Melioidosis in the Torres Strait Islands, Australia: Exquisite Interplay between Pathogen, Host, and Environment

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Abstract. *Burkholderia pseudomallei*, a bacterium that lives in the soil of the tropics, causes the disease melioidosis. This retrospective study investigated the temporospatial epidemiology of the 49 laboratory-confirmed melioidosis cases in the Torres Straits Islands of tropical Australia between 1997 and 2017. An identifiable risk factor for the disease was present in 43/49 (88%) cases and in 35/36 (97%) cases with complete clinical data. The mean incidence of melioidosis varied across the region, from 0/100,000 persons/year in the Eastern Island Cluster to 116.1/100,000 persons/year in the Near Western Island Cluster. An environmental suitability score for the growth of *B. pseudomallei*—constructed using the rainfall, vegetation, and soil type on each island—correlated with disease incidence (Spearman's rho 0.51; $P = 0.035$). Melioidosis is an opportunistic disease that occurs in patients with specific risk factors, but its incidence is also strongly influenced by environmental factors that favor the growth of the causative organism.

Melioidosis is an opportunistic infection caused by the environmental Gram-negative bacterium *Burkholderia pseudomallei*. Infection is usually asymptomatic, but it can be rapidly fatal in individuals with specific comorbidities including diabetes mellitus, hazardous alcohol use, and chronic kidney disease (CKD).¹ Even where there is access to sophisticated intensive care support, the case-fatality rate can exceed 10%.^{2,3} Meanwhile in resource-poor and remote locations, the case-fatality rate can approach 35%.⁴ Melioidosis has no effective vaccine, so it is important to identify other strategies to prevent the disease.

Burkholderia pseudomallei lives in the soil and surface water of tropical and subtropical regions, with rainfall and the physicochemical properties of soil and vegetation all appearing to influence the organism's growth. The association with rainfall is strong and is emphasized by the clustering of cases after severe weather events and the observation that almost 90% of human cases in northern Australia present during the wet season.^{5,6} The influence of soil and vegetation type on the growth of *B. pseudomallei* is less well defined, but both also appear to be important. Some investigators have noted that fine-textured soils with a higher proportion of silt and clay particles, and a lower pH and carbon: nitrogen ratio, provide conditions preferred by the bacteria.⁷ However, other studies have found a positive association with the proportion of sand.⁸ Conversely, increasing soil salinity limits the bacterium's growth.⁸ There are fewer data that define the effect of vegetation; however, the organism appears to thrive in rice fields and in the presence of grasses of the *Aristida* species.^{9,10}

The Torres Strait archipelago in tropical northern Australia covers an area of 48,000 km². There are 17 inhabited islands, grouped into five geographically and culturally distinct areas: an Eastern Cluster of volcanic islands; a Central Cluster of low sandy islands; a Top Western Cluster comprising predominantly alluvial muds overlying old coral platforms; a Near Western Cluster composed of volcanic and granitic rocks; and an Inner Cluster (Thursday Island Cluster) comprising basement igneous and volcanic rock (Figure 1).¹¹ The mean daily temperature ranges from 28.3°C to 32.1°C (82.9–89.7°F). The

December–April wet season accounts for approximately 91% of the annual rainfall.¹²

Only 4,514 people inhabit the islands, with approximately 92% of the residents identifying as Indigenous Torres Strait Islanders, ethnically a Melanesian population.¹³ There is a high prevalence of risk factors for melioidosis: approximately one-third have diabetes, while up to 49% consume excess alcohol.¹⁴ The precise local prevalence of CKD is uncertain, although there is a significant local burden that necessitates a nine-chair hemodialysis unit and an outreach peritoneal dialysis service.¹⁵ There are health clinics on all 17 inhabited islands; however, their remote location means that clinic staff frequently have to rely on telephone advice from medical staff based in the region's main hospital on Thursday Island.

Previous work suggest that the annual incidence of melioidosis in the Torres Straits Islands is 42.7/100,000, one of the highest in the world.¹⁶ However, the distribution of cases is quite heterogeneous, with local clinicians observing that melioidosis is very rare in the Eastern Cluster of islands, despite a similar prevalence of risk factors for the disease.¹⁷

To determine whether differences in local environmental factors might account for this apparent disparity, all microbiologically confirmed cases of melioidosis diagnosed in the Torres Strait between 1997 and 2017 were evaluated. This period was chosen as it coincided with the establishment of a statewide electronic database, which ensured that all cases were captured. Additional patient data were collected from their medical records, where they were available. Disease incidence was determined using population data from the Australian Bureau of Statistics.¹³ A variety of sources were used to collect environmental data: Australian Bureau of Meteorology data were used to determine the rainfall for each of the 17 islands, whereas vegetation and soil data for the one-kilometer radius around the primary community settlement on each island were collated from an environmental survey performed in 2009.^{11,12} To determine the environmental suitability for *B. pseudomallei*, a score was calculated from these data (Supplemental Table 1). A score between 1 (least suitable for the growth of *B. pseudomallei*) and 5 (most suitable) for rainfall was determined (Supplemental Table 2). A blinded reviewer, with environmental microbiological expertise, based in mainland Australia, was provided with a list of the soil and

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FIGURE 1. Map of the Torres Strait region showing the annual incidence (cases/100,000) of melioidosis during the study period on each of the inhabited islands and the environmental suitability of each of the islands for the growth of *Burkholderia pseudomallei*. This figure appears in color at www.ajtmh.org.

vegetation types found in the region, although he was unaware of their distribution. Each soil and vegetation type was also assigned a score between 1 and 5 (Supplemental Tables 3–5). The three 5-point scores were added together, and a percentage was generated. Data were entered into an electronic database (Microsoft Excel; Microsoft Corp., Redmond, WA) and analyzed using statistical software (Stata 14.0; StataCorp., College Station, TX). Associations between continuous variables were examined using Spearman's rho. The Far North Queensland Human Research and Ethics Committee provided ethical approval for the study (HREC/15/QCH/46–977).

