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Antimicrobial Susceptibility of Bloodstream Isolates of *Staphylococcus aureus*: Global Results from the Tigecycline Evaluation and Surveillance Trial, 2004-2008

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Abstract: Problem statement: The Tigecycline Evaluation and Surveillance Trial (TEST) commenced in 2004 to monitor the activity of tigecycline, a new glycylcycline and numerous comparators against major hospital-and community-associated pathogens. In this report we examine the efficacy of tigecycline and comparators against isolates of *Staphylococcus aureus* collected from blood. **Approach:** Almost 4000 blood-derived isolates of *Staphylococcus aureus* were collected from participating centers globally between 2004-2008. **Results:** All isolates were susceptible to tigecycline (MIC_{90} 0.25 mg L^{-1}) and linezolid (MIC_{90} 4 mg L^{-1}); 99.9% of isolates were susceptible to vancomycin (MIC_{90} 1 mg L^{-1}). Tigecycline and linezolid activity were unaffected by resistance to methicillin, ICU vs non-ICU isolate collection or the age of patients from which the isolates were collected. Although 95.3% of MSSA were levofloxacin susceptible, only 14.4% of MRSA isolates were susceptible to levofloxacin in this study. **Conclusion:** Tigecycline is shown here to be active against *S. aureus* isolates collected from blood and is unaffected by methicillin resistance. However, tigecycline is not as yet approved for the treatment of bacteremic infections.

Key words: MRSA, surveillance, bacteremia, resistance, tigecycline

INTRODUCTION

Antimicrobial resistance among a variety of bacterial pathogens is now well documented and is an increasingly important consideration when evaluating therapeutic choice and healthcare cost (McDonald, 2006; Chastre, 2008; Isturiz, 2008). Increases in antimicrobial resistance have led to increased patient morbidity and mortality as well as increased length of hospital stay and health care costs (Cosgrove, 2006). The escalations in antimicrobial resistance have presented challenges to healthcare providers, making the selection of effective empiric therapy increasingly difficult (Deasy, 2009).

Staphylococcus aureus continues to be a common cause of serious infections, including those involving the bloodstream and antimicrobial therapy of this organism is complicated by the evolution of Methicillin (MRSA) and Multi-Drug (MDR) resistant strains (Lodise and McKinnon, 2005; Rehm *et al*., 2009). MRSA is an important risk factor for other serious illnesses, including novel H1N1 influenza infection (Shannon *et al*., 2009). MRSA can also be a significant contributor to mortality: Klein *et al*. (2007) estimated that 5500 MRSA-related deaths occurred annually in the US between 1999 and 2005, while the Office for national statistics in the UK has reported a maximum of 1629 MRSA-related deaths, occurring in 2005 (Office for National Statistics, 2009). In Australia and New Zealand where invasive *S. aureus* infection is associated with substantial mortality, significant rates of MRSA and the suboptimal antimicrobials available for treatment of these strains have been shown to exacerbate the problem (Turnidge *et al*., 2009).

Tigecycline (Wyeth Pharmaceuticals, Collegeville, PA, USA) is the first clinically available representative of a new class of antimicrobials, the glycylcyclines, which are derived from the tetracycline nucleus. Tigecycline (Fig. 1) is characterized by a broad spectrum of potent antibacterial activity and remains active against many strains expressing tetracycline and multi-drug resistance (Felmingham, 2005; Zhanel *et al*., 2006).

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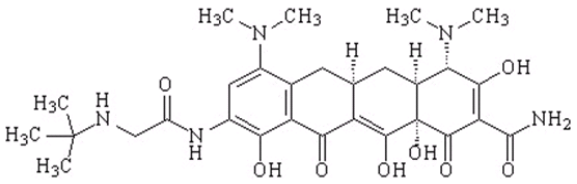

