

Antimicrobial Susceptibility among Pathogens Collected from Hospitalized Patients in the United States and In Vitro Activity of Tigecycline, a New Glycylcycline Antimicrobial

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Received 17 February 2006/Returned for modification 15 May 2006/Accepted 23 July 2006

The activities of tigecycline and comparators against isolates collected from 76 U.S. centers between January 2004 and September 2005 were assessed. Tigecycline MIC₉₀s were ≤2 μg/ml for *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Escherichia coli*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Serratia marcescens*, *Acinetobacter baumannii*, *Staphylococcus aureus*, *Enterococcus faecalis*, *Enterococcus faecium*, and *Streptococcus agalactiae*.

Tigecycline (Wyeth Pharmaceuticals, Collegeville, PA) is a novel antimicrobial with an expanded broad spectrum of in vitro activity. It is the first glycylcycline to be approved in the United States for use in the treatment of complicated skin and skin structure and intra-abdominal infections. The Tigecycline Evaluation and Surveillance Trial (TEST) is a global multicenter surveillance program designed to assess the in vitro activities of tigecycline and comparators against a range of clinically important pathogens from both the community and hospital settings. This study reports on the in vitro activities of tigecycline and comparators against a variety of organisms collected in 2004/2005 from U.S. centers of the TEST program.

Bacterial isolates. Isolates were collected between January 2004 and September 2005 from 76 centers across the United States. The following states were included in the study (numbers of centers are in parentheses): Washington (one), Oregon (two), California (two), Utah (one), Arizona (two), New Mexico (one), North Dakota (one), Nebraska (one), Kansas (one), Oklahoma (one), Texas (three), Minnesota (one), Missouri (one), Arkansas (one), Louisiana (two), Wisconsin (one), Illinois (one), Michigan (three), Indiana (one), Kentucky (one), Tennessee (three), Mississippi (one), Alabama (one), Georgia (four), Ohio (six), West Virginia (one), Virginia (one), North Carolina (two), Florida (five), Pennsylvania (one), Maryland (two), Delaware (one), New Jersey (four), New York (nine), Connecticut (two), Massachusetts (two), New Hampshire (one), Vermont (one), and the District of Columbia (one). Consecutive isolates were collected from patients with a documented infection, and only isolates that were determined by the center to be clinically significant (using institutional criteria) were included. One isolate per patient was permitted.

Isolates were identified to the species level by the participating laboratory. Organism collection and verification of organism identity (for approximately 10% of isolates received) were carried out by a central laboratory (Laboratories International for Microbiology Studies, a division of International Health Management Associates, Inc., Schaumburg, IL).

Antimicrobial susceptibility testing. MICs were determined locally, and the information was returned to the central laboratory for inclusion in the centralized database. MICs were determined according to the broth microdilution methodology of the Clinical and Laboratory Standards Institute (CLSI) (formerly NCCLS) (13).

Quality control was carried out by each testing site, on each day of testing, and submitted to the central laboratory. The quality control strains were *Escherichia coli* ATCC 25922, *Staphylococcus aureus* ATCC 29213, *Pseudomonas aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, and *Streptococcus pneumoniae* ATCC 49619.

Susceptibility determinations. Susceptibility was determined according to the interpretive criteria of the CLSI (8). For tigecycline, the FDA-approved criteria were applied for those organisms listed in the package insert (18). No interpretive criteria have been approved for tigecycline when testing against *Acinetobacter* spp. or *Pseudomonas* spp. Isolates of *E. coli*, *Klebsiella pneumoniae*, and *Klebsiella oxytoca* were tested for extended-spectrum β-lactamase (ESBL) production according to CLSI methods (8).

