Melioidosis

Melioidosis is bacterial infection with a high case fatality rate that is endemic in Thailand (1). Melioidosis is a highly virulent disease which is categorized by the US Centers for Disease Control and Prevention (CDC) as a select agent capable of being used in a bioterrorism attack (2). Melioidosis is known to be very difficult to accurately diagnose, and a microbiology laboratory is required to perform definite diagnostic testing by bacterial cultures (2). Melioidosis needs to be treated by specific antibiotics (3). Findings from studies have indicated that the vast majority of melioidosis cases and its deaths from meliodosis in Thailand have not been reported as part of Thailand's national surveillance system (Report 506).

Melioidosis is caused by Burkholderia pseudomallei, a Gram-negative bacilli bacteria. which can normally be found in soil and water. B. pseudomallei is prevalent in soil and water in all regions of Thailand, particularly in the northeastern, eastern, and southern parts of the country (4). Patients can 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, or pulmonary infection, or single organ involvement, or multiple organ infections such as lesions and abscesses in the lung, liver, or spleen. The average incubation period after acquiring the organism is approximately nine days, but can also be as short as one day, or as long as years. Melioidosis must be diagnosed and confirmed by bacterial culture from clinical samples which contain the organism such as sputum and urine. It is important that culture media specific to *B. pseudomallei* be used in the culture process. Specific treatment is required for Melioidosis patients by using antimicrobial agents like ceftazidime and carbapenems. These antibiotics must be continuously administered for approximately five months in order to prevent relapse of the disease. Effective disease prevention measures include wearing of personal protective gear, 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 before drinking, avoiding drinking rain water, tap water or unboiled water from natural water sources, and eating only clean and thoroughly cooked foods.

So far the most common problems in the prevention and control of Melioidosis have been: (a) the lack of capacity on the part of many laboratories to accurately identify *B. pseudomallei*; it is likely that this causative agent might potentially be misidentified as a contaminant, *Pseudomonas spp.*, or other pathogens. Based on studies in Thailand it is recommended that **any Gram-negative oxidase-positive bacilli isolated from clinical specimens should always be initially identified and confirmed whether it is not** *B. pseudomallei* **before being reported as contaminant,** *Pseudomonas spp.* **or other organisms; (b) Melioidosis diagnosis using antibody method has been found to have low sensitivity and specificity, resulting in a high level of false positive results; and (c) It has been found that fatal cases of melioidosis usually died very quickly within 1-3 days following hospital admission, while it typically takes 4-7 days for bacterial culture results to become available. This resulted in patient's relatives not being aware that the patient had died of melioidosis, melioidosis not being documented as a cause of death in their medical record by attending**

physician, and fatal cases of melioidosis not being reported by surveillance officer as part of the disease surveillance system maintained by the Ministry of Public Health (MOPH).

In 2015, based on the data from its existing surveillance system (Report 506), the Bureau of Epidemiology (BOE) reported a total of 3,242 cases of melioidosis, representing a morbidity rate of 4.96 per 100,000 populations (5). The vast majority of cases were in the northeast, particularly in Mukdahan province, where the morbidity rate was 50.71 per 100,000 populations, followed by Amnat Charoen, Sisaket, Ubon Ratchathani, and Roi Et provinces, with the morbidity rates of 32.19, 29.65, 25.93, and 22.70 per 100,000 populations, respectively (see Figure 1). Among these patients, 112 were fatal cases, representing a mortality rate of 0.17 death per 100,000 populations, or case fatality rate of 3.45 percent. It has been found the case fatality rate significantly increased when compared with the previous year (see Figure 2), particularly in Ubon Ratchathani province, where as high as 107 deaths were reported.

Reported cases of melioidosis included 1,165 females and 2,077 males or a female-tomale ratio of 1:1.8. The pattern of disease distribution by different age groups was found to be similar to that of the previous year, i.e. the highest morbidity rate was found among individuals \geq 65 years of age, at 11.17 cases per 100,000 populations. This was followed by those 55-64 and 45-54 years of age, whose morbidity rates were 10.41 and 7.52 per 100,000 populations, respectively (see Figure 3). Most patients (80.57 percent) resided in Tambon Administration Organization (TAO) areas, followed by municipality areas (19.43 percent). The occupation most affected by the disease was farmer (54.63 percent), followed by casual laborer and dependents, at 13.33 and 12.99 percent, respectively. Thai nationals accounted for 98.09 percent of the patients, followed by Laotians at 1.42 percent. The vast majority of patients (60.33 percent) sought medical care at community hospitals, followed by regional/general hospitals (38.31 percent). Among these patients, 69.12 percent received their medical care at the outpatient department, whereas all fatal cases were admitted to hospital and died 0-43 days (median 4 days) following case identification.

The disease is being reported throughout the year. In 2015 seasonal pattern of melioidosis was similar to those of the year 2014 and consistent with the patterns over 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 2014 and the trend continued through March 2015. Subsequently a decrease in new cases was reported during late summer (April-May). This was then followed by another rise in meliodosis activity in the next rainy season (see Figure 4).

