related with hypercytokinemia [5]. Whether antiviral treatment for these patients will provide benefit is not yet clear. More studies on viral load profiles among hospitalized patients with influenza and clinical trials of late antiviral therapy are needed to resolve the issue.

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N. Lee,[1] C. S. Cockram,[1] P. K. S. Chan,[2] D. S. C. Hui,[1] K. W. Choi,[1] and J. J. Y. Sung[1]

Departments of [1]Medicine and Therapeutics and [2]Microbiology, The Chinese University of Hong Kong, Hong Kong

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Reprints or correspondence: Dr. Nelson Lee, Div. of Infectious Diseases, Dept. of Medicine and Therapeutics, The Chinese University of Hong Kong, 9/F, Clinical Sciences Bldg., Prince of Wales Hospital, Shatin, Hong Kong Special Administrative Region, People's Republic of China (leelsn@cuhk.edu.hk).

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Increased Antimicrobial Susceptibility Profiles among Polymyxin-Resistant *Acinetobacter baumannii* Clinical Isolates

To the Editor—We read with great interest the article by Li et al. [1], in which the authors reported promising therapeutic options for treatment of infections caused by colistin-resistant *Acinetobacter baumannii*. The authors observed overall increased antimicrobial susceptibility among colistin-resistant strains, compared with the parent colistin-susceptible strains. Because of the potential therapeutic importance of this observation, we evaluated the susceptibility profiles of polymyxin-resistant and -susceptible *A. baumannii* clinical isolates collected as part of the global SENTRY Antimicrobial Surveillance Program during the period 2001–2007 [2].

A collection of 3707 *A. baumannii* isolates were tested for susceptibility to numerous antimicrobial agents using validated broth microdilution panels with cation-adjusted Mueller-Hinton medium (TREK Diagnostics) [3]. Testing and incubation were performed according to the methods of the Clinical and Laboratory Standards Institute [4]. MICs were interpreted as specified by the Clinical and Laboratory Standards Institute [5], except for tigecycline MICs, which were interpreted according to breakpoints approved by the US Food and Drug Administration (breakpoint for susceptibility, $\leqslant 2$ μg/mL; breakpoint for resistance, $\geqslant 8$ μg/mL). For comparison purposes, geographically unrelated polymyxin-resistant isolates were included in this study, and the resistance phenotype was confirmed by Etest (AB Biodisk). Susceptibility rates for polymyxin-resistant isolates were compared with those for polymyxin-susceptible isolates by χ^2 test, using EpiInfo, version 3.4.1 (Centers for Disease Control and Prevention). $P < .05$ was considered to be statistically significant.

The distribution of MIC_{50} and susceptibility rates among polymyxin-resistant and -susceptible *A. baumannii* for selected antimicrobial agents are shown in table 1. Most drugs demonstrated limited spectrums of activity against the polymyxin-susceptible group (susceptibility rate, $\leqslant$53.8%), except for the carbapenems (imipenem [71.6% susceptible] and meropenem [68.0% susceptible]), tetracyclines (doxycycline [74.6% susceptible], minocycline [88.4% susceptible], and tigecycline [97.0% inhibited at $\leqslant 2$ μg/mL]). Overall, compared with the polymyxin-susceptible group, the polymyxin-resistant group showed higher susceptibility rates for the majority of antimicrobial agents (16 of 22 antimicrobial agents). The differences were mostly observed among those drugs showing lower susceptibility rates ($\leqslant$48.8%) and were statistically significant for the β-lactams ampicillin-sulbactam, aztreonam, cefoxitin, cefepime, ceftriaxone, and cefuroxime ($P < .05$). In contrast, antimicrobial agents with better activity, such as imipenem, meropenem, tobramycin, minocycline, and tigecycline, showed similar or slightly higher activity against the polymyxin-susceptible isolates, compared with the polymyxin-resistant isolates.

Overall, these results corroborate with those previously reported by Li et al. [1], except for the results for ticarcillin-clavulanate and carbapenems, for which the authors noted substantially lower MICs among the colistin-resistant group, compared with the colistin-susceptible group. On the other hand, compared with our group of polymyxin-susceptible isolates, our collection of polymyxin-resistant clinical isolates showed higher susceptibility rates for amikacin, tetracycline, and trimethoprim-sulfamethoxazole—results not observed previously by Li et al. [1].