Table 1 shows the activities of tigecycline and comparators against *K. pneumoniae*, *K. oxytoca*, *E. coli*, *Enterobacter aerogenes*, *Enterobacter cloacae*, *Serratia marcescens*, *Acinetobacter baumannii*, and *P. aeruginosa*. A total of 126 isolates of *K. pneumoniae* were identified as ESBL producers (126/1,460 [8.6%]), and against these isolates, the lowest MIC₉₀ was for tigecycline (2 μg/ml). A total of 1,334 (91.4%) *K. pneumoniae* isolates were identified as non-ESBL-producing isolates; the lowest MIC₉₀s were for ceftriaxone, cefepime, imipenem, and levofloxacin (≤0.5 μg/ml) (Table 1). Tigecycline activity was unaffected by ESBL production. In addition, tigecycline was the only compound to which more than 90% of ESBL-producing isolates were susceptible.

Among the 1,785 *E. coli* isolates collected, more than 95% of isolates were susceptible to tigecycline, piperacillin-tazobactam, ceftriaxone, cefepime, imipenem, and amikacin; 94.6% of isolates were susceptible to ceftazidime. Overall, 20.5% of isolates were resistant to levofloxacin; in the subset of isolates identified as ESBL producers ($n = 31$), this increased to 83.9% (data not shown).

Among *A. baumannii* isolates, the lowest MIC₉₀ was for

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TABLE 1. Susceptibilities of gram-negative pathogens to the TEST panel of antimicrobial agents^a

