

Thailand Laos Melioidosis Network Meeting I

Date and Venue: 22 March 2012, Mahidol-Oxford Research Unit (MORU), BKK, Thailand

Aim: Close meeting among leading scientists in melioidosis research and policy makers in Thailand and Laos. Main purposes are to (1) update information among participants, (2) form collaboration among research institutes and government authorities, and (3) discuss on the important issues related to situations of melioidosis in Thailand, including epidemiology, diagnosis, treatment, prevention, public awareness and public engagement.

Participated organizations: Bureau of Emerging Infectious Disease and Bureau of Epidemiology, Ministry of Public Health (MoPH), Thailand; Center of Disease Control (CDC), Thailand; Khon Kaen University; Mahosot-Oxford Research Unit, Laos; Faculty of Medicine, Siriraj hospital, Mahidol-Oxford Research Unit, and Faculty of Tropical Medicine, Mahidol University

Executive summary:

- 1) Melioidosis is an important cause of death in Thailand. Estimated total death due to this disease is more than 1,000 people per year. The number reported by national statistics are underestimated because of the difficulty in disease diagnosis, patients died prior to diagnosis or died at home, and failure to report to MoPH by the hospitals.
- 2) Knowledge of prevention for melioidosis is available and drinking untreated water is a risk. This includes well water, borehole water, and un-chlorinated tap water.
- 3) Melioidosis is an urgent issue that requires a raise in public awareness of the disease and to improve their knowledge on the prevention scheme of this disease countrywide. Chlorination of all village tap water supply and campaign for drinking only clean water is also urgently needed. Melioidosis will be included into the campaign for emerging diseases by MoPH and also promoted under ONE HEALTH campaign. Faculty of Tropical Medicine, Mahidol University will promote this disease via MELIODOSIS CLIP CONTEST, which will be launched in May 2012.
- 4) “Melioid” was chosen as Thai name for melioidosis and this name will be used for all campaigns.
- 5) Melioidosis vaccine is desperately needed for Thailand but it is not currently available. Bottlenecks of vaccine development include lack of, but not limit to, knowledge on immunology, good vaccine candidates and appropriate animal models.
- 6) Next meeting (TLMNM II) will be held at MORU, Bangkok in October 2012. Doodle will be sent out among participants in June to set the best date.

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Agenda of the meeting

Date: 22 March 2012

Venue: 420/6 Rajvithi Rd, BKK (<http://www.tropmedres.ac/about-moru-summary/contact-us>)

Date: Thursday 22 March 2012

Time	Agenda	Speakers
09.30-09.45	Registration and coffee	
09.45-10.00	Welcome & Introduction	DL
10.00-12.00	Current and future studies in melioidosis	
	10.00 – 10.30 MORU	DL, AJ, PC
	10.30 – 11.00 KKU	SW, GL
	11.00 – 11.15 Siriraj	SK
	11.15 – 11.30 CDC Thailand	KB
	11.30 – 11.45 LOMWRU	DD
11.45-12.00	Situation of melioidosis in Thailand by MOPH	SL
12.00-13.00	Lunch Break	
13-00-14.30	Close discussion	Thai participants
	1. Viewpoints on melioidosis	
	2. Thai name for melioidosis	
	3. Public engagement: How can we increase public awareness and improve prevention for melioidosis?	
14.30-16.00	Open discussion	Everyone
	Future trends of Melioidosis Research in Thailand:	
	Topics:	
	1. Research: What can we do to improve the diagnosis, treatment and prevention of melioidosis?	
	2. Melioidosis vaccine: Where are the bottlenecks in the development of melioidosis vaccine?	
	3. Collaboration and Networking: how can we help each other?	
	4. Next meeting: When and where?	

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List of participants

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Summary of the morning session (research update)

Mahidol-Oxford Research Unit (MORU) and Faculty of Tropical Medicine, Mahidol University. The unit focuses on epidemiology, environmental factors, immunology, diagnosis, treatment and public engagement of melioidosis. Website: <http://www.tropmedres.ac>

Direk Limmathurotsakul (DL) presented recent evidence of routes of melioidosis acquisition and activities of daily living associated with melioidosis acquisition. Key finding is that 10% of well water, borehole water, and tap water supply is contaminated with *B. pseudomallei* and that the population at risk are drinking those water without treatment. Filtration is not effective in elimination of this organism, and this could be due to poor maintenance of the machine.