Li et al. suggested that *A. baumannii* showing phenotypic resistance to colistin may possess outer-membrane modifications, consequently increasing permeability for antimicrobial agents, which may also explain the results obtained in our study. Regardless of the changes, they were not favorable for those antimicrobial agents frequently used for treatment of infections caused by multidrug-resistant *A. baumannii*, such as the carbapenems and tobramycin. Furthermore, minocycline and the novel glycylcycline tigecycline, which may represent a valuable antimicrobial for treatment of infections caused by multidrug-resistant *A. baumannii* [6], were highly active independently of the polymyxin susceptibility profile.

Table 1. MIC_{50}, antimicrobial susceptibility profile, and susceptibility rates of 3683 polymyxin-susceptible and 24 polymyxin-resistant *Acinetobacter baumannii* isolates.

Antimicrobial agent	Polymyxin-susceptible phenotype[a]		Polymyxin-resistant phenotype[a]		P[b]	OR (95 CI%)[c]
	MIC_{50}, μg/mL	Susceptibility rate, %	MIC_{50}, μg/mL	Susceptibility rate, %		
Ampicillin-sulbactam	16	45.4	4	70.8	.013	2.92 (1.14–7.76)
Piperacillin	>64	21.0	64	33.3	.138	1.88 (0.74–4.69)
Piperacillin-tazobactam	>64	33.2	32	45.8	.187	1.71 (0.71–4.07)
Ticarcillin-clavulanate	128	29.3	64	33.3	.762	1.14 (0.54–2.83)
Aztreonam	>16	4.9	>16	20.8	<.001	5.21 (1.68–15.0)
Cefoxitin	>16	0.9	>16	20.8	<.001	30.0 (9.18–92.4)
Cefepime	16	38.4	4	58.3	.046	2.24 (0.93–5.44)
Ceftazidime	>16	34.5	>16	45.8	.240	1.61 (0.67–3.84)
Ceftriaxone	>32	16.2	32	41.6	<.001	3.7 (1.52–8.89)
Cefuroxime	>16	2.6	>16	25.0	<.001	12.72 (4.41–34.97)
Imipenem	1	71.6	1	66.6	.589	0.79 (0.32–2.02)
Meropenem	2	68.0	4	58.3	.314	0.66 (0.28–1.60)
Ciprofloxacin	>4	32.7	1	50.0	.072	2.06 (0.86–4.90)
Levofloxacin	>4	35.6	≤0.5	50.0	.142	1.81 (0.76–4.31)
Amikacin	32	48.8	8	58.3	.355	1.46 (0.61–3.55)
Gentamicin	>8	37.0	4	50.0	.190	1.70 (0.71–4.05)
Tobramycin	4	53.8	8	45.8	.434	0.73 (0.30–1.73)
Minocycline	≤1	88.4	≤1	87.5	.885	0.91 (0.26–3.89)
Tigecycline	0.5	97.0	0.5	95.8	.729	0.70 (0.10–14.16)
Doxycycline	≤1	74.6	≤1	87.5	.150	2.37 (0.67–10.03)
Tetracycline	8	43.1	≤4	58.3	.133	1.85 (0.77–4.49)
Trimethoprim-sulfamethoxazole	>2	37.9	≤2	54.2	.420	1.39 (0.58–3.31)

[a] The category of susceptibility for polymyxin was determined as specified by the Clinical and Laboratory Standards Institute [5], except for tigecycline, which was interpreted according to the breakpoints approved by the US Food and Drug Administration (≤2 μg/mL for susceptible and ≥8 μg/mL for resistant).

[b] Calculated by χ^2 test.

[c] ORs and respective 95% CIs refer to comparisons of susceptibility rates between polymyxin-resistant *A. baumannii* and polymyxin-susceptible *A. baumannii* for each antimicrobial agent.

In addition, it is important to mention that other resistance mechanisms were present among the polymyxin-resistant isolates when the antimicrobial agents did not become satisfactorily more active; however, the susceptibility rate for ampicillin-sulbactam increased substantially among those isolates (from 45.4% to 70.8%) (table 1). In summary, this study complements the data reported previously [1], providing additional insights for combination therapeutic options and for possible novel antimicrobial agents in development, and indicates that local susceptibility testing results will be important in guiding treatment.

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Rodrigo E. Mendes,[1] Thomas R. Fritsche,[1] Helio S. Sader,[1,2] and Ronald N. Jones[1,3]

[1]JMI Laboratories, North Liberty, Iowa; [2]Universidade Federal de São Paulo, São Paulo, Brazil; and [3]Tufts University School of Medicine, Boston, Massachusetts

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Reprints or correspondence: Dr. Rodrigo E. Mendes, JMI Laboratories, 345 Beaver Kreek Centre, Ste. A, North Liberty, IA 52317 (rodrigo-mendes@jmilabs.com).

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