Fig. 1: Structural formula of tigecycline

Antimicrobial susceptibility surveillance is an important strategy in understanding the evolution of antimicrobial resistance and providing information as an aid to optimizing the empirical therapy of bacterial infections (Felmingham, 2002). The Tigecycline Evaluation and Surveillance Trial (TEST), established in 2004, is a global surveillance study designed to compare the *in vitro* activity of tigecycline with a panel of antimicrobials used in daily practice, against a range of clinically important bacterial species including *S. aureus*. Tigecycline is indicated in the treatment of complicated Skin and Skin Structure Infections (cSSSIs), complicated Intra-Abdominal Infections (cIAIs) and Community-Acquired Bacterial Pneumonia (CABP) caused by penicillin-susceptible *S. pneumoniae* or β-lactamase negative *H. influenzae* (Wyeth Pharmaceuticals Inc, 2009a; 2009b). This study reports on the comparative *in vitro* susceptibility of bloodstream isolates of *S. aureus* examined during the sampling period 2004-2008. Tigecycline is not indicated for the treatment of bloodstream infections (Wyeth Pharmaceuticals Inc, 2009a; 2009b).

MATERIALS AND METHODS

Bacterial isolates: Bloodstream isolates of *S. aureus* were collected consecutively by centers participating in TEST, with only one isolate per patient included in the study. Data on a total of 3927 bloodstream isolates of *S. aureus* were submitted to the TEST during the period 2004-2008. Of this total, 3629/3927 (92.4%) provided data enabling division of isolates into those sourced from patients treated on either non-ICU or ICU and 3544/3927 (90.2%) could be separated into those patients aged 18-64 years and those ≥65 years of age (Table 1).

Collection, transport and confirmation of isolate identification were organized by Laboratories International for Microbiology Studies, a division of International Health Management Associates (IHMA, Schaumburg, Ill., USA) which also managed a centralized database of isolate information.

Isolates were identified according to the American Society for Microbiology procedure for *S. aureus* (Murray, 2007).

Antimicrobial susceptibility testing: Minimum Inhibitory Concentrations (MICs) of the antimicrobials included in the analysis were determined locally by participating centers using the Clinical Laboratory Standards Institute (CLSI) broth microdilution method (CLSI, 2009a) with either Microscan® panels (Dade Behring, Sacramento, Calif., USA) or Sensititre® plates (TREK Diagnostic Systems, East Grinstead, UK). Isolates of *S. aureus* were tested against the following antimicrobials (concentration ranges tested expressed in mg L^{-1}): penicillin (0.06-8); amoxicillin/clavulanic acid (0.03/0.015-8/4); piperacillin/tazobactam (0.25/4-16/4); ceftriaxone (0.03-64); imipenem (0.12-16, Microscan® only); meropenem (0.12-16, Sensititre® only); levofloxacin (0.06-32); linezolid (0.5-8); vancomycin (0.12-32); minocycline (0.25-8) and tigecycline (0.008-16). Imipenem was removed from the TEST and replaced by meropenem in 2006 because of imipenem stability issues. Quality control testing was carried out on each day of testing using *S. aureus* strain ATCC 29213. For all antimicrobials except tigecycline, MICs were interpreted using criteria published by the CLSI (2009b). In the case of tigecycline, isolates of *S. aureus* requiring MIC of ≤0.5 mg L^{-1} were interpreted as susceptible, as recommended by the US Food and Drug Administration (Wyeth Pharmaceuticals Inc, 2009a; 2009b).

Determination of methicillin resistance: All isolates of *S. aureus* were tested for the methicillin-resistant phenotype using the cefoxitin disk diffusion method (30 µg disks; Remel, Lenexa, KA, USA) by IHMA's central laboratory (Murray, 2007).

Quality assurance: All isolates were subjected to a Quality Assurance Programme (QAP) designed by IHMA, which incorporated more than 150 individual QA checks to screen for atypical susceptibility patterns or other discrepant results. In the case of *S. aureus*, some of these checks included tigecycline MIC >0.25 mg L^{-1}, penicillin-susceptible and carbapenem or any beta-lactam-resistance and non-susceptibility to linezolid or vancomycin; some specific checks for MRSA were non-resistance to penicillin, susceptibility to carbapenems and resistance to amoxicillin/clavulanic acid and non-susceptibility to quinupristin/dalfopristin.