Anchalee Jatapai (AJ) presented how to diagnose melioidosis and showed that culture is gold standard for diagnosis but time consuming and low sensitivity. Serological test such as IHA (indirect hemagglutination test) could give false positive result. Culture result may come back after patients died and the hospital may fail to report to MoPH. Study is being conducted for the true mortality of melioidosis and it shows that the true death due to melioidosis in NE Thailand is very high.

Praveen Chansrichavala (PC) presented on the development of melioidosis research communities and on-going work of melioidosis public engagement. These include website for melioidosis (www.melioidosis.info) and facebook page for melioidosis in both English (www.facebook.com/melioidosis.info) and Thai (www.facebook.com/melioid). PC presented the upcoming “Melioid Clip Contest” that will be launched in May 2012.

Melioidosis Research Center (MRC) and Khon Kaen University. The unit focuses on epidemiology, environmental factors, immunology, treatment and bacteriology. Website: <http://www.md.kku.ac.th/melioid2>

Dr Surasakdi Wongratanacheewin (SW) presented recent studies conducted by Melioidosis Research Center (MRC). The MRC members recently found that the LL-31 and LL-37, and cathelicidin, are more effective in killing biofilm form of *B. pseudomallei* than ceftazidime. Moreover, numerous bacteriophages specifically lysed *B. pseudomallei* were isolated from soil in the endemic area. These bacteriophages were found to interfere with the infectivity of *B. pseudomallei* in A549 cells. The MRC team also constructed metagenomic library for screening the products that can inhibit *B. pseudomallei*.

Dr Ganjana Lertmemongkolchai (GL) presented an overview of their research interests on human cellular, cytokine and antibody immune responses, searching for vaccine candidates and development of diagnostic tools using high throughput technology such as proteomics and transcriptomics analysis. The work in their group has received an initiative fund for research and development from the Wellcome Trust, UK and currently from the US NIAID/NIH funds in collaborations with overseas colleagues (UK, US and EU). Their collaborations in Thailand include colleagues at Siriraj Hospital, Sappasitthiprasong Hospital, Khon Kaen Regional Hospital, Sakol Nakorn Hospital and Primary Health Care Units/Hospitals in the upper Northeast Region. However, the obstacle in searching for vaccine is the lack of animal models for diabetes that are suitable for melioidosis.

Siriraj Hospital.

Dr Sunee Korbsrisate (SK) presented the scope of research conducting at Siriraj Hospital. This includes construction of *B. pseudomallei* mutant and characterization of mutation on the intracellular survival of this bacterium. *B. pseudomallei* mutations including genes encoding for BimA, phospholipase C, sigma factor E, and ABC transporter. The projects were done in collaboration with colleagues from UK, Singapore, Dr. Ganjana and Dr. Narisara. In addition, we are currently working on the isolation and characterization of bacteriophages which infect *B. pseudomallei*.

CDC Thailand. The unit of CDC in Thailand has been conducting research in causes and outcomes of pneumonia and bacteremia in Thailand. The unit has been focusing on epidemiology and health economic impact of melioidosis in Thailand.

Kip Baggett (KB) presented the recent study of epidemiology of melioidosis, “Burden and seasonal distribution of bacteremic melioidosis in Eastern, NE, Thailand: Sa Kaeo and Nakorn Panom”. Incidence of melioidosis is largely underestimated if blood culture is not performed in all patients suspected pneumonia or sepsis. The financial burden of melioidosis in terms of hospital cost, morbidity and mortality are extremely high and concerns for this disease need to be raised by the local health authorities.

Mahosot Oxford Research Unit (LOMWRU). The unit is located at Mahosot Hospital, Vientian, Laos. This unit is a sister unit of MORU, Bangkok and has been conducting melioidosis research for more than 10 years.

Dr David Dance (DD) presented the situation of melioidosis in Laos, which has more than 400 culture confirmed melioidosis patients in the last 10 years. It is important that there is a

better understanding about uneven distribution in melioidosis. Current ongoing work: collaborate with a French soil scientist to look at the different of soil types and association with *B. pseudomallei*.

