusions: 2020 has shown us how thin the line between day to day life and disaster truly is. While Thailand has fared remarkably well in the face of COVID-19 pandemic.

Wednesday 16 December 2020

S47: Facing COVID-19 situation around the world by CTM Alumni

16.10-17.40hr

Room A

Chairpersons:

1. Wirongrong Chierakul
2. Prakaykaew Charunwatthana

Invited speakers:

1. Facing COVID-19 situation in the UK (no abstract)
   Simon Peter Boyd
   Department of Gastroenterology, Luton and Dunstable Hospital, Bedfordshire, UK

2. Facing COVID-19 situation in Sudan and Saudi Arabia (no abstract)
   Mohammed Yasein Elamin
   Ministry of Health, Saudi Arabia

3. Facing COVID-19 situation in Nepal (no abstract)
   Anup Bastola
   Sukraraj Tropical and Infectious Disease, Hospital Teku, Kathmandu, Nepal

4. A public health perspective of COVID-19 from Nepal (no abstract)
   Biraj Karmacharya
   Department of Public Health, Kathmandu University, School of Medical Sciences, Kathmandu, Nepal

5. Facing COVID-19 situation in Japan
   Yoshiro Hadano and Hirotake Mori
   Tokyo Medical and Dental University; Department of General Medicine, Juntendo University

6. Facing COVID-19 situation in Malaysia (no abstract)
   Muhamad Yazli Yuhana
   UiTM Medical Specialist Centre

Title: Facing COVID-19 situation in Japan-management of patients and health-care workers

Author: Yoshiro Hadano (Presenter), Tokyo Medical and Dental University Medical Hospital, Japan

Background: After the first laboratory-confirmed COVID-19 case, involving a patient who had returned from Wuhan, was reported in Japan on January 14, 2020, 74,544 laboratory-confirmed cases were identified subsequently throughout Japan until September 10, 2020. Among them, 22857 (30.6%) COVID-19 patients were identified in Tokyo. Most of the tertiary care hospitals had to prepared sufficient beds and appropriate treatment protocols to maintain the quality of intensive care for COVID-19 patients At Tokyo Medical and Dental University (TMDU) medical hospital, the entire hospital staff coordinated to optimize the hospitalized care of COVID-19 patients, and several wards have been re-engineered as designated COVID-19 treatment facilities by installing temporary shields and partitions.

Study Design & Methods: Narrative review

Results: As for the treatment strategy of COVID-19, favipiravir (Avigan), a possible antiviral drug for influenza or Ebola virus diseases, was given as 1st choice of treatment in the initial phase as well as hydroxychloroquine/chloroquine. However, favipiravir did not produce statistically meaningful outcomes based on the study in Japan. Current treatment guidelines in Japan recommend dexamethasone and remdesivir. Management of health-care workers is also an important problem to maintain the quality of care and to prevent their health problems. In TMDU, the mental support team was launched to prevent burnout, and a weekly PCR test was mandatory for all staff who were involved in COVID-19 patient care to guarantee their safety.

Conclusions: Our strategy has been successful with regard to no collapse of the medical care system and the absence of intra-hospital SARS-CoV-2 transmission. We expect this review to be helpful for improving the planning of hospitals during the COVID-19 and other infectious pandemics.

Wednesday 16 December 2020

S48: Ivermectin for malaria: characterizing pharmacokinetics, metabolites and impacts on *Anopheles* and *Plasmodium*

16.10-17.40hr

Room B

Chairpersons:

1. Kesinee Chotivanich
2. Joel Tarning

Invited speakers:

1. Ivermectin and its metabolites
   Phornpimon Tipthara Wong
   Mahidol Oxford Tropical Medicine Research Unit, Thailand

2. Ivermectin metabolites and *Anopheles*
   Kevin Kobylinski
   Armed Forces Research Institute of Medical Sciences, Department of Entomology, Thailand

3. Ivermectin metabolite pharmacokinetics
   Richard Hoglund
   Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand

4. Ivermectin and artemisenin resistant *Plasmodium falciparum*
   Achaporn Yipsirimetee
   Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand

Title: Ivermectin and its metabolites

Author: Phornpimon Tipthara (Presenter), Mahidol Oxford Tropical Medicine Research Unit, Thailand

Background: Mass drug administration of ivermectin has been proposed as a possible malaria elimination tool. Ivermectin exhibits a mosquito lethal effect well beyond its biological half-life, suggesting the presence of active slowly eliminated metabolites.

