Clinical and Vaccine Immunology

Surprisingly Low Seroprevalence of Burkholderia pseudomallei in Exposed Healthy Adults in the Darwin Region of Tropical Australia Where Melioidosis Is Highly Endemic

Gemma L. James, Ben Delaney, Linda Ward, Kevin Freeman, Mark Mayo and Bart J. Currie

Updated information and services can be found at:
http://cvi.asm.org/content/20/5/759

These include:

REFERENCES	This article cites 11 articles, 7 of which can be accessed free at: http://cvi.asm.org/content/20/5/759#ref-list-1
CONTENT ALERTS	Receive: RSS Feeds, eTOCs, free email alerts (when new articles cite this article), more»

Information about commercial reprint orders: **http://journals.asm.org/site/misc/reprints.xhtml**
To subscribe to to another ASM Journal go to: **http://journals.asm.org/site/subscriptions/**

Journals.ASM.org

Surprisingly Low Seroprevalence of *Burkholderia pseudomallei* in Exposed Healthy Adults in the Darwin Region of Tropical Australia Where Melioidosis Is Highly Endemic

Gemma L. James,[a] Ben Delaney,[a] Linda Ward,[b] Kevin Freeman,[c] Mark Mayo,[b] Bart J. Currie[b,d]

Emergency Department, Royal Darwin Hospital, Darwin, Northern Territory, Australia[a]; Division of Global and Tropical Health, Menzies School of Health Research, Casuarina, Northern Territory, Australia[b]; Pathology Department, Royal Darwin Hospital, Darwin, Australia[c]; Infectious Diseases Department, Northern Territory Medical Program, Royal Darwin Hospital, Darwin, Australia[d]

In the Darwin region of Australia where melioidosis is highly endemic, only 11/354 (3%) healthy residents were seropositive by indirect hemagglutination assay, despite extensive exposure to *Burkholderia pseudomallei*. None developed melioidosis, but some described a prior self-limiting illness. This seropositivity rate is much lower than that seen in northeast Thailand, where melioidosis is similarly highly endemic, potentially reflecting important differences between these two locations in the epidemiology of melioidosis.

Melioidosis, which is caused by the environmental bacterium *Burkholderia pseudomallei*, is endemic in northern Australia and other tropical regions in southeast Asia (1). Serology studies from Thailand suggest that for each diagnosed case of melioidosis there are many asymptomatic infections (2). However, while seropositivity rates in northeast Thailand have been described to increase with age in children to levels of over 50% (3), a large community survey in northern Queensland, Australia, showed only 5.7% seropositivity overall, with higher rates seen in those with risk factors for melioidosis such as diabetes (8.6%) and chronic alcoholism (15%) (4). Furthermore, while the incidence of melioidosis in the tropical Top End of the Northern Territory of Australia is at least as high as in northeast Thailand (5), limited data suggest that seropositivity rates in the Top End are as low as those seen in Queensland (reference 6 and unpublished data). Melioidosis is increasingly being recognized as an opportunistic infection, with diabetics particularly at risk and healthy people rarely dying from melioidosis when early diagnosis and state-of-the-art intensive care facilities are available (7). Nevertheless, in the Darwin Prospective Melioidosis Study, 106/540 (20%) cases had no identifiable medical risk factor for melioidosis, with the majority of these cases having a history of recreational and/or occupational exposure to monsoonal wet-season soils and surface water (8). We therefore performed a serological study on healthy Darwin residents to assess both seropositivity and potential associations with asymptomatic infection with *B. pseudomallei*.

We recruited healthy adults living in the Darwin region who self-identified as being active and having exposure to wet-season soils and surface water. We excluded anyone with a known risk factor for melioidosis, including diabetes, hazardous alcohol use, chronic respiratory or renal disease, and malignancy or immunosuppressive therapy, as identified in the Darwin Prospective Melioidosis Study (8). An extensive questionnaire documented the number of years living in the region of endemicity, specific occupational and recreational activities, and estimated quantification of potential exposure events, including immersion of hands or feet in surface water, direct contact of skin with wet-season soil, and cuts and abrasions during outdoor activities. Serology was performed using the indirect hemagglutination assay (IHA) as previously described, with the IHA antigen derived from a combination of three local clinical *B. pseudomallei* strains and a positive titer being 1:40 or higher (4, 6). The study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health and the Menzies School of Health Research.

