

## RESEARCH NOTE

### LACK OF CORRELATION OF *BURKHOLDERIA PSEUDOMALLEI* QUANTITIES IN BLOOD, URINE, SPUTUM AND PUS

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**Abstract.** We evaluated the correlation of *Burkholderia pseudomallei* quantities in blood versus urine, sputum or pus. Correlations between bacterial counts in blood and other samples were not found. It is likely that an initial seeding event to extracellular organs is followed by independent growth of *B. pseudomallei*, and that bacteria in the urine were not passively filtered from the bloodstream.

#### INTRODUCTION

Melioidosis, an infectious disease caused by the gram-negative bacterium *Burkholderia pseudomallei*, accounts for 20% of all community-acquired bacteremias in northeast Thailand and is the most common cause of fatal community-acquired bacteremic pneumonia in northern Australia (Cheng *et al*, 2005). The organism is present in surface water and soil in areas that are endemic for melioidosis. Disease is acquired through bacterial inoculation or contamination of wounds, or through inhalation or more rarely ingestion (Currie *et al*, 2000). Pneumonia, urinary tract infection,

hepatosplenic abscesses, septic arthritis or subcutaneous abscesses may occur secondary to bacterial dissemination (Currie *et al*, 2000). Individuals with suspected melioidosis are recommended to have cultures of blood, urine, throat swab, respiratory secretions, pus, or swabs from skin lesions if available. Isolation of *B. pseudomallei* from any specimen is diagnostic for melioidosis since this organism is not part of the colonizing flora (Walsh and Wuthiekanun, 1996; Wuthiekanun *et al*, 2001).

The pathogenesis of bacteremic melioidosis remains unclear. It seems likely that after gaining entry into the host, *B. pseudomallei* proliferates locally. We hypothesized that the bacteria then gains entry into the bloodstream from where it seeds to extracellular sites. A previous study showed that median counts of *B. pseudomallei* in sputum and pus specimens were considerably higher than in the blood (Wuthiekanun *et al*, 2007), which supports this possibility. Urinary tract infection in melioidosis was suspected to be caused by bacteremia, and very

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low number of *B. pseudomallei* found in urine may be caused by overflow of the bacteremia (Wuthiekanun *et al*, 2001). The association between presence of *Staphylococcus aureus* bacteremia and secondary bacteriuria has been observed (Lee *et al*, 1978; Ekkelenkamp *et al*, 2007). The aim of this study was to use data on *B. pseudomallei* count in different clinical samples taken from patients with melioidosis to determine whether the bacterial count in blood was correlated with bacterial load in the urinary tract, respiratory tract or abscesses.

#### MATERIALS AND METHODS

Data collected during a previous study determining the quantitative count of *B. pseudomallei* in clinical specimens were used (Wuthiekanun *et al*, 2001). In brief, 414 adult patients with culture-confirmed melioidosis had a total of 730 specimens (414 blood samples, 268 urines, 120 respiratory secretions and 28 pus samples) taken on admission for quantitative culture. Quantitative culture results are summarized in Table 1. Of 268 patients with urine samples collected for culture, 145 (54%) had either blood or urine culture positive for *B. pseudomallei* and were included in the analysis of correlation between CFU counts of *B. pseudomallei* in blood and urine (Fig 1A). No correlation was

found for bacterial load in the two specimen types (Spearman's  $\rho=0.03$ ,  $p=0.75$ ). Of 120 patients with respiratory secretion collected for culture, 109 patients (91%) had either blood culture or respiratory secretion culture positive for *B. pseudomallei*. There was no correlation between bacterial load in blood and respiratory secretions (Fig 1B,  $\rho=0.07$ ,  $p=0.52$ ). Of 28 patients with pus samples collected for quantitative culture, 26 (93%) had either blood culture or pus culture positive for *B. pseudomallei*. No correlation was found between bacterial load in blood and pus samples (Fig 1C,  $\rho=0.11$ ,  $p=0.59$ ). The analyses were repeated in only bacteremic melioidosis and the results were not different.

#### DISCUSSION

The lack of correlation between blood and other specimen types provides further support for the idea that infection and independent growth of *B. pseudomallei* at extracellular sites is a dominant part of disease pathology. These data do not support the idea that bacteria in the bloodstream passively filter into the urine, and are more consistent with active infection of the renal parenchyma. This study has the limitation that we could not control for variable route of infection, antimicrobial administration, and differences in bacterial strain and host sus-

Table 1  
Summary of *B. pseudomallei* quantitative culture result of four clinical specimen types obtained from 414 patients with melioidosis.