Isolates with atypical results were re-evaluated with regard to purity and identification followed by re-testing by the central laboratory using the same antimicrobial panel supplied to the investigator labs.

Table 1: Comparative distribution of MRSA amongst blood isolates of *Staphylococcus aureus* cultured from non-ICU and ICU patients and patients of 18-64 or ≥65 years of age, examined in the TEST programme, 2004-2008

Year(s) of study	2004	2005	2006	2007	2008	2004-2008
Non-ICU and ICU patient isolates	495	658	772	1063	641	3629
S. aureus from non-ICU patients (%)	393 (79.4)	505 (76.7)	603 (78.1)	847 (79.7)	495 (77.2)	2843 (78.3)
MRSA from non-ICU patients (%)	171 (43.5)	232 (45.9)	234 (38.8)	285 (33.6)	163 (32.9)	1085 (38.2)
S. aureus from ICU patients (%)	102 (20.6)	153 (23.3)	169 (21.9)	216 (20.3)	146 (22.8)	786 (21.7)
MRSA from ICU patients (%)	54 (52.9)	70 (45.8)	80 (47.3)	99 (45.8)	55 (37.7)	358 (45.5)
Isolates from patients aged 18-64 and ≥65 years	478	633	740	1033	660	3544
S. aureus from patients aged 18-64 years (%)	259 (54.2)	355 (56.1)	391 (52.8)	577 (55.9)	368 (55.8)	1950 (55.0)
MRSA from patients aged 18-64 years (%)	112 (43.2)	155 (43.7)	143 (36.6)	209 (36.2)	102 (27.7)	721 (37.0)
S. aureus from patients aged ≥65 years (%)	219 (45.8)	278 (43.9)	349 (47.2)	456 (44.1)	292 (44.2)	1594 (45.0)
MRSA from patients aged ≥65 years (%)	113 (51.6)	136 (48.9)	162 (46.4)	187 (41.0)	116 (39.7)	714 (44.8)

Isolates generating atypical results on retesting were reviewed by an in-house panel of microbiologists and either accepted and re-inserted into the database or re-tested a second time. Atypical results generated on three separate occasions were accepted into the TEST database.

RESULTS

Bloodstream isolates of *S. aureus* submitted to TEST and reported in this study were collected from centers in the following regions during the period 2004-2008: Africa, the Asia/Pacific Rim, Europe, Latin America, the Middle East and North America (Fig. 2). In view of the relatively small numbers of isolates submitted annually from individual regions (with the exception of methicillin resistance) susceptibility data are reported on combined isolates from all years and regions.

While isolates of *S. aureus* from patients treated on non-ICU outnumber those from ICU almost 4-fold (2843 (78.3%) Vs 786 (21.7%)), isolates from patients aged 18-64 years and from those of ≥65 years are more evenly distributed (1950 (55.0%) Vs 1594 (45%)) (Table 1).

Overall rates of methicillin resistance (MRSA) are somewhat higher in patients treated in ICUs compared with the non-ICU setting (45.5% Vs 38.2%, respectively) (Table 1).

Of the combined total of 3927 bloodstream isolates of *Staphylococcus aureus* submitted to TEST during the period 2004-2008, 2397 (61.0%) are methicillin susceptible (MSSA) and 1530 are MRSA (Table 2). All isolates of MSSA and MRSA are susceptible to tigecycline (MIC_{90} 0.25 mg L^{-1}; MIC_{100} 0.5mg L^{-1}) and linezolid (MIC_{90} 4 mg L^{-1}; MIC_{100} 4 mg L^{-1}). Predictably, tigecycline retains activity against the small number of isolates not fully susceptible to minocycline. Most (99.9%) of the isolates of MSSA and of MRSA are susceptible to vancomycin with only three isolates of MSSA and one of MRSA requiring an MIC of 4 mg L^{-1}, 2 fold greater than the susceptibility breakpoint of 2 mg L^{-1} (but not above the CLSI-defined resistant breakpoint of 16 mg L^{-1}) (Table 2).