Strain and antimicrobial	MIC ($\mu\text{g/ml}$)			% S	% I	% R
	50%	90%	Range			
Non-ESBL-producing <i>Klebsiella pneumoniae</i> (n = 1,334)						
Tigecycline	0.5	2	≤ 0.008 –8	95.0	4.3	0.7
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	0.8	19.0	80.2
Amoxicillin-clavulanate	2	8	0.25 – ≥ 64	90.2	3.5	6.3
Piperacillin-tazobactam	2	8	≤ 0.06 – ≥ 256	95.2	0.9	3.9
Ceftazidime	≤ 8	≤ 8	≤ 8 – ≥ 64	95.0	1.1	3.9
Ceftriaxone	≤ 0.06	0.25	≤ 0.06 – ≥ 128	96.6	1.3	2.1
Cefepime	≤ 0.5	≤ 0.5	≤ 0.5 – ≥ 64	97.7	0.2	2.1
Imipenem	0.5	0.5	≤ 0.06 – ≥ 32	98.7	0.4	0.9
Levofloxacin	0.06	0.5	≤ 0.008 – ≥ 16	94.1	1.2	4.7
Amikacin	2	2	≤ 0.5 –32	98.8	1.2	0.0
Minocycline	2	8	≤ 0.5 – ≥ 32	86.1	5.9	8.0
ESBL-producing <i>Klebsiella pneumoniae</i> (n = 126)						
Tigecycline	1	2	0.12–8	92.1	6.3	1.6
Ampicillin	≥ 64	≥ 64	16 – ≥ 64	0.0	0.8	99.2
Amoxicillin-clavulanate	16	≥ 64	2 – ≥ 64	27.0 ^b	26.2	46.8
Piperacillin-tazobactam	128	≥ 256	1 – ≥ 256	42.9 ^b	4.8	52.4
Ceftazidime	≥ 64	≥ 64	≤ 8 – ≥ 64	5.6	1.6	92.9
Ceftriaxone	64	≥ 128	0.25 – ≥ 128	24.6	24.6	50.8
Cefepime	8	≥ 64	≤ 0.5 – ≥ 64	53.2	8.7	38.1
Imipenem	0.5	8	0.25 – ≥ 32	76.2	15.1	8.7
Levofloxacin	≥ 16	≥ 16	0.03 – ≥ 16	25.4	2.4	72.2
Amikacin	8	32	≤ 0.5 –32	82.5	17.5	0.0
Minocycline	4	≥ 32	1 – ≥ 32	70.6	8.7	20.6
<i>Klebsiella oxytoca</i> (n = 248)						
Tigecycline	0.25	1	0.06–4	98.8	1.2	0.0
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	4.4	7.7	87.9
Amoxicillin-clavulanate	2	16	0.25 – ≥ 64	87.1	4.0	8.9
Piperacillin-tazobactam	1	8	≤ 0.06 – ≥ 256	92.7	0.8	6.5
Ceftazidime	≤ 8	≤ 8	≤ 8 – ≥ 64	93.5	0.4	6.0
Ceftriaxone	≤ 0.06	4	≤ 0.06 –32	95.6	4.4	0.0
Cefepime	≤ 0.5	1	≤ 0.5 –16	99.6	0.4	0.0
Imipenem	0.5	0.5	0.25–8	99.6	0.4	0.0
Levofloxacin	0.03	1	≤ 0.008 – ≥ 16	96.0	2.4	1.6
Amikacin	2	4	≤ 0.5 –16	100	0.0	0.0
Minocycline	1	4	≤ 0.5 – ≥ 32	93.5	5.2	1.2
<i>Escherichia coli</i> (n = 1,785)						
Tigecycline	0.12	0.25	0.015–4	99.8	0.2	0.0
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	46.9	1.3	51.8
Amoxicillin-clavulanate	4	32	0.25 – ≥ 64	75.4	12.7	11.9
Piperacillin-tazobactam	1	4	≤ 0.06 – ≥ 256	95.7	2.2	2.1
Ceftazidime	≤ 8	≤ 8	≤ 8 – ≥ 64	94.6	1.7	3.7
Ceftriaxone	≤ 0.06	0.25	≤ 0.06 – ≥ 128	95.4	2.3	2.4
Cefepime	≤ 0.5	≤ 0.5	≤ 0.5 – ≥ 64	98.5	0.3	1.1
Imipenem	0.25	0.5	0.12–4	100	0.0	0.0
Levofloxacin	0.03	≥ 16	≤ 0.008 – ≥ 16	78.1	1.4	20.5
Amikacin	2	4	≤ 0.5 –32	99.6	0.4	0.0
Minocycline	1	8	≤ 0.5 – ≥ 32	86.4	7.6	5.9
<i>Enterobacter aerogenes</i> (n = 419)						
Tigecycline	0.5	1	0.06–8	95.7	3.3	1.0
Ampicillin	≥ 64	≥ 64	1 – ≥ 64	1.0	5.5	93.6
Amoxicillin-clavulanate	≥ 64	≥ 64	1 – ≥ 64	3.8	3.1	93.1
Piperacillin-tazobactam	2	32	0.12 – ≥ 256	87.8	8.4	3.8
Ceftazidime	≤ 8	32	≤ 8 – ≥ 64	82.6	4.8	12.6
Ceftriaxone	0.12	8	≤ 0.06 – ≥ 128	92.1	6.2	1.7
Cefepime	≤ 0.5	1	≤ 0.5 – ≥ 64	98.1	1.2	0.7
Imipenem	1	2	0.25–8	99.5	0.5	0.0
Levofloxacin	0.06	0.5	≤ 0.008 – ≥ 16	94.3	2.6	3.1
Amikacin	2	4	≤ 0.5 –32	99.0	1.0	0.0
Minocycline	2	8	≤ 0.5 – ≥ 32	90.0	4.8	5.3