Study Design & Methods: Human liver microsomes, primary human hepatocytes, and whole blood from healthy volunteers given oral ivermectin were used to identify
ivermectin metabolites by ultra-high performance liquid chromatography coupled with high resolution mass spectrometry. The molecular structures of metabolites were determined by mass spectrometry and verified by nuclear magnetic resonance. Pure cytochrome P450 enzyme isoforms were used to elucidate the metabolic pathways.

Results: Thirteen different metabolites were identified after incubation of ivermectin with human liver microsomes. The 3″-O-demethyl ivermectin, 4-hydroxymethyl ivermectin, and 3″-O-demethyl, 4-hydroxymethyl ivermectin were the dominant metabolites found in microsomes, hepatocytes, and blood from volunteers after oral ivermectin administration. Metabolic pathway evaluations with characterized cytochrome P450 enzymes showed that 3″-O-demethyl ivermectin was produced by CYP3A4 and CYP3A5, and that 4-hydroxymethyl ivermectin and 3″-O-demethyl, 4-hydroxymethyl ivermectin were produced by CYP3A4.

Conclusions: Demethylated and hydroxylated ivermectin are the main human metabolites in vivo.

Title: Ivermectin metabolites and *Anopheles*

Author: Kevin Kobylinski (Presenter) Armed Forces Research Institute of Medical Sciences, Department of Entomology, Thailand

Background: Ivermectin is lethal to blood feeding *Anopheles* mosquitoes and mass drug administration is currently under investigation in numerous countries, including Thailand, for its potential role as a vector control tool. Previously, ivermectin was shown to be x20 times more lethal to *Anopheles dirus* when fed blood from ivermectin-treated volunteers (400 µg/kg) compared to the same concentrations of ivermectin artificially spiked into membrane feeders. We suspect that this is due to ivermectin metabolites with mosquito-lethal efficacy which compounds the mosquito mortality effect beyond parent compound alone. Ivermectin is a racemic mixture of ivermectin B1a (>90%) and B1b (<10%), differing by an ethyl or methyl group at C26, respectively. Intriguingly, an earlier report found that the snail-lethal effect of ivermectin was entirely attributable to ivermectin B1b. Thirteen ivermectin metabolites were identified and described from human liver microsomes, hepatocytes, and treated volunteer plasma. The two most abundant metabolites were 3″-O-demethyl ivermectin and 4-hydroxymethyl ivermectin, and thus may be critical to the mosquito-lethal effect of ivermectin. The 4-hydroxymethyl ivermectin has been synthesized and fed to *Anopheles dirus*, a primary malaria vector found in the Greater Mekong Subregion. Several other ivermectin structures were acquired commercially including, pure ivermectin B1a and B1b, ivermectin aglycone, and ivermectin monosaccharide and their mosquito-lethal effect has been assessed and will be presented here. Mosquito-lethal results establish the proof-of-concept that ivermectin metabolites possess mosquito-lethal activity, and the mosquito-lethal effect of various structures provide insight into how ivermectin interacts with its target in *Anopheles*, the glutamate-gated chloride ion channel.

Title: Ivermectin and metabolite pharmacokinetics

Author: Richard Hoglund (Presenter), (1) Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Joel Tarning

Background: Ivermectin has shown great promise as a mosquito-lethal drug, which could be used in future mass drug administrations for malaria eradication. To optimise such trials, it is important to understand the pharmacokinetic properties of both ivermectin and its metabolites as well as the relationship between drug exposure and mosquito-lethal effect.

Study Design & Methods: Dense pharmacokinetic data from two clinical trials in healthy volunteers was used to develop the pharmacokinetic and pharmacodynamic models. The first study was a healthy volunteer trial investigating potential drug-drug interactions between ivermectin, dihydroartemisinin-piperaquine, and primaquine. The second study was a study in healthy volunteers designed to measure the metabolites of ivermectin. A total of 16 volunteers participated in the first study and 10 in the second, dense pharmacokinetic samples were collected in both studies and the levels of ivermectin and three metabolites were quantified at the department of clinical Pharmacology, MORU, Bangkok. In addition to the pharmacokinetic data, blood from the volunteers were fed to mosquitos and the mosquito mortality were measured. The collected data was used to develop pharmacometric models in NONMEM.