Based on the event-based surveillance data obtained from the outbreak verification program in 2015, three events of melioidosis were reported, which included two probable cases in [Chiang Mai's] Hang Dong and Doi Saket districts, and five confirmed cases of melioidosis in Pichit's Taphan Hin district. All patients were children aged 3-14 years and most of them developed only mild symptoms, with a high-grade fever lasting 2-3 days prior to hospital visit. According to attending physicians, dengue was initially suspected but results of tourniquet test were negative. Melioidosis infection was then suspected. Clinical samples were collected and submitted for laboratory analysis using IHA method at a private hospital and confirmatory tests were performed at the Department of Medical Sciences (DMSc) utilizing IFA technique. Test

results came back positive from both laboratories. Outbreak investigation could neither identify the relationship between each individual patient nor pinpoint definite risk factors.

Based on the laboratory data provided by the Department of Medical Sciences (DMSc) and its 14 regional medical science centers, a total of 131 serum samples were submitted for antibody tests, 27 of which tested positive for the organism, representing 20.61 percent. Utilizing IFA technique, tests were performed on 121 samples, 21 of which tested positive. IHA method was used to test 11 samples and six of them tested positive for melioidosis (6).

According the study conducted by Melioidosis Research Unit, Sunpasitthiprasong Hospital, it was found that at Sunpasitthiprasong Hospital in Ubon Ratchathani province alone around 200-300 cases of culture-confirmed melioidosis had been reported annually from 1997-2006 and 40 percent of these patients had fatal outcomes (7). Findings from this study suggested that incidence rates of melioidosis infection rose steadily every year. In 2006, a total of 380 cases of culture-confirmed melioidosis were reported, including 154 deaths. Approximately two thirds of patients were local residents of Ubon Ratchathani province and about one third were those referred from neighboring provinces. Another study conducted in collaboration with Melioidosis Research Center at Khon Kaen University has found that in 2007 there were 1,865 cases of culture-confirmed melioidosis in the northeast. Similarly, the case fatality rate was approximately 40 percent (7). Findings from the study conducted by researchers under Thailand Melioidosis Network (www.melioidosis.info/th) indicated that in 2015 the number of culture-confirmed melioidosis cases at the following health facilities were as follows: Sappha Sitthiprasong Hospital, Ubon Ratchathani province, 378 cases (including 134 deaths), Udon Thani Hospital, Udon Thani province, 107 cases (including 49 fatal cases), and Srinagarind Hospital, Khon Kaen province, 95 cases (including 8 deaths) (see Table 1).

Based on a modeling study, it has been found that if every single patient who died of melioidosis infection in Thailand sought medical care at hospital with microbiology laboratory, and if microbiology laboratories across the country collected all relevant specimens, used culture media specific to *B. pseudomallei* and accurately identified and characterized the organism, and all melioidosis cases were properly reported, annually Thailand would have an estimated 2,838 fatal cases due to melioidosis infection (4).

In 2015, an increase in the number of fatal cases of melioidosis reported in the surveillance system (Report 506) from the previous years was primarily attributed to collaboration from Melioidosis Research Unit at Sunpasitthiprasong Hospital that successfully reported melioidosis cases into the system for the first year, thus resulting in higher overall morbidity and mortality rates. Based on these new data, it may not be possible to confirm whether the number of melioidosis cases actually increased in 2015. However, we can at least safely say that (a) 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 include public awareness campaign to educate the general public about how to prevent themselves from getting infected by the organism, or alerting and raising awareness among staff of health facilities so that specimens are collected for laboratory culture and proper treatment provided in a timely manner, and (b) confirmed and fatal cases of melioidosis from all hospitals with microbiology laboratories have been significantly underreported. **It is, therefore, important to educate and remind laboratory**

staff, clinicians, statisticians, and epidemiologists to comply with the requirements of the existing surveillance system by including in their Report 506 every single case of melioidosis with *B. pseudomallei*-positive culture.







Udon Thani Nakhon Phanom Sa Kaeo Ubon Ratchathani Khon Kaen Year Morbidity Mortality Morbidity Morbidity Mortality Morbidity Mortality Mortality Morbidity Mortality 1997 198 97 -------_ 257 124 1998 --------173 71 1999 --------141 67 2000 -_ _ _ --_ -152 2001 61 --_ --_ _ -2002 184 83 --------2003 235 90 --------250 99 2004 --------273 2005 110 -_ _ -_ ---380 154 2006 --_ ---475 2007 167 90 23 7 26 ----25 401 107 130 48 13 2008 ----2009 383 119 30 11 _ 110 23 ---393 96 2010 140 -------2011 405 143 93 -------405 157 2012 89 -------2013 450 79 97 199 105 44 ----2014 444 174 149 75 92 10 57 -_ _ 2015 378 95 107 49 8 134 ----

Table 1. The number of reported cases and fatal cases of melioidosis confirmed by *B. pseudomallei*-positive culture from clinical specimens at research study sites with Thailand Melioidosis Network (<u>www.melioidosis.info/th</u>)

* For Ubon Ratchathani province, data was obtained from Sappha Sitthiprasong Hospital; Udon Thani province, data obtained from Udon Thai Hospital; Khon Kaen province, data obtained from Srinagarind Hospital; Nakhon Phanom and Sa Kaeo provinces, data obtained from Nakhon Phanom Hospital, Sa Kaeo [Crown Prince] Hospital and from Thailand MOPH-U.S.CDC Collaboration

** - means "No data available"

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