SHORT REPORT: DEVELOPMENT OF ANTIBODIES TO 
BURKHOLDERIA PSEUDOMALLEI DURING CHILDHOOD IN 
MELIOIDOSIS-ENDEMIC NORTHEAST THAILAND

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Abstract. A cross-sectional serological survey of 2,214 children living in northeast Thailand was conducted to define 
the antibody response to Burkholderia pseudomallei from birth to 14 years. There was a sharp rise in detectable 
antibodies from birth to 4 years followed by reactivity in approximately 60–70% of children thereafter.

Burkholderia pseudomallei is a soil saprophyte and the cause of melioidosis.1 This organism exists in soil and water in 
association of melioidosis-endemic regions of the tropics, and infection is 
acquired through bacterial inoculation, inhalation, and aspiration. Clinical manifestations of infection are very broad 
ranging, but the most frequent presentation is that of a septicemic illness associated with bacterial dissemination to 
distant sites.1 One fifth of cases in northeast Thailand occur in 
children. Overall mortality is 50% in northeast Thailand (35% in children) and 19% in Australia.2

Children have extensive contact with B. pseudomallei in 
endeMIC areas. Two previous studies have examined the 
antibody response to B. pseudomallei during childhood in melioidosis-endemic northeast Thailand; testing was performed 
using the indirect hemagglutination assay (IHA).3,4 Of 295 
children 1 day to 15 years of age who presented to a well baby 
clinic or were admitted to hospital for illnesses excluding me-
liallisis, 83% had an IHA titer of 1:10 or more, and 7.4% had 
a titer of 1:160 or greater.3 This indicates widespread expo-
sure of children but suggests that a titer of ≥ 1:160 (a titer 
commonly used in Thailand to support a diagnosis of melio-
dosis in patients with clinical feathures consistent with this di-
gnosis) is relatively uncommon. However, children 10 years 
of age numbered only 46 and were grouped together. A sec-
ond larger study of 1,000 children presenting to pediatric 
wards who did not have melioidosis reported a detectable 
titer in 12% of children ≤ 6 months of age, with a linear 
increase to reach a plateau of 80% by 4 years of age.5

The proportion of children with IHA titers of 1:160 or greater rose 
from 2-3% in children under the age of 1 year to 25% in the 
10- to 15-year age group. Again, children between 10 and 15 
years of age were grouped and were under-represented in 
that they made up only 17% of the population. We propose 
that equal numbers of children in each year group are 
required to define more accurately the immune response to B. pseudomallei during childhood. The purpose of this study was to 
perform the IHA in a large cohort of children in which each year was equally represented.

A prospective, cross-sectional study was conducted be-
 tween October 2004 and September 2005, during which un-
selected consecutive serum samples from children between 

birth and 14 years of age were collected from the biochemi-
stry departments of Sappasitiprasong Hospital and Udon 
Thani Hospital in northeast Thailand. Approximately 80% of 
residents belong to rice farming families. Blood samples were 
derived from out- and in-patients from all departments, 
where duplicate samples from the same patient were ex-
cluded. An anonymous database was used to record sex and 
age. Children who were known from the request form to have 
a diagnosis of melioidosis were excluded. Target sample num-
bers were approximately 70 samples in each year group for 
each of the two centers. Collection ceased for a given year 
group once sufficient samples had been identified. Serum 
samples were subsequently tested in random order. The pre-
ence and titer of antibodies to B. pseudomallei were defined 
using the IHA as previously described,5 using pooled antigens 
prepared from B. pseudomallei clinical isolates 199a and 207a 
cultured from patients with melioidosis in northeast Thailand.

Ethical approval for this study was obtained from The Faculty 
of Tropical Medicine, Mahidol University, Thailand, and the 
Oxford Tropical Research Ethics Committee.

Sera were obtained from 2,214 children, of whom 1,266 
(57%) were boys. The number collected per year group is 
shown in Figure 1. The proportion of children with any de-
tectable titer rose sharply in the first 4 years of life (Figure 1). 
The proportion with detectable titers showed little variation 
overall between the age of 4 and 14 years, ranging from 60% 
to 71% positive, with the exception of the 11- and 13-year age 
groups. The proportion of children with a titer of ≥ 1:160 rose 
with increasing years; 9% of those 9 years of age had a titer of 
≥ 1:160, rising to about one fifth of children between 13 and 
14 years of age. Girls had a significantly higher IHA titer than 
boys; the median (interquartile range) was 1:20 (0–1:80) for 
girls and 1:10 (0–1:40) for boys (P = 0.0001). This was noted 
overall across the age spectrum and for different titers.

These data confirm previous findings that an antibody re-
ponse occurs early in childhood in northeast Thailand, with 
a sharp increase in the first 4 years of life. In addition, this 
study provides insights into antibody titers in a large popula-
tion of older children. The proportion with any detectable 
titer was virtually static after the age of 4 years. A significant 
proportion of children failed to develop an antibody re-
response. Parental occupation and living conditions were not 
recorded, but it is unlikely that any children living in north-

east Thailand remain unexposed throughout childhood. We 
have observed previously that a proportion of patients with
culture-proven melioidosis failed to develop an antibody response that is detectable by IHA. We suggest, therefore, that a proportion of people may either fail to mount an antibody response or respond to bacterial antigens that are not present in the IHA test. The significance of this observation for the risk of disease is unclear and warrants further study.

The increase in the proportion of children who had a titer of $1:160$ may relate to repeated exposure to $B. pseudomallei$ in the environment and boosting of the immune response. An alternative possibility is that this is caused by the presence of a bacterial focus that is not associated with clinical features of infection. The majority of the study population with a detectable immune response is unlikely to develop melioidosis during their lifetime, but the relative risk for future disease in those with a low versus high IHA titer is not known. This requires long-term, prospective longitudinal follow-up of a healthy population with known antibody titers. These data clearly show the futility of using an IHA titer of $1:160$ as a diagnostic test for melioidosis in endemic regions.

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