Results: The pharmacokinetic properties of ivermectin and its metabolites were successfully described by the developed population pharmacokinetic model. The model described the observed data adequately and showed good precision in parameter estimates. The pharmacokinetic model was fixed and linked to a population pharmacodynamic model describing mosquito mortality. This pharmacokinetic-pharmacodynamic model described successfully the observed concentration measurements of ivermectin and its metabolites, as well as their relationship to mosquito mortality.

Conclusions: A pharmacometric model was developed successfully, which could be used to simulate different dosing scenarios of ivermectin treatment and mass drug administration, and inform optimal use in malaria elimination campaigns.

Title: Ivermectin and artemisinin resistant *Plasmodium falciparum*

Author: Achaporn Yipsirimetee (Presenter), Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
Co-authors: Phornpimon Tipthara Wong, Amornrat Promsongsil, Pornpawee Chiewpoo, Patpannee Khanthagan, Sirinatda Sanguan, Tianrat Piteekan, Arjen Dondrop, Kesinee Chotivanich, Kevin Kobylinski, Joel Tarning

Background: Artemisinin resistance of *Plasmodium falciparum* has emerged and spread widely in Southeast Asia. Ivermectin was introduced to mass drug administration program in order to interrupt malaria transmission through its mosquito-lethal effects. However, the effect of ivermectin and its metabolites on the asexual blood stage of the parasite is unclear. The aim of this study was to investigate the effects of ivermectin on the asexual blood stage of artemisinin-sensitive and artemisinin-resistant *P. falciparum* isolates.

Study Design & Methods: The susceptibility of artemisinin-sensitive and artemisinin-resistant *P. falciparum* parasite isolates to artesunate and ivermectin were investigated using the trophozoite and schizont maturation inhibition assay. Parasites were incubated with ivermectin (0.1-100 µg/mL), artesunate (0.4-400 ng/mL), and artesunate (0.4-400 ng/mL) plus ivermectin (fixed concentration at 50 ng/mL) for 24 and 48 hours. Susceptibility testing of parasite isolates with ivermectin and its common metabolites (ivermectin-B1a-aglycone, ivermectin-monosaccharide and ivermectin-4-OHMe) were also evaluated at varying concentrations using the SYBR green assay (incubation for 72 hours). Data were evaluated by a sigmoidal dose-response analysis, and results presented as concentrations associated with 50% inhibition (IC50).

Results: The effect of ivermectin on the asexual blood stage (N=8) was relatively low, resulting in a high IC50 value (IC50=817.82±149.87 nM) compared to that of artesunate (IC50=3.80±1.33 nM). Furthermore, there was no difference in ivermectin effect when evaluated with artemisinin-resistant and artemisinin-sensitive isolates. None of the evaluated ivermectin metabolites showed an increased potency compared to ivermectin.

Conclusions: Ivermectin and its metabolites did not show any clinically relevant parasite-inhibition effects on the asexual blood stage of *P. falciparum* parasites. These results were not different in artemisinin-resistant and artemisinin-sensitive isolates. Further investigation is needed to evaluate the effects of ivermectin and its metabolites on other parasite stages such as gametocytes.

Wednesday 16 December 2020

S49: Biologics development for prevention and treatment of viral diseases

16.10-17.40hr

Room C

Chairperson: Pongrama Ramasoota

Invited speakers:

1. RGD-AAV bacteriophage delivery system for vaccine and therapeutic development
   Amin Hajitou
   Imperial College, London, United Kingdom

2. *In silico* and *in vitro* analysis of small molecules and natural compounds targeting feline coronavirus (CoV) main protease, a surrogate platform for CoVs
   Sirin Theerawatanasirikul
   Faculty of Veterinary Medicine, Kasetsart University. Thailand

3. Therapeutic antibody against dengue virus: toward commercialization
   Pongrama Ramasoota
   Center of Excellence for Antibody Research, Faculty of Tropical Medicine, Mahidol University, Thailand

4. Characterization of human anti-dengue NS1 monoclonal antibodies derived from Thai DENV2 patients
   Pannamthip Pitaksajjakul
   Center of Excellence for Antibody Research, Faculty of Tropical Medicine, Mahidol University, Thailand

Title: *In silico* and *in vitro* analysis of small molecules and natural compunds targeting feline coronoavirus (CoV) main protease, a surrogate platform for CoVs