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TABLE 1—Continued

Strain and antimicrobial	MIC ($\mu\text{g/ml}$)			% S	% I	% R
	50%	90%	Range			
<i>Enterobacter cloacae</i> (n = 1,089)						
Tigecycline	0.5	2	≤ 0.008 –8	93.0	4.6	2.4
Ampicillin	≥ 64	≥ 64	1– ≥ 64	1.7	4.1	94.2
Amoxicillin-clavulanate	≥ 64	≥ 64	1– ≥ 64	2.8	1.3	96.0
Piperacillin-tazobactam	2	64	≤ 0.06 – ≥ 256	81.9	9.5	8.6
Ceftazidime	≤ 8	≥ 64	≤ 8 – ≥ 64	73.5	4.0	22.5
Ceftriaxone	0.25	64	≤ 0.06 – ≥ 128	77.2	9.3	13.5
Cefepime	≤ 0.5	4	≤ 0.5 – ≥ 64	95.7	1.9	2.4
Imipenem	0.5	1	0.25–16	99.8	0.1	0.1
Levofloxacin	0.06	2	≤ 0.008 – ≥ 16	90.4	3.0	6.5
Amikacin	2	2	≤ 0.5 – ≥ 128	99.7	0.2	0.1
Minocycline	2	8	≤ 0.5 – ≥ 32	83.7	6.8	9.5
<i>Serratia marcescens</i> (n = 658)						
Tigecycline	1	1	0.12–8	97.0	2.7	0.3
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	2.9	4.0	93.2
Amoxicillin-clavulanate	≥ 64	≥ 64	≤ 0.12 – ≥ 64	2.4	1.7	95.9
Piperacillin-tazobactam	1	8	0.12– ≥ 256	96.7	2.1	1.2
Ceftazidime	≤ 8	≤ 8	≤ 8 – ≥ 64	93.5	2.1	4.4
Ceftriaxone	0.25	4	≤ 0.06 – ≥ 128	94.7	2.6	2.7
Cefepime	≤ 0.5	1	≤ 0.5 – ≥ 64	98.0	0.9	1.1
Imipenem	1	2	0.25– ≥ 32	99.5	0.3	0.2
Levofloxacin	0.12	1	0.015– ≥ 16	96.2	1.8	2.0
Amikacin	2	4	≤ 0.5 –16	100	0.0	0.0
Minocycline	2	4	≤ 0.5 – ≥ 32	91.6	4.9	3.5
<i>Acinetobacter baumannii</i> (n = 851)						
Tigecycline	0.5	1	0.03–8	— ^c	— ^c	— ^c
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	— ^d	— ^d	— ^d
Amoxicillin-clavulanate	32	≥ 64	≤ 0.12 – ≥ 64	— ^d	— ^d	— ^d
Piperacillin-tazobactam	8	≥ 256	≤ 0.06 – ≥ 256	58.2	16.6	25.3
Ceftazidime	16	≥ 64	≤ 8 – ≥ 64	46.9	5.1	48.1
Ceftriaxone	32	≥ 128	≤ 0.06 – ≥ 128	29.1	23.4	47.5
Cefepime	16	≥ 64	≤ 0.5 – ≥ 64	44.8	16.6	38.7
Imipenem	0.5	16	≤ 0.06 – ≥ 32	87.0	1.5	11.5
Levofloxacin	4	≥ 16	0.015– ≥ 16	47.6	5.3	47.1
Amikacin	4	32	≤ 0.5 – ≥ 128	83.9	7.5	8.6
Minocycline	≤ 0.5	8	≤ 0.5 – ≥ 32	88.0	9.8	2.2
<i>Pseudomonas aeruginosa</i> (n = 1,338)						
Tigecycline	8	≥ 32	≤ 0.008 – ≥ 32	— ^c	— ^c	— ^c
Ampicillin	≥ 64	≥ 64	≤ 0.5 – ≥ 64	— ^d	— ^d	— ^d
Amoxicillin-clavulanate	≥ 64	≥ 64	2– ≥ 64	— ^d	— ^d	— ^d
Piperacillin-tazobactam	4	64	≤ 0.06 – ≥ 256	91.1	— ^d	8.9
Ceftazidime	≤ 8	32	≤ 8 – ≥ 64	84.8	5.2	10.1
Ceftriaxone	64	≥ 128	≤ 0.06 – ≥ 128	17.0	25.3	57.8
Cefepime	4	16	≤ 0.5 – ≥ 64	79.7	12.9	7.4
Imipenem	1	8	≤ 0.06 – ≥ 32	88.5	8.7	2.8
Levofloxacin	1	≥ 16	≤ 0.008 – ≥ 16	65.8	7.5	26.8
Amikacin	4	8	≤ 0.5 – ≥ 128	97.3	1.2	1.5
Minocycline	≥ 32	≥ 32	≤ 0.5 – ≥ 32	4.0	12.6	83.5

^a S, susceptible; I, intermediate; R, resistant. Susceptible, intermediate, and resistant values may add to 99.9 or 100.1 due to rounding.