Ministry of Public Health, Thailand

Soawapak Laosiritaworn (SL): presented the national statistics and methods to gather the data from every hospitals in Thailand. It is clear that the total number of melioidosis patients and the total number of death due to melioidosis are under reported. Melioidosis is also found in a number of zoos in Thailand and animal melioidosis, and is also an important cause of death for farmers in Thailand.

Summary of the afternoon session (1st half, among Thai participants)

1. Viewpoint of melioidosis from Ministry of Public Health

The numbers reported by national statistics are clearly underestimated because the disease is difficult to diagnose, patients died prior to diagnosis or died at home, and failure to report to MoPH by the hospitals.

Melioidosis is considered as an important emerging disease of Thailand. It is an urgent issue that requires a raise in public awareness of the disease and to improve their knowledge on the prevention scheme of this disease countrywide. Chlorination of all village tap water supply and campaign for drinking only clean water is also urgently needed countrywide. Melioidosis will be included into the campaign for emerging diseases by MoPH and also promoted under ONE HEALTH campaign.

It is suggested that there should be recommendation for water treatment with chlorination before consumption, especially water sources from well, borehole, river and tap water supply. The evidence-based finding of *B. pseudomallei* in untreated water and death-cases of melioidosis in non-endemic area are enough concerns to drive an effective prevention and control measurement and raise public awareness. The local authority, public health officer, government and non-government persons should collaborate and discuss these findings and how to handle the increasing incidence of melioidosis effectively.

2. Thai Name for Melioidosis in Thai

“Melioid” (โรคเมลลิออยด์) has been agreed upon by MOPH and researchers until otherwise decided. Public have previously adopted English names for other diseases, e.g. Malaria, Legionnaires; therefore, there are no foreseeable problems in adopting the word “Melioid”. Other names have been suggested, for example “โรคไข้ดิน” and “โรคฝีดิน” but these names do not capture the nature of melioidosis sufficiently. “Melioid” has three syllables and has been widely used among melioidosis patients and melioidosis clinics countrywide. Therefore, it is the best name for all of public engagement campaigns presently.

3. Collaboration among Thai researchers

Melioidosis researchers in Thailand are reducing. It is important to have collaboration particularly in issues that have high impact on the country as a whole. Public health prevention and control program is essential. Bureau of Epidemiology and MOPH should use the existing data on incidence and prevention that is already available (for example, data shared by Dr. Direk, Dr Wironrong and Dr Surasak at this meeting) and translate these raw data into communication to the general public. Besides collaboration and networking, capacity building is also very

important. Young researchers should be educated and supported towards melioidosis research in the future. Moreover, international collaboration is also very important.

4. World Melioidosis Congress 2013

Next World melioidosis congress (7th) will be on 18-20 Sept 2013 in Bangkok Thailand. The pre-meeting workshop will be melioidosis case observations at Ubon Ratchathani and Khon Kaen if possible. Reduction of price for Thai students will be done in order to increase the amount of Thai participants.

Summary of the afternoon session (2nd half, all participants)

1. What can we do to improve the diagnosis, treatment and prevention of melioidosis?

Dr. Kip Baggett from CDC Thailand has raised a very important concern that there is a lack of current guideline in treatment of Melioidosis in Thailand. There is a need for treatment guideline as Melioidosis is a prominent disease in Thailand. This guideline will also reduce over or under prescription of antibiotics in the non-melioidosis and melioidosis patients.

Action point: Dr. Pleonchan Chetchotisak will coordinate a meeting with “Infectious Disease Association of Thailand (สมาคมโรคติดเชื้อแห่งประเทศไทย www.idthai.org)” and discuss this to set up a national guideline for diagnosis and treatment of Melioidosis in Thailand

Concerns regards potential underdiagnosis of melioidosis in hospital laboratories in Thailand has been raised. **Dr. David Dance** suggested that the problems may lie within the identification of *Burkholderia pseudomallei* and drug sensitivities rather than the capacity of growing the bacteria. Provincial hospitals have good system and knowledgeable laboratory technicians, however, this may not be the case in hospitals outside of northeast of Thailand. In UK, there is a national standard bacteriology methods and laboratory accreditation scheme.

