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Letters to the Editor

Aminoglycoside and Macrolide Resistance in *Burkholderia pseudomallei*

We were very interested in the recent paper by Moore et al. (3) in which the authors used transposon mutants to demonstrate efflux-mediated resistance to aminoglycosides and macrolides in *Burkholderia* (formerly *Pseudomonas*) *pseudomallei*. Melioidosis is very difficult to treat because of intrinsic resistance to many antimicrobial agents, particularly the aminoglycosides. Aminoglycoside–β-lactam combinations are used empirically to treat suspected community-acquired sepsis in many areas of the world, but they are ineffective in melioidosis.

We have been conducting clinical and laboratory studies of melioidosis in Thailand since 1986. During this time we have collected over 3,700 clinical isolates of *B. pseudomallei* from more than 1,800 patients with melioidosis admitted to Sappasitprasong Hospital, Ubon Ratchathani, northeast Thailand. We have performed susceptibility testing using the disk diffusion method on most of these isolates, according to the guidelines of the National Committee for Clinical Laboratory Standards (4), for ceftazidime, co-amoxiclav, chloramphenicol, doxycycline, ciprofloxacin, gentamicin, polymyxin B, and, more recently, imipenem. MIC determinations, using an agar incorporation method (5), have been performed for representative isolates.

During this time we have isolated three strains of *B. pseudomallei*, from two patients, which were susceptible to gentamicin by disk testing. The isolates were from a splenic aspirate of one patient (708a) (2) and from blood and knee aspirate cultures of the second (2188a and b).

All other isolates were resistant to gentamicin by disk testing (disk content, 10 μg). *B. pseudomallei* is usually highly resistant to aminoglycosides, with a gentamicin MIC at which 50% of the isolates are inhibited of 128 mg/liter (1), and also to the macrolide antibiotics. The MIC results for 100 clinical isolates of *B. pseudomallei*, collected during 1998, for the macrolides erythromycin, clarithromycin, and azithromycin are listed in Table 1. In contrast, the three gentamicin-susceptible isolates were also susceptible to these macrolide antibiotics (Table 1).

For all three isolates the MICs of ceftazidime, imipenem, chloramphenicol, ciprofloxacin, and doxycycline were within the expected ranges for each agent. All three were resistant to polymyxin B.

Thus, there are very rare wild strains of *B. pseudomallei* which exhibit antibiotic susceptibility patterns similar to those of the transposon mutants created by Moore et al. (3), i.e., with linked loss of resistance to aminoglycosides and macrolides. By definition the three clinical isolates described here are virulent. This is consistent with the evidence for retention of virulence in hamsters by the mutant strains. Whether these findings have therapeutic implications remains to be seen.

TABLE 1. MICs[a] for isolates of *B. pseudomallei*

Antibiotic	MIC_{50}	MIC_{90}	MIC		
			708a	2188a	2188b
Gentamicin	128[b]	128[b]	0.5	0.5	0.5
Erythromycin	256[c]	256[c]	16	4	4
Azithromycin	256[c]	256[c]	2	<0.5	<0.5
Clarithromycin	128[c]	256[c]	16	4	4

[a] In milligrams per liter.
[b] For 10 NCTC strains and 211 clinical isolates of *B. pseudomallei* (1).
[c] For 100 clinical isolates of *B. pseudomallei* isolated during 1998.

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