Specimen	Median (cfu/ml)	Q1 and Q3 (cfu/ml)	Range (cfu/ml)	Number of positive specimens (% total specimen collected)
Blood	1.1	0.2 - 7.7	<0.1- $\geq 100$	203 (49%, 414)
Urine	$1.5 \times 10^4$	$2.0 \times 10^3$ - $2.3 \times 10^5$	< $10^3$ - $\geq 10^6$	56 (21%, 268)
Sputum	$1.1 \times 10^5$	< $10^2$ - $9.4 \times 10^6$	< $10^2$ - $5.0 \times 10^9$	94 (78%, 120)
Pus	$1.1 \times 10^7$	$6.2 \times 10^5$ - $6.8 \times 10^7$	< $10^2$ - $2.3 \times 10^8$	23 (82%, 28)

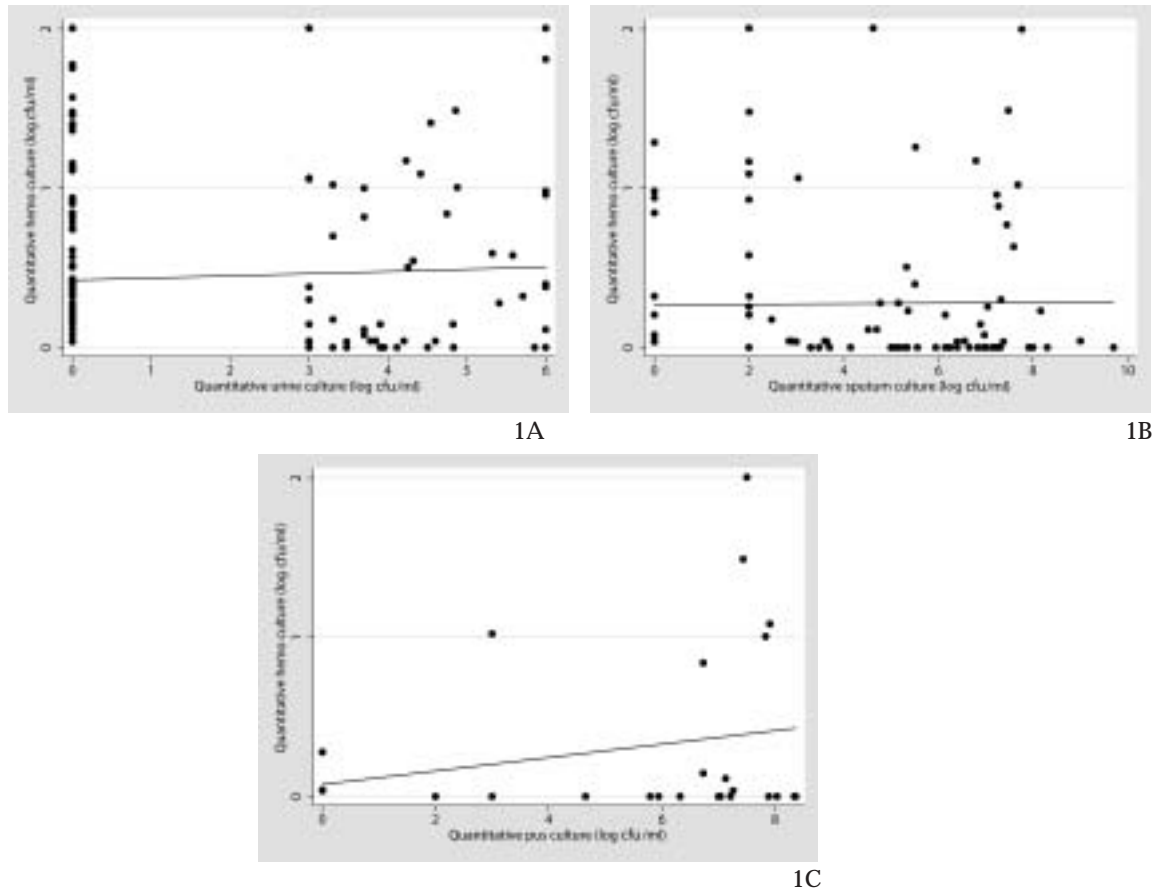


Fig 1—Scatter plot with liner regression curve of *B. pseudomallei* quantitative culture of blood and urine (1A), blood and respiratory secretion (1B), and blood and pus (1C) from 145, 109 and 29 patients, who had either blood or another clinical specimen culture positive for *B. pseudomallei*, respectively. No correlation was found between quantitative counts of blood and other specimen types.

ceptibility. These may be associated with the different patterns of disease progression. Studies in mouse models in which such factors were controlled also observed a lack of correlation in *B. pseudomallei* cfu counts in blood and other infected organs. Tan *et al* (2008) found rising cfu counts in the liver and spleen but a decline of *B. pseudomallei* counts in blood at one week after aerosol inoculation into mice. However, variation in clinical presentation of melioidosis in individual patients suggests that route of infec-

tion, bacterial strain and host susceptibility are major factors associated with infection and progression of *B. pseudomallei* at primary and disseminated organs in individual.

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