Melioidosis

Melioidosis is caused by *Burkholderia pseudomallei,* gram negative bacilli bacteria with a characteristic "safety pin" appearance (bipolar staining) on Gram staining. Generally, *B. pseudomallei* is prevalent in soil and water in all regions of Thailand, particularly in the northeastern, eastern, and southern parts of the country.(1) Patients could become infected with the organism via prolonged exposure to soil and water, e.g. from rice farming or via cuts and sores in the skin, drinking and ingestion of contaminated water and food, or inhalation of dust contaminated with the organism.

Melioidosis patients generally have no specific signs and symptoms. They may present with only high fever and shock due exclusively to the infection. In addition, this can potentially be accompanied by pulmonary infection, or multiple organ infections such as lesions and abscesses in the lung, liver, or spleen at the same time. Its average incubation period after acquiring the organism is approximately nine days, but could also be as short as one day, or even as long as years.(2) Signs and symptoms of melioidosis are typically similar to those of other infectious diseases, e.g. bloodstream infections due to other bacterial species, leptospirosis, scrub typhus, and malaria. It has been found that patients with acute bloodstream infection usually died very quickly within 1-3 days following hospital admission.(3) It is therefore very important that melioidosis be diagnosed and confirmed by bacterial culture from clinical samples infected with the organism such as blood, sputum, and urine. This is because bacterial culture is the most accurate diagnostic method available that will determine the clinical outcomes and survival of the patients. However, bacterial culture also has its limitations as it will rely solely on the availability of microbiology laboratory and highly skilled laboratorians to perform the diagnostic test and bacterial characterization and typically it will take approximately 3-7 days for the results to become available.

Melioidosis diagnosis using antibody method, for instance, testing for antibodies to *B. pseudomallei* using indirect hemagglutination (IHA) technique, has been found to have low sensitivity and specificity. Approximately 10-30 percent of Thai populations have been found to be intrinsically *B. pseudomallei* positive as the vast majority of Thais are farmers who are exposed to this soil-dwelling bacterium in their daily life activities, thus resulting in a high level of false positive results. Given this confirmatory tests must be performed using bacterial culture method only.

Effective disease prevention measures include wearing of personal protective gears, e.g. rubber boots and gloves while working in paddy fields or being exposed to soil and water for an extended period of time, boiling water from all water sources (rain water, tap water, water from natural water sources) before drinking, and eating only clean and thoroughly cooked foods. Those who have survived from acute melioidosis will need to be treated continuously by antibiotics co-trimoxazole for five months in order to prevent relapse of the disease.

Recently Melioidosis Research Center, Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University and Melioidosis Research Center, Khon Kaen University have developed and introduced a diagnostic test for *in vitro* bacterial detection and characterization using a latex agglutionation test (LA test). This diagnostic technique is being implemented in a pilot phase in a number of health facilities in Thailand's northeastern region. It is capable of accurately identifying *B. pseudomallei* in just two minutes, while identification of this melioidosis causative agent using biochemical reaction-based methods will take 24 hours. It should also be noted that for those laboratories with a lack of necessary capacity it is more likely that this causative agent might potentially be misidentified as a contaminant, *Pseudomonas spp.*, or other pathogens. In addition, a diagnostic test has also been developed and implemented for detection and characterization of the pathogen directly from clinical samples using an immunofluorescence assay (IFA). Currently this diagnostic test is being implemented in a pilot phase in some research units in the northeastern region and to date it has proved relatively effective in accurately diagnosing the disease in a more timely manner, thus resulting in better clinical outcomes.(4) Still, in order for the immunofluorescence assay (IFA) to be properly performed, a specialized microscope, which is usually not available in microbiology laboratories in general, is also needed.

At present, all microbiology laboratories across the country are recommended that any gram-negative, motile rod-shaped, oxidase-positive bacilli isolated from clinical specimens should always be initially identified and confirmed as non-*Burkholderia pseudomallei.* Specifically, the organism isolated from blood sample that resembles soil-dwelling bacteria should not be immediately identified as a contaminant and gram-negative, motile rod-shaped, oxidase-positive bacilli should not be identified as only *Pseudomonas* spp*.,* without adequately verifying that the organisms are not *Burkholderia pseudomallei.* In the event that the organism is sensitive to ceftazidime, amoxicillin-clavulanic acid, while it is resistant to gentamycin and colistin, more attention should be paid to *Burkholderia pseudomallei.* Additionally, laboratories should be made aware that *Burkholderia pseudomallei* is prevalent in all regions of Thailand and remains one of the important causes of death.