^b Although ESBL-producing *K. pneumoniae* may appear susceptible to cephalosporins in vitro, such isolates should be treated as resistant clinically, irrespective of MICs (8).

^c No FDA-approved interpretive criteria are available.

^d No CLSI-approved interpretive criteria are available.

tigecycline (1 $\mu\text{g/ml}$) (Table 1). The MIC₉₀ for imipenem was 16 $\mu\text{g/ml}$, and 11.5% of isolates were resistant to imipenem. In the case of *P. aeruginosa*, piperacillin-tazobactam and amikacin were the only agents to which more than 90% of isolates were susceptible (91.1% and 97.3%, respectively) (Table 1).

Table 2 shows the activities of tigecycline and comparators against *S. aureus*, *E. faecalis*, *Enterococcus faecium*, and *Strep-*

tococcus agalactiae. Among the *S. aureus* isolates collected, 813 (48.0%) were methicillin susceptible (methicillin-susceptible *S. aureus* [MSSA]) and 879 (52.0%) were methicillin resistant (methicillin-resistant *S. aureus* [MRSA]). Against both MSSA and MRSA, the lowest MIC₅₀s and MIC₉₀s were for tigecycline and minocycline (Table 2). Similarly, a low MIC₅₀ and a low MIC₉₀ were recorded for imipenem against MSSA isolates

TABLE 2. Susceptibilities of gram-positive pathogens to the TEST panel of antimicrobial agents^a

