

Letters to the Editor

Positive Serologic Test Results for *Burkholderia pseudomallei* in Asymptomatic Persons

Dear Sir:

We note with interest the recent paper by Kronmann and others in the *American Journal of Tropical Medicine and Hygiene* showing antibodies to *Burkholderia pseudomallei* in 13 of 38 US Marines, only one of whom had culture-confirmed melioidosis.¹ We caution against the use of a poorly validated serologic test to provide evidence of melioidosis in asymptomatic persons.

The authors use the indirect fluorescent antibody (IFA) assay, which has not been used in disease-endemic countries for many years, and no validation of this assay is presented. Although we may assume that the test is broadly similar to the previous descriptions of the IFA assay,² the bacterial strains used (or if purified antigen was used, the nature of the antigen) are not defined. The authors cite earlier work by Ashdown and others who described a high specificity of the IFA assay, but in this report, only 11 of 89 patients had culture-confirmed melioidosis, with the remaining 78 diagnosed with subclinical melioidosis on the basis of serologic test results.³ The clinical significance of asymptomatic persons with positive serologic results is unclear; whether such people have truly been infected and harbor latent infection is not known. Nevertheless, as the authors note, it is apparent that overt melioidosis does not develop in most of such patients.

Furthermore, there may have been confounding by exposure to the antigenically similar but less virulent *B. thailandensis* that is present in Thailand but not in Australia. The higher prevalence of positive indirect hemagglutination (IHA) test results using *B. pseudomallei* antigen in Thai patients compared with those from northern Australia, with a broadly similar incidence of disease, may suggest that exposure to *B. thailandensis* may result in detectable antibodies against *B. pseudomallei*.^{4,5} Studies of cross-reactivity between the IHA using *B. thailandensis* as the antigen in patients with culture-confirmed melioidosis have not been consistent.^{6,7}

We suggest that the quantification of risk in groups exposed to mud and pooled surface water should be based on surveillance of culture-confirmed melioidosis in the population at risk. The authors do not offer any data on the incidence of melioidosis in occupationally exposed groups in the same area, such as during previous military exercises or in rice farmers. Approximately 20 cases of melioidosis per year are reported at the Chonburi Hospital approximately 80 km from the study site (with an unknown denominator), and a low rate of melioidosis has been documented in a hospital survey in the central region of Thailand compared with the northeast Issan region.^{8,9}

In summary, the clinical significance of seropositive asymptomatic persons in this study is doubtful, given the use of a poorly characterized serologic test, possible confounding by exposure to *B. thailandensis*, the lack of a non-exposed control group, and the lack of a clinical picture characteristic of melioidosis in all but one of these patients.

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Dear Sir:

We appreciate the interest of Currie and others in our report of a case of melioidosis and cases with positive serologic test

results for melioidosis among a group of US Marines deployed to Thailand.¹ We concur with a number of their remarks and acknowledged most of these as limitations in our article, but there are a few comments that we would like to specifically address.

Cheng and others question the validity of our specific serologic test, the immunofluorescent antibody (IFA) assay. The test we report was performed by Focus Diagnostics using the method of Ashdown and a strain obtained from the American Type Culture Collection. Cheng and others also question the findings of Ashdown and others² by stating that they used only 11 culture-confirmed cases for determining specificity. Ashdown and others 140 longitudinal serum samples from 42 culture-confirmed patients to calculate the cited specificity, whereas Cheng and others refer to a separate analysis of prospective samples in the same reference. They also state that the IFA assay has not been used in disease-endemic countries for many years. Although the indirect hemagglutination (IHA) test remains the most widely used test despite its poor sensitivity and specificity, investigators from some disease-endemic regions, such as Malaysia, have cited the routine use of the more technically demanding IFA assay since 1995.³⁻⁵ Other authors have concluded that that IFA assay is at least as good as the IHA test for melioidosis diagnosis.^{6,7}

We agree that the clinical significance of positive serologic test results for asymptomatic persons with melioidosis is unknown and acknowledged this in our original paper, although we would emphasize that this uncertainty does not exclude its potential significance. Cheng and others note the relative infrequency of confirmed melioidosis at a regional hospital in the same general vicinity the US Marines visited, but it is obvious to us that the group had plausible exposure to melioidosis; the group traveled as a unit, and one of them developed culture-confirmed disease.

It is unlikely that all our test results represented false-positive results because one member of the exposure group was a culture-confirmed case and because the prevalence of false-positive test results is generally low in previously non-exposed populations. We appreciate that the possibility of cross-reacting antibodies to *B. thailandensis* and other limi-

tations of the study do not enable us to provide a definitive answer on the precise incidence of melioidosis. However, our study does suggest that exposure during short-term exercises similar to those described in our report may occur, and occasionally result in clinically significant disease. We hope that our report will stimulate future prospective studies of melioidosis associated with travel to disease-endemic countries.

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