Action points:

1. There should be at least SOPs for bacterial identification in English and Thai version. Dr. Direk Limmathurotsakul suggested that a draft should be made and circulates amongst the network members to finalize the SOP. This could then be implemented nationally. These SOPs will also be uploaded onto the melioidosis website (www.melioidosis.info).
2. Annual training workshop should be planned to adjoin big annual meetings belonged to The Association of Medical Technologists of Thailand (www.amtt.org). This can improve the knowledge of lab technicians and medical technologists regarding the identification of *B. pseudomallei*.
3. To improve public awareness and knowledge of melioidosis prevention, “Melioid Clip Contest” will be launched by Faculty of Tropical Medicine, Mahidol University. Partners and sponsors are more than welcome.

2. Progression of melioidosis vaccine

Dr Ganjana Lertmemongkolchai summarized that there are several vaccine candidates but none has shown absolute protection. A conjugated vaccine is being investigated but it is too early to conclude. The vaccine most likely would target the population groups that are at risk of developing melioidosis, e.g. diabetics patients. Moreover, there is a lack of well described diabetic mice model and non-human primate model, which is very desirable to evaluate vaccines.

Although there is a very clear need for melioidosis vaccine in Thailand, there are a number of bottlenecks in the vaccine development. This includes lack of, but not limit to, knowledge on immunology, good vaccine candidates and appropriate animal models.

3. Next meeting: Where, When and How often?

It is suggested and agreed by all members that the network meeting should be kept small and every 6 months. Next meeting will be at MORU in October 2012.

Action point: Praveen and Anchalee will send out doodle in the next 2 months.

Conclusion of the meeting

At the TLMNM meeting held on Thursday 22 March 2012 at Mahidol-Oxford Research Unit (MORU), Bangkok, Thailand, where Researchers Meet Policy Makers, a consensus agreement on assigning a Thai name for melioidosis have been agreed upon “Meliod” or “โรคเมลลิออยด์”. Other important issues that have been raised include the importance of translating the existing evidence regards the incidence and reports of melioidosis outbreak into an effective prevention and control measurement and policy. This will only be achievable through a strong link and collaboration between the researchers and MOPH. Contamination in water supply sources with *B. pseudomallei* has been reported in the endemic areas (Northeast and South of Thailand) and it is imperial that MOPH implements water supply management nationally. Under report of melioidosis incidence have been acknowledged in the meeting and a national surveillance system needs to be updated, so that a true incidence rate of melioidosis is reported. It is only through these recognitions that a health control and prevention program can arise and implement and thus, benefit the public.

Currently, there is a lack of National Guideline for Treatment of Melioidosis in Thailand and a Standard Clinical Microbiology Diagnostic Methods. Writing up these guidelines will provide clinicians and laboratory technicians with a better recognition and identification of melioidosis in patients. It is agreed that drafts of the guideline in treatment and standard clinical microbiology diagnostic method would be written up by clinicians (this will be brought up in the Infectious Disease Association of Thailand) and researchers within this group, respectively, and circulate for comments and revisions before final agreement is reached.

Due to high morbidity and mortality rate of melioidosis in Thailand, this stimulates the need for melioidosis vaccine. However, this is still a long road as mechanism of immune responses to *B. pseudomallei* in different group of patients needs to be dissected. In addition, there is a lack of a good diabetic mice model (this represents the target group of patients who are highly susceptible to melioidosis) in which evaluating vaccines in natural infection is needed.

At the end of the meeting, it was concluded that there is a need of an ongoing collaboration between the researchers and MOPH in order to drive implementation of melioidosis health control and prevention program forward, e.g. water supply management supply and promoting preventive measures. The other important area that would prove fruitful is the national guideline and SOPs in the treatment and diagnosis of Melioidosis. Several vaccine candidates have been identified but there is a lack of well described diabetic mice model and non-human primate model. However, if there is a promising vaccine, this could prove to be one aspect of public health initiative to reduce the incidence of melioidosis.

The next meeting is to be held in October 2012 at MORU.