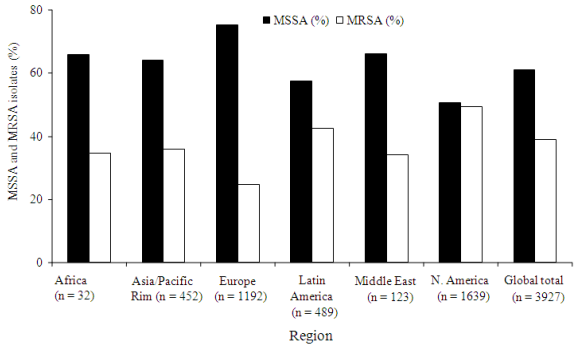

Fig. 2: Geographical distribution of blood isolates of methicillin-susceptible (MSSA) and methicillin-resistant *Staphylococcus aureus* (MRSA) examined in the TEST programme: 2004-2008 combined isolates

While only 17.6% of isolates of MSSA are susceptible to penicillin, the staphylococcal beta-lactamase-stable compounds included in the study are generally highly active against these strains (amoxicillin/clavulanic acid, 99.9% of isolates tested susceptible; piperacillin/tazobactam, 100% susceptible; ceftriaxone, 98.9% susceptible; imipenem, 99.9% of 945 isolates tested susceptible; meropenem, 99.9% of 1452 susceptible) (Table 2). All isolates of MRSA are considered clinically resistant to these compounds according to CLSI guidelines (CLSI, 2009a: 2009b).

The most obvious difference in susceptibility between MSSA and MRSA is with the fluoroquinolone, levofloxacin. Most (95.3%) isolates of MSSA are susceptible to this compound, compared with only 14.4% of MRSA (Table 2). Levofloxacin susceptibility increased significantly among *S. aureus* isolates from blood between 2004 (59.2% S) and 2008 (68.7% S) ($p<0.0001$. MRSA susceptibility to levofloxacin increased ($p = 0.001$) while MSSA susceptibility decreased ($p = 0.0167$) during this interval. Data for 2008 are incomplete at this point, however, so the reliability of these trends is uncertain.

Table 2: Comparative *in vitro* activity of tigecycline against 3927 blood isolates of *Staphylococcus aureus* examined in the TEST programme, 2004-2008

	MSSA MIC (mg L^{-1})					MRSA MIC (mg L^{-1})				
Antimicrobial	n	50%	90%	Range	S (%)	n	50%	90%	Range	S (%)
Penicillin	2397	4.00	≥16.00	≤0.06-≥16	17.6	1530	≥16.00	≥16.00	0.25-≥16	0.0*
Amoxycillin/clavulanic acid	2397	1.00	2.00	≤0.03-8	99.9	1530	8.00	≥16.00	0.25-≥16	0.0*
Piperacillin/tazobactam	2397	1.00	2.00	≤0.25-8	100.0	1530	≥32.00	≥32.00	≤0.25-≥32	0.0*
Ceftriaxone	2397	2.00	4.00	0.25-≥128	98.9	1530	64.00	≥128.00	≤0.03-≥128	0.0*
Imipenem	945	≤0.12	0.25	≤0.12-8	99.9	717	1.00	≥32.00	≤0.12-≥32	0.0*
Meropenem	1452	≤0.12	0.25	≤0.12-8	99.9	813	4.00	≥32.00	≤0.12-≥32	0.0*
Levofloxacin	2397	0.12	0.50	≤0.06-≥64	95.3	1530	8.00	≥64.00	≤0.06-≥64	14.4
Linezolid	2397	2.00	4.00	≤0.5-4	100.0	1530	2.00	4.00	≤0.5-4	100.0
Vancomycin	2397	1.00	1.00	≤0.12-4	99.9	1530	1.00	1.00	≤0.12-4	99.9
Minocycline	2397	≤0.25	0.50	≤0.25-≥16	99.4	1530	≤0.25	4.00	≤0.25-≥16	94.4
Tigecycline	2397	0.12	0.25	0.015-0.5	100.0	1530	0.12	0.25	≤0.008-0.5	100.0