In 2016, based on the data from its existing surveillance system (Report 506), the Bureau of Epidemiology (BOE) reported a total of 3,045 cases of melioidosis, representing a morbidity rate of 4.63 per 100,000 populations (including 100 deaths). These fatal cases were reported from Ubon Ratchathani (87), Surat Thani (6), Songkhla (2), Pichit, Uthai Thani, Maha Sarakham, Nakhon Si Thammarat, and Phang Nga (1 fatal case each), representing a mortality rate of 0.15 per 100,000 populations and case fatality rate of 3.28 percent. Retrospectively, over the past 10 years (from 2007-2016), the case fatality rate from melioidosis was found to have peaked in 2015 and dropped slightly in 2016 (Figure 1).

Nevertheless, the number of reported cases available from the existing surveillance system has yet to include the number of morbidity and mortality due to melioidosis from other provincial and regional hospitals with microbiology laboratory at their disposal. In the northeast, for instance, the number of reported cases of melioidosis in the existing surveillance system was based only on the data provided by Sappha Sitthiprasong Hospital in Ubon Ratchathani, which included only the data of this northeastern province. Additionally, the surveillance system did not receive the data on melioidosis cases from other neighboring provinces, of which patients had been referred to Sappha Sitthiprasong Hospital and eventually died of melioidosis.

The reported cases of melioidosis included 1,087 females and 1,958 males, representing a female-to-male ratio of 1:1.8. The highest morbidity rate was found among individuals $\geq$ 65 years of age, at 9.60 cases per 100,000 populations. This was followed by those 55-64 years of age, at 9.35 cases per 100,000 populations, and people aged 45-54 years old, at 7.30 cases per 100,000 populations (Figure 2). The occupation most affected by the disease was farmer (49.95%), followed by casual laborer (13.63%), and student (9.26%). Thai nationals accounted for 98.36 percent of the patient population, followed by Burmese (0.36 percent), and Laotians (1.25 percent).

The disease is being reported throughout the year. In 2016 a seasonal pattern of melioidosis activity was found to be similar to that of the year 2015 and consistent with the medians within the last five years, which indicated that melioidosis activity typically peaks during the rainy season. In other words, a spike in melioidosis cases started from July and the trend continued through November. Subsequently a decrease in new cases was reported and it was then followed by another rise in meliodosis activity in January of the following year (see Figure 3).

The top five provinces in terms of the number of reported cases of melioidosis were in the northeast, namely Ubon Ratchathani (523 cases), Sisaket (455 cases), Roi Et (209 cases), Buriram (177 cases), and Mukdahan (144 cases). Based on the number of morbidity rate per 100,000 populations, however, the first five provinces included Mukdahan (41.29), Sisaket (30.96), Ubon Ratchathani (28.12), Amnat Charoen (25.48), and Roi Et (15.98) (Figure 4).

According to the data from the existing surveillance system (Report 506), the year 2016 has seen a slight decrease in the morbidity and case fatality rates of melioidosis from the year 2015. Nevertheless, to ensure the accuracy of the number of fatal cases from melioidosis, case reporting is also needed from other hospitals with microbiology laboratory capacity. Based on the data currently available, we can at least safely say that it is likely that in Thailand melioidosis cases can be found all year round, particularly during the rainy season. Given this fact disease surveillance and prevention efforts should be stepped up at the start of the rainy season. These may include public awareness campaign to educate the general public about how to prevent themselves from getting infected by the organism, e.g. by wearing rubber boots while tending to their rice fields and plantations, avoiding working during rainstorm and flooding, drinking clean water, and alerting and raising awareness among staff of health facilities so that clinical samples are collected from patients at risk for *B. pseudomallei* infection for laboratory analysis and proper treatment provided in a timely manner.

References:

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Fig.1 Reported cases of meliodosis per 100,000 population and case fatality rate by year, Thailand, 2007-2016