Strain and antimicrobial	MIC ($\mu\text{g/ml}$)			% S	% I	% R
	50%	90%	Range			
Methicillin-susceptible <i>Staphylococcus aureus</i> (n = 813)						
Tigecycline	0.12	0.12	0.015–0.5	100	— ^d	— ^d
Penicillin	8	≥ 16	≤ 0.06 – ≥ 16	13.9	— ^e	86.1
Ampicillin	4	≥ 32	≤ 0.06 – ≥ 32	15.9	— ^e	84.1
Amoxicillin-clavulanate	1	2	≤ 0.03 –4	100	— ^e	0.0
Piperacillin-tazobactam	1	2	≤ 0.25 –8	100	— ^e	0.0
Imipenem	0.25	0.25	≤ 0.12 –2	100	0.0	0.0
Ceftriaxone	4	4	0.12–32	96.9	3.1	0.0
Levofloxacin	0.12	4	≤ 0.06 – ≥ 64	87.6	2.3	10.1
Minocycline	≤ 0.25	≤ 0.25	≤ 0.25 –8	99.0	1.0	0.0
Linezolid	2	2	≤ 0.5 –4	100	— ^e	— ^e
Vancomycin	0.5	1	≤ 0.12 –4	100	0.0	0.0
Methicillin-resistant <i>Staphylococcus aureus</i> (n = 879)						
Tigecycline	0.12	0.25	0.03–0.5	100	— ^d	— ^d
Penicillin	≥ 16	≥ 16	0.25– ≥ 16	0.0	— ^e	100
Ampicillin	≥ 32	≥ 32	0.5– ≥ 32	0.0	— ^e	100
Amoxicillin-clavulanate	8	≥ 16	1– ≥ 16	25.1 ^b	— ^e	74.9
Piperacillin-tazobactam	16	≥ 32	1– ≥ 32	31.9 ^b	— ^e	68.1
Imipenem	0.5	16	≤ 0.12 – ≥ 32	82.6	3.8	13.7
Ceftriaxone	32	≥ 128	8– ≥ 128	0.2	58.5	41.3
Levofloxacin	16	≥ 64	≤ 0.06 – ≥ 64	18.5	2.3	79.2
Minocycline	≤ 0.25	0.5	≤ 0.25 – ≥ 16	99.3	0.6	0.1
Linezolid	2	4	≤ 0.5 –4	100	— ^e	— ^e
Vancomycin	1	1	0.25–4	100	0.0	0.0
<i>Enterococcus faecalis</i> (n = 740)						
Tigecycline	0.06	0.12	0.015–0.5	— ^c	— ^d	— ^d
Penicillin	2	4	0.12– ≥ 16	97.2	— ^e	2.8
Ampicillin	1	1	0.12– ≥ 32	97.8	— ^e	2.2
Amoxicillin-clavulanate	0.5	1	≤ 0.03 – ≥ 16	— ^e	— ^e	— ^e
Piperacillin-tazobactam	2	4	≤ 0.25 – ≥ 32	— ^e	— ^e	— ^e
Imipenem	1	1	≤ 0.12 – ≥ 32	— ^e	— ^e	— ^e
Ceftriaxone	≥ 128	≥ 128	0.5– ≥ 128	— ^e	— ^e	— ^e
Levofloxacin	1	≥ 64	≤ 0.06 – ≥ 64	55.3	1.1	43.6
Minocycline	8	8	≤ 0.25 – ≥ 16	44.2	46.2	9.6
Linezolid	2	2	≤ 0.5 –16	97.6	1.9	0.5
Vancomycin	1	2	≤ 0.12 – ≥ 64	94.6	0.7	4.7
<i>Enterococcus faecium</i> (n = 280)						
Tigecycline	0.06	0.12	0.015–0.5	— ^d	— ^d	— ^d
Penicillin	≥ 16	≥ 16	0.12– ≥ 16	11.4	— ^e	88.6
Ampicillin	≥ 32	≥ 32	0.12– ≥ 32	13.9	— ^e	86.1
Amoxicillin-clavulanate	≥ 16	≥ 16	0.06– ≥ 16	— ^e	— ^e	— ^e
Piperacillin-tazobactam	≥ 32	≥ 32	1– ≥ 32	— ^e	— ^e	— ^e
Imipenem	≥ 32	≥ 32	0.25– ≥ 32	— ^e	— ^e	— ^e
Ceftriaxone	≥ 128	≥ 128	2– ≥ 128	— ^e	— ^e	— ^e
Levofloxacin	≥ 64	≥ 64	0.5– ≥ 64	8.9	1.4	89.6
Minocycline	0.5	8	≤ 0.25 – ≥ 16	67.9	23.9	8.2
Linezolid	2	2	≤ 0.5 –4	96.4	3.6	0.0
Vancomycin	≥ 64	≥ 64	0.25– ≥ 64	31.4	0.7	67.9
<i>Streptococcus agalactiae</i> (n = 655)						
Tigecycline	0.03	0.25	0.015–1	99.5	— ^d	— ^d
Penicillin	≤ 0.06	0.12	≤ 0.06 –0.25	99.8	— ^e	— ^e
Ampicillin	0.12	0.12	≤ 0.06 –0.25	100	— ^e	— ^e
Amoxicillin-clavulanate	0.06	0.12	≤ 0.03 –1	— ^e	— ^e	— ^e
Piperacillin-tazobactam	≤ 0.25	≤ 0.25	≤ 0.25 –2	— ^e	— ^e	— ^e
Imipenem	≤ 0.12	0.25	≤ 0.12 –1	— ^e	— ^e	— ^e
Ceftriaxone	0.06	0.12	≤ 0.03 –2	99.8	— ^e	— ^e
Levofloxacin	0.5	1	≤ 0.06 –32	99.4	0.5	0.2
Minocycline	8	≥ 16	≤ 0.25 – ≥ 16	— ^e	— ^e	— ^e
Linezolid	1	1	≤ 0.5 –2	100	— ^e	— ^e
Vancomycin	0.5	0.5	≤ 0.12 –1	100	— ^e	— ^e

^a S, susceptible; I, intermediate; R, resistant. Susceptible, intermediate, and resistant values may add to 99.9 or 100.1 due to rounding.

^b For methicillin-resistant *S. aureus*, β -lactam/ β -lactamase inhibitor combinations may appear active in vitro but are not effective clinically (8).

^c The FDA-approved interpretive criteria for tigecycline and *E. faecalis* apply only to vancomycin-susceptible isolates.

^d No FDA-approved interpretive criteria are available.

^e No CLSI-approved interpretive criteria are available.