A total of 354 individuals were enrolled and completed the questionnaire. Of the 354 individuals, 207 (58%) were female; the median age was 38 years (range, 18 to 61 years), and the median time living in the region of northern Australia where melioidosis is endemic was 13 years (range, 1 to 57 years). While 88% of the individuals worked predominantly indoors, 71% spent the majority of their recreational time outdoors. A total of 310 (88%) lived in urban residences in Darwin, and 321 (91%) used the chlorinated town water supply. Exposure to wet-season soil and water was estimated as extensive in 77%, moderate in 18%, and low in only 5%. A total of 334 (94%) participants had knowledge of melioidosis prior to the study, but only 21 (6%) claimed to always cover their hands and/or feet during exposure-prone outdoor activities in the wet season.

Despite extensive exposure to the Darwin environment where the presence of *B. pseudomallei* is known to be widespread in soils and surface water (9), only 11/354 (3.1%) people were seropositive (Table 1). IHA titers in those who were seropositive ranged from 1:80 to 1:2,560. None had a titer of 1:40, and the only person with a titer of 1:20 had a repeat titer of <1:20. Of the 11 seropositive individuals, 7 were male, 10 were in the extensive-exposure group, 1 was in the moderate-exposure group, and 9 had experienced >10 wet seasons in Darwin (Table 1).

The 11 seropositive individuals were recalled for repeat testing, and all were assessed for evidence of melioidosis by full blood count, C-reactive protein analysis, urine analysis, chest X-ray, and urine culture for *Burkholderia pseudomallei*. In each case the re-

TABLE 1 Summary for 11 *Burkholderia pseudomallei*-seropositive individuals[a]

Patient no.	Age (yr)/sex	Occupation	No. of yrs in tropics	Urban/rural residence	Town mains/bore water	Possible infecting event	Initial titer	Titer upon review
1	59/M	Environmental scientist	52	Urban	Mains	Direct contact with soil through occupational activities	1/160	1/160
2	40/M	Public servant	15	Urban	Mains	Remote tourism guide or rugby	1/80	1/80
3	39/M	Firefighter	20	Urban	Mains	Remote tourism guide or football	1/640	1/320
4	41/M	Pharmacist	15	Urban	Mains	Cross-country running	1/160	1/160
5	28/M	Planning engineer	4	Urban	Mains	Work overseeing bore dig	1/160	1/40
6	24/F	Lawyer	24	Rural	Mains	None identified	1/160	1/80
7	34/F	Environment officer/scientist	16	Urban	Mains	Direct contact with soil through occupational activities	1/160	1/80
8	47/F	Administration manager	29	Rural	Bore & mains	Gardening	1/1,280	1/640
9	25/M	Linesman	25	Urban	Mains	Football, goose shooting, or direct contact with soil through occupational activities	1/640	1/640
10	47/F	Nurse	11	Urban	Mains	Previous remote nursing or gardening	1/320	1/640
11	25/M	Environmental scientist	3	Urban	Mains	Occasional visits to rural communities	1/2,560	1/2,560

[a] The result of a screen for melioidosis was negative for all 11 individuals. M, male; F, female.

peat serology confirmed the positive result (Table 1), but all were healthy and none was found to have melioidosis, although 3 had nonspecific scarring on the chest X-ray. All but 1 (who had lived 24 years in the region of endemicity) had substantial exposure to *B. pseudomallei* through occupational and/or recreational activities (Table 1), but none identified a specific event more likely to be their infecting event. Four individuals described a prior prolonged (>2-week) episode of influenza-like symptoms which could have been consistent with primary infection with *Burkholderia pseudomallei*, but in all cases this illness resolved without any specific melioidosis treatment. Over the 3 years subsequent to the study, none has developed melioidosis.