There were 49 cases of laboratory-confirmed melioidosis that occurred relatively evenly across the study period (Figure 2). The patients' median age was 44.9 years, and 69% were male. In nine cases, limited clinical data were available (five charts had been destroyed and four of the charts were inaccessible or contained minimal detail). Despite this, there were only 6/49 (12%) patients who had no identifiable or documented risk factor for melioidosis. In the 36 patients for whom complete risk factor data were available, only two (6%) patients did not have diabetes mellitus, CKD, or recent hazardous alcohol consumption, and one of these two had another recognized predisposing factor (chronic lung disease). In the patients in whom the presence of specific risk factors could be confidently determined, 35/46 (76%) were diabetic,

25/37 (68%) reported hazardous alcohol consumption, and 7/46 (15%) had CKD. Of the 49 cases, 41 (84%) occurred during the December–April wet season; four (8%) patients died.

The mean annual incidence of melioidosis varied across the region, ranging from 0/100,000 in the Eastern Cluster (there were no cases during the entire study period) to 116.1/100,000 in the Near Western Cluster (Supplemental Table 1). On one of the islands in the Near Western Cluster, there were nine separate individuals of a mean population of 234 affected during the study period, translating to a cumulative risk in the general population of 3.9% (95% CI: 2.0–7.2%). The suitability score varied across the region from 50 to 72 and correlated with the incidence on each island (Spearman's rho 0.51; $P = 0.035$) (Figure 3). The association between incidence and mean annual rainfall (Spearman's rho 0.61; $P = 0.01$) was stronger than the association between incidence and vegetation (Spearman's rho 0.42; $P = 0.09$), and soil (Spearman's rho -0.13 ; $P = 0.61$) (Figures 2 and 3).

This study highlights the important interplay between the pathogen, the host, and the environment in the local incidence of melioidosis. A recognized risk factor was present in 97% of patients with complete data, and 84% of cases occurred during the region's wet season, emphasizing the status of *B. pseudomallei* as a seasonal, opportunistic pathogen. In this context, the marked heterogeneity of cases across the region is striking. There is very little variation in the prevalence of the

FIGURE 2. (A) Distribution of the cases by year. (B) Mean annual rainfall by island cluster during the study period. This figure appears in color at www.ajtmh.org.

comorbidities that predispose to the disease, and yet on several islands there were no cases during the study period at all, whereas on others the disease incidences are among the highest ever reported.^{1,17} The association between the environmental suitability score and disease incidence is, therefore, notable.

Public health campaigns to prevent melioidosis have had mixed success but may be more effective if they can be targeted more precisely to populations at higher risk of the disease. The case-fatality rate of 8% underscores the organism's virulence and emphasizes the importance of including agents with activity against *B. pseudomallei* in the empirical regimen

FIGURE 3. (A) Relationship between calculated suitability score and annual disease incidence on each island. (B) Relationship between mean annual rainfall and annual disease incidence on each island. This figure appears in color at www.ajtmh.org.

of local cases of sepsis and severe community-acquired pneumonia. On islands where the incidence is greatest, it is essential to have reliable access to meropenem or ceftazidime. However, these data support the impression of local clinicians that melioidosis is much less common in other parts of the region. This may encourage them to seek alternative diagnoses, and in an era when antibiotic stewardship is increasingly important, it might also permit earlier de-escalation.

The study has several limitations. The study's suitability score is crude; the relationship between rainfall and melioidosis cases is not linear, the rainfall's timing is critical, and other factors including fluctuations in dewpoint and groundwater levels are also important.^{9,18} The impact that soil and vegetation have on *B. pseudomallei* persistence—in addition to rainfall—remains poorly understood, and the suitability score assumes an equal weighting for these variables, which may not be appropriate. Indeed, of the three factors, only rainfall had an independently statistical association with disease incidence in this small dataset. There are other potential weaknesses: the small population on each of the islands affects the reliability of the reported disease incidence, and although most infections are suspected to be the result of percutaneous inoculation, our score did not take patient behavior into account. Furthermore, even if an environment is notionally suitable for *B. pseudomallei*, this does not necessarily mean that the organism will be found there.^{19,20} Previously, genetic characterization of *B. pseudomallei* from soil and cases of melioidosis in the Torres Strait Islands has identified sequence types common to both Papua New Guinea and mainland Australia, suggesting a nonrandom distribution of the microbe.²¹ It is postulated that historical trade and migration between Papua New Guinea and mainland Australia have influenced the distribution of *B. pseudomallei*.¹⁶ However, notwithstanding these caveats, the score was determined in a blinded manner, by a microbiologist with extensive experience in the environmental determinants of *B. pseudomallei* growth. The correlation between the score and disease incidence is at least hypothesis-generating, and there are plans to prospectively sample soil from the Torres Straits Islands to confirm the findings and to inform disease prevention strategies.

In summary, this study illustrates the exquisite interaction between the pathogen, host, and environment in the local incidence of melioidosis. On a broader level, it emphasizes the importance of understanding the temporospatial epidemiology of infectious diseases, particularly in remote and poorly resourced locations, to facilitate prevention, expedite detection, and optimize management.

Received October 6, 2018. Accepted for publication December 9, 2018.

Published online January 21, 2019.

Note: Supplemental tables appear at www.ajtmh.org.

Acknowledgments: We thank Peter Horne for assistance with the production of Figure 1 and Jeff Warner and Robyn McDermott for expert advice during the manuscript's preparation.

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