Author: Sirin Theerawatanasirikul (Presenter), Kasetsart University, Thailand
Co-authors: Chalermpol Lekcharoensuk, Chih Jung Kuo, Jullada Chootip, Nanthawan Phetcharat, Porntippa Lekcharoensuk

Background: The novel emerging coronavirus or SARS-CoV-2, the causative agent of the pandemic COVID-19, rapidly spreads worldwide. Recently, remdesivir was the only antiviral drug authorized by FDA for emergency treatment of COVID-19. Thus, the researchers rush to discover other potential antiviral agents to conquer this CoV. In addition, the cell-based screening for anti-SARS-CoV-2 requires the biosafety level 3 (BSL-3) laboratory for safety of workers and environment. Feline coronavirus (FCoV) belongs to family Coronaviridae and causes severe fatal disease in cats. A mutated FCoV variant–feline infectious peritonitis virus (FIPV)– can be handled and performed in a BSL-2 laboratory.

Study Design & Methods: We investigated interaction between the FIPV main protease and small molecules or natural compound from libraries using in silico virtual screening. The potential molecules with good binding affinities were retrieved from the libraries for protease inhibition and antiviral activity assays.

Results: Our results showed that the small molecules (NSC71097, NSC629301 and NSC282187) and the natural compounds (7-methylluteolin, stictic acid, quercetin 7-rhamnoside and chaetochromin) were good inhibitors. The results demonstrated that antiviral activity of stictic acid (NSC87511), chaetochromin (NSC345647), and small molecules (NSC71097 and NSC629301) could inhibit viral replication using IPMA and RT-qPCR assays. Moreover, the compounds structurally fit in the substrate binding site of the main protease of FIPV and other CoVs including SARS-CoV, SARS-CoV-2 and MERS-CoV, respectively.

Conclusions: Our investigations have revealed the potential antiviral compounds for novel drug development against FCoV or other emerging CoVs in both humans and animals. This study also showed that FCoV can be exploited as a surrogate platform for CoVs.

Title: Therapeutic human monoclonal antibody against dengue virus; toward commercialization

Author: Pongrama Ramasoota (Presenter), Center of Excellence for antibody research (CEAR), Faculty of tropical medicine, Mahidol University, Thailand

Background: Dengue hemorrhagic 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.

Study Design & Methods: 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 established at CEAR.

Results: Two candidates NhuMAb (clones 19 and 54) were successfully pre-clinically tested in vitro by 95-100 % neutralized all 4 serotypes of 20 clinical isolates DENV and in vivo tested by significantly decreased mortality of prior DENV intra-cranially mice and eliminated DENV (from 1010 to be 0) in blood of DENV challenged Marmoset monkeys within 2 days. To make NhuMAb without causing ADE, FC-modified at LALA position of both NhuMAb clones was established. Industrial scale production of NhuMAbs using the Food and drug administration (FDA) accepted method of Stable expressed Chinese Hamster Ovary (CHO) cell produced at GMP facility was prepared at the licensing company. AG129 mice that 24 hr. prior subcutaneously injected with 105 FFU DENV followed by treated with Fc-modified NhuMAb clone 54 showed almost 100 % survival

Conclusions: The licensing company is ongoing to test this Fc-modified NhuMAb clone 54 for further safety and toxicity tests, followed by Phase 1 clinical trial in the near future (2024).

Title: Characterization of human anti-dengue NS1 monoclonal antibodies derived from Thai DENV2 patients

Author: Pannamthip Pitaksajjakul (Presenter), Faculty of Tropical Medicine, Mahidol University, Thailand
Co-authors: Siriporn Kowaboot, Surachet Benjathummarak, Wilarat Poungmanee, Khwanchit Boonha, Urai Chaisri, Pongrama Ramasoota

Background: Dengue is one of the most important mosquito-borne disease in the tropics and subtropics. Severe dengue cases usually occur among patients secondarily infected with different serotypes. Recently, antibodies targeted to dengue NS1 protein have been interested due to their absence of ADE. Mouse antibodies specific to NS1 have been widely studied for their cross-reactivity with several human molecules. In this study, the first cross-reactivity study of dengue NS1 specific human monoclonal antibodies (HuMAbs), isolated from DENV2 infected patients were reported.

Study Design & Methods: Nine anti-NS1 HuMAbs derived mainly from convalescent-phase patients with secondary DENV-2 infections were characterized. The target epitopes were determined against truncated-NS1-protein-expressing Escherichia coli lysates. Their cross-reactivity with plasminogen, thrombin, and endothelial cells was investigated, and then plasmin-formation assays were performed.