Fig.2 Reported cases of meliodosis by age-group, Thailand, 2012-2016

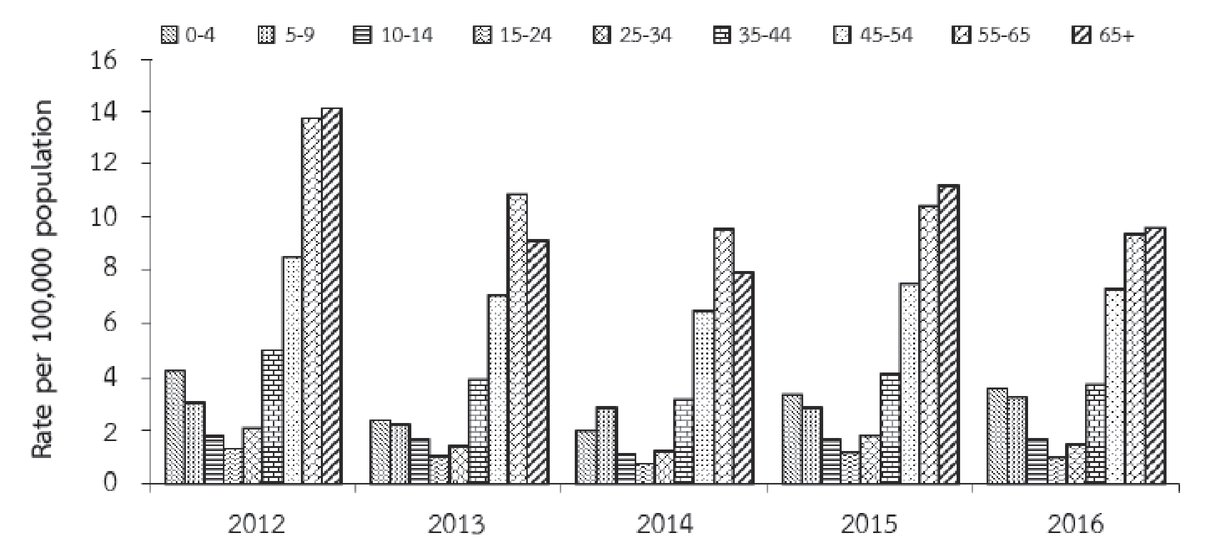


Fig.3 Reported cases of meliodosis by month, Thailand, 2015-2016

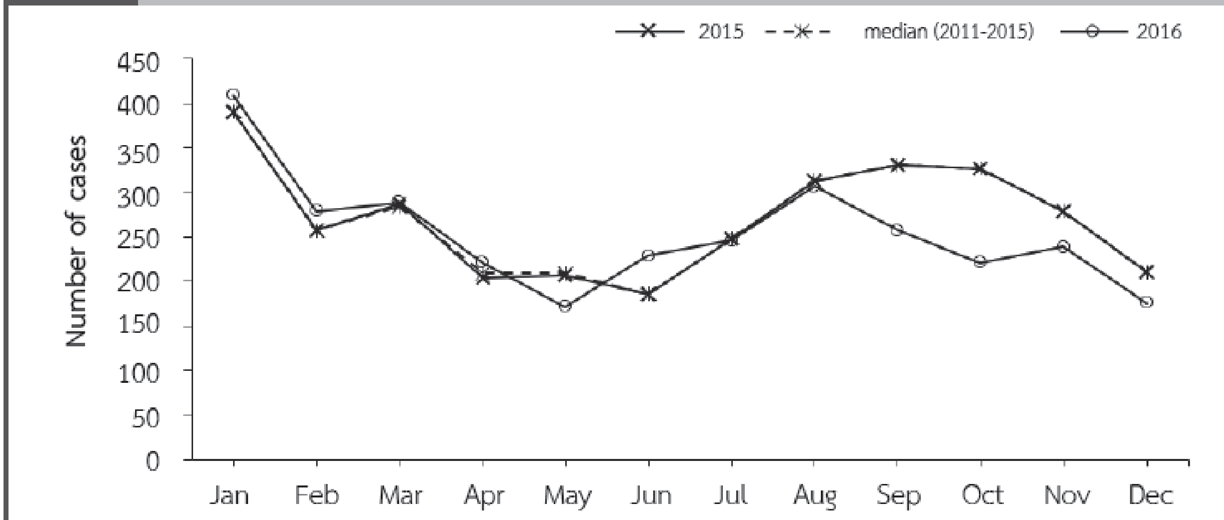
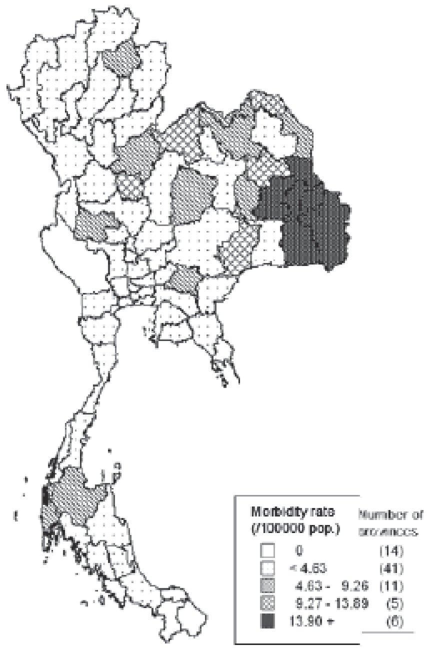


Fig.4 Reported cases of melioidosis per 100,000 population by province, Thailand, 2016



Top Ten Leading Rate

1	Mukdahan	144	41.29
2	Si Sa Ket	455	30.96
3	Ubon Ratchathani	523	28.12
4	Amnat Charoen	96	25.48
5	Roi Et	209	15.98
6	Yasothon	81	15.00
7	Bungkan	57	13.53
8	Phichit	64	11.75
9	Kalasin	112	11.37
10	Buri Ram	177	11.16