The surprisingly very low *B. pseudomallei* IHA seropositivity rate in this study of heavily exposed healthy people in a region with among the highest documented incidence rates for melioidosis (5, 8) is in sharp contrast to the high seropositivity rates seen in northeast Thailand (3), where incidence rates of melioidosis are also high (10). Possible explanations include exposure to non-pathogenic cross-reacting environmental *Burkholderia* species in Thailand and differing epidemiologies between the regions, with possible differences in the route of infection and repeated exposure in Thai children even potentially conferring some immunity to disease (melioidosis) later in life and possible differences in virulence of *B. pseudomallei* between Australia and Thailand. While most cases are attributed to percutaneous inoculation, the potential roles of inhalation during severe weather events and ingestion from contaminated water supplies are receiving increasing attention (7). What is clear is that the estimate from Thailand that only approximately 1 in 4,600 antibody-producing exposures results in clinical infection (i.e., melioidosis) is not applicable to Australia (2).

In conclusion, infection with *B. pseudomallei* is uncommon in healthy individuals in the Darwin region where melioidosis is highly endemic, but self-limiting clinical illness from primary infections may be occasionally occurring. The proportion of seropositive individuals who harbor latent *B. pseudomallei* remains entirely unclear, but while activation from latency with melioidosis occurring many years after infection is well described (11), prospective studies suggest that such events are very uncommon (8).

REFERENCES

1. **Cheng AC, Currie BJ.** 2005. Melioidosis: epidemiology, pathophysiology, and management. Clin. Microbiol. Rev. **18**:383–416.
2. **Cheng AC, Wuthiekanun V, Limmathurotsakul D, Chierakul W, Peacock SJ.** 2008. Intensity of exposure and incidence of melioidosis in Thai children. Trans. R. Soc. Trop. Med. Hyg. **102**(Suppl 1):S37–S39.
3. **Wuthiekanun V, Chierakul W, Langa S, Chaowagul W, Panpitpat C, Saipan P, Thoujaikong T, Day NP, Peacock SJ.** 2006. Development of antibodies to Burkholderia pseudomallei during childhood in melioidosis-endemic northeast Thailand. Am. J. Trop. Med. Hyg. **74**:1074–1075.
4. **Ashdown LR, Guard RW.** 1984. The prevalence of human melioidosis in Northern Queensland. Am. J. Trop. Med. Hyg. **33**:474–478.
5. **Parameswaran U, Baird RW, Ward LM, Currie BJ.** 2012. Melioidosis at Royal Darwin Hospital in the big 2009–2010 wet season: comparison with the preceding 20 years. Med. J. Aust. **196**:345–348.
6. **Cheng AC, O'Brien M, Freeman K, Lum G, Currie BJ.** 2006. Indirect hemagglutination assay in patients with melioidosis in northern Australia. Am. J. Trop. Med. Hyg. **74**:330–334.
7. **Wiersinga WJ, Currie BJ, Peacock SJ.** 2012. Melioidosis. N. Engl. J. Med. **367**:1035–1044.
8. **Currie BJ, Ward L, Cheng AC.** 2010. The epidemiology and clinical spectrum of melioidosis: 540 cases from the 20 year Darwin prospective study. PLoS Negl. Trop. Dis. **4**:e900. doi:10.1371/journal.pntd.0000900.
9. **Kaestli M, Mayo M, Harrington G, Ward L, Watt F, Hill JV, Cheng AC, Currie BJ.** 2009. Landscape changes influence the occurrence of the melioidosis bacterium Burkholderia pseudomallei in soil in northern Australia. PLoS Negl. Trop. Dis. **3**:e364. doi:10.1371/journal.pntd.0000364.
10. **Limmathurotsakul D, Wongratanacheewin S, Teerawattanasook N, Wongsuvan G, Chaisuksant S, Chetchotisakd P, Chaowagul W, Day NP, Peacock SJ.** 2010. Increasing incidence of human melioidosis in Northeast Thailand. Am. J. Trop. Med. Hyg. **82**:1113–1117.
11. **Ngauy V, Lemeshev Y, Sadkowski L, Crawford G.** 2005. Cutaneous melioidosis in a man who was taken as a prisoner of war by the Japanese during World War II. J. Clin. Microbiol. **43**:970–972.