(0.25 µg/ml). However, against MRSA, while the MIC₅₀ of imipenem remained low (0.5 µg/ml), the MIC₉₀ was 16 µg/ml. Of the 740 isolates of *E. faecalis* and 280 isolates of *E. faecium* collected, the lowest MIC₅₀ and MIC₉₀ were recorded for tigecycline (0.06 and 0.12 µg/ml, respectively) (Table 2).

The prevalence of ESBL-producing *K. pneumoniae* reported in this study (8.6%) is similar to that reported previously by Paterson et al. for *Klebsiella* spp. collected in 2003 as part of the SMART study (7%; the stated frequency for *K. pneumoniae* was similar, although the data were not reported) (14). Of concern are the 8.7% of ESBL-producing *K. pneumoniae* isolates that were identified as being resistant to imipenem. The majority of these isolates came from centers in the New York and New Jersey areas and may possess the *bla*_{KPC} gene. Such isolates have been previously reported by Bratu et al. (5, 6, 7), and further investigation of these isolates is warranted. The only agent to which more than 90% of ESBL-producing isolates were susceptible was tigecycline, which suggests that the consideration of tigecycline for use in infections due to ESBL producers may be reasonable. In a recently published study, tigecycline was shown to achieve bacterial eradication in 80% (12/15) of patients with intra-abdominal infections caused by ESBL-producing *E. coli* or *K. pneumoniae* (1).

In comparison with the 20.5% of *E. coli* isolates reported as being resistant to levofloxacin in this study, other programs have previously reported a lower prevalence among hospitalized patients. Paterson et al. (14) reported 9.5% nonsusceptibility to levofloxacin for *E. coli* isolates collected in 2003, and Biedenbach et al. reported a prevalence of 9.8% nonsusceptibility to ciprofloxacin for *E. coli* isolates from blood cultures collected in 2002 (3). This apparent increase is worrisome and highlights the importance of continued surveillance of antimicrobial resistance.

Acinetobacter spp. give cause for concern due to their innate resistance to many antimicrobials (9, 10). A total of 11.5% of the *A. baumannii* isolates collected as part of TEST were resistant to imipenem, which is higher than the 8.5% among *Acinetobacter* spp. reported by the MYSTIC program for 2004 (15). Among the *A. baumannii* isolates collected as part of this TEST study, tigecycline was the only antimicrobial that inhibited more than 90% of isolates at a concentration of ≤1 µg/ml. As with *Acinetobacter* spp., *P. aeruginosa* is resistant to a number of antimicrobial classes either innately or through acquired resistance. As has been reported by other studies, the MICs of tigecycline for *P. aeruginosa* were elevated (MIC₉₀ ≥ 32 µg/ml) (4, 16).

Many studies have reported the increasing occurrence of MRSA both in the United States and globally. This TEST study reports an MRSA prevalence of 52.0% in the United States, similar to the prevalence reported by a number of studies of intensive care unit (ICU) pathogens collected between 2000 and 2002 (52.3%, 51.9%, and 51.4%) (11, 12, 17) and higher than that found from a recent collection (2002) from hospitalized patients (39.1%) (3). Pathogens isolated from patients in the ICU typically have higher rates of resistance than isolates from other hospital wards (2). Given that the TEST program collected MRSA isolates from hospitalized patients (18.4% from ICU patients and 81.6% from non-ICU patients), this study suggests an increase in the prevalence of MRSA within the general hospital population. Only three

agents tested in this study were active against all isolates of MRSA (100% susceptible): tigecycline, linezolid, and vancomycin.

In conclusion, these data from the TEST program report the continued development of resistance among many pathogens. There is a real need for new agents for the effective treatment of infections due to resistant pathogens. Given its broad spectrum of activity, which is maintained against clinically relevant resistant gram-positive and gram-negative pathogens, tigecycline is likely to be a welcome addition to the treatment of serious infections.

We acknowledge the staff of International Health Management Associates, Inc., Schaumburg, IL, for their coordination of the TEST study.

This study was funded by Wyeth Pharmaceuticals.

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