Results: All HuMAbs recognized the NS1 C-terminus located in the region defined by residues 301–352 and were cross-reactive with human plasminogen (Plg), but not thrombin. Some clones showed cross-reactivity with endothelial cells. Moreover, all HuMAbs that showed cross-reactivity with Plg converted Plg to plasmin in a plasmin-formation assay.

Conclusions: These results suggest the potential implications and drawbacks of anti-NS1 antibodies for immunotherapy.

Wednesday 16 December 2020

S50: Emerging viruses

16.10-17.40hr

Room D

Chairperson: Jonas Schmidt-Chanasit

Invited speakers:

1. Sars-CoV-2 vaccine development**:** progress and challenges (no abstract)
   Marylyn Addo
   University of Hamburg, Germany

2. Lassa fever in Africa
   Stephan Guenther
   Bernhard Nocht Institute for Tropical Medicine, Germany

3. Sars-CoV-2 animal models (no abstract)
   Martin Beer
   Friedrich-Loeffler-Institut, Germany

Title: Lassa fever in Africa

Author: Stephan Guenther (Presenter), Bernhard-Nocht-Institute for Tropical Medicine, Germany

Background: Lassa fever is an acute febrile illness associated with bleeding, encephalopathy and multiple organ failure. It is caused by the Lassa virus, a member of the Arenaviridae family. The natural host of Lassa virus is rodents of the species Mastomys natalensis. The disease is endemic in the West African countries of Sierra Leone, Guinea, Liberia, Mali, Benin and Nigeria. Some 100,000-300,000 estimated infections occur annually, with an overall mortality rate of 1-2%. Hospital mortality rates are around 20-30%, but can be as high as 65% in nosocomial Lassa fever epidemics caused by human-to-human transmission of the virus. The only drug available is the broad-spectrum nucleoside analogue ribavirin, although its clinical effectiveness is being questioned. Vaccines for use in humans are not available. The pathophysiological cascade leading to organ failure and death from Lassa fever is still poorly understood. Due to the high pathogenicity of Lassa virus and the limitations in preventing or treating infections, the virus is classified as a level 4 pathogen.

Study Design & Methods: The long-term cooperation with our partner institution in an endemic area in Nigeria - the Irrua Specialist Teaching Hospital (ISTH) - including the establishment of a laboratory for molecular diagnostics of Lassa fever and a ward for the treatment of Lassa fever patients more than 10 years ago has laid the foundation for observational studies and clinical trials.

Results: Studies have been conducted on the diagnosis, pathophysiology, immunology and molecular epidemiology of Lassa fever. Clinical trials are underway to improve patient management, drug treatment and prevention of Lassa fever.

Conclusions: Our partners in Africa and we have gained new insights into different aspects of Lassa fever and improved the management of this deadly disease.

Wednesday 16 December 2020

S51: COVID-19 response in relation to other disease control program (Thai/Eng session)

16.10-17.40hr

Room E

Chairperson: Wanna Hanshaoworakul

Invited speakers:

1. Developing tools for enhancing the surveillance of bat-borne pathogens in livestock and surveillance of COVID-19 in animals (no abstract)
   Weerapong Thanapongtharm
   Bureau of Disease Control and Veterinary Services, Department of Livestock Development, Thailand

2. The new normal: prevention and control of non-communicable diseases in the COVID-19 mitigating (no abstract)
   Sasithorn Tungsawat
   Division of Non Communicable Disease, Department of Disease Control, MOPH

3. Tobacco control program and COVID-19 (no abstract)
   Chayanan Sittibusaya
   Office of Tobacco Products Control Committee, DDC, MOPH

4. TB control and COVID-19 (no abstract)
   Phalin Kamolwat
   Division of Tuberculosis Department of Disease Control, MOPH

5. HIV, STIs and COVID – 19: impact on sex workers and people living with HIV (no abstract)
   Taweesap Siraprapasiri and Surang Janyam
   Disease Control Department of the Ministry of Public Health; Workers in Group (SWING) Foundation

S52: Closing Ceremony

17.40-18.40

Chairperson: Weerapong Phumratanaprapin

“Recent advances in antiparasitic chemotherapy”

Keynote Speaker

Prof. Sir Nicholas White
Professor of Tropical Medicine, Mahidol University and University of Oxford