*: All MRSA defined as resistant to penicillinase-labile penicillins, according to CLSI guidelines (11)

Table 3: Comparative *in vitro* activity of tigecycline against 3629 blood isolates of *Staphylococcus aureus* from non-ICU and ICU patients examined in the TEST programme, 2004-2008

	Non-ICU patient isolates MIC (mg L^{-1})					ICU patient isolates MIC (mg L^{-1})				
Antimicrobial	n	50%	90%	Range	S (%)	n	50%	90%	Range	S (%)
Methicillin-suceptible isolates										
Penicillin	1758	4.00	≥16.00	≤0.06-≥16	17.6	428	8.00	≥16.00	≤0.06-≥16	16.8
Amoxycillin/clavulanic acid	1758	1.00	2.00	≤0.03-8	99.9	428	1.00	2.00	0.06-8	99.8
Piperacillin/tazobactam	1758	1.00	2.00	≤0.25-8	100.0	428	1.00	1.00	≤0.25-8	100.0
Ceftriaxone	1758	2.00	4.00	0.25-≥128	99.1	428	2.00	4.00	0.25-≥128	97.9
Imipenem	697	≤0.12	0.25	≤0.120-1	100.0	179	≤0.12	0.25	≤0.12-8	99.4
Meropenem	1061	≤0.12	0.25	≤0.12-8	99.8	249	≤0.12	0.25	≤0.12-4	100.0
Levofloxacin	1758	0.12	0.50	≤0.06-≥64	94.9	428	0.12	0.50	≤0.06-32	96.7
Linezolid	1758	2.00	4.00	≤0.5-4	100.0	428	2.00	2.00	≤0.5-4	100.0
Vancomycin	1758	1.00	1.00	≤0.12-4	99.9	428	1.00	1.00	≤0.12-4	99.8
Minocycline	1758	≤0.25	0.50	≤0.25-≥16	99.5	428	≤0.25	0.50	≤0.25-≥16	98.8
Tigecycline	1758	0.12	0.25	0.03-0.5	100.0	428	0.12	0.25	0.015-0.5	100.0
Methicillin-resistant isolates										
Levofloxacin	1085	16.00	≥64.00	≤0.06-≥64	13.9	358	8.00	≥64.00	≤0.06-≥64	14.8
Linezolid	1085	2.00	4.00	≤0.5-4	100.0	358	2.00	2.00	≤0.5-4	100.0
Vancomycin	1085	1.00	1.00	≤0.12-4	99.9	358	1.00	1.00	≤0.12-2	100.0
Minocycline	1085	≤0.25	4.00	≤0.25-≥16	94.8	358	≤0.25	4.00	≤0.25-≥16	91.9
Tigecycline	1085	0.12	0.25	≤0.008-0.5	100.0	358	0.12	0.25	≤0.008-0.5	100.0

Table 4: Comparative *in vitro* activity of tigecycline against 3544 blood isolates of *Staphylococcus aureus* from patients aged 18-64 years and ≥65 years examined in the TEST programme, 2004-2008

	Patients aged 18-64 years MIC (mg L^{-1})					Patients aged ≥65 years MIC (mg L^{-1})				
Antimicrobial	n	50%	90%	Range	S (%)	n	50%	90%	Range	S (%)
Methicillin-susceptible isolates										
Penicillin	1229	4.00	≥16.00	≤0.06-≥16	16.7	880	4.00	≥16.00	≤0.06-≥16	19.9
Amoxycillin/clavulanic acid	1299	1.00	2.00	0.06-8	99.8	880	0.50	1.00	≤0.03-8	99.9
Piperacillin/tazobactam	1299	1.00	2.00	≤0.25-8	100.0	880	1.00	1.00	≤0.25-8	100.0
Ceftriaxone	1299	2.00	4.00	0.5-≥128	98.9	880	2.00	4.00	0.25-16	99.1
Imipenem	473	≤0.12	0.25	≤0.12-8	99.8	365	≤0.12	0.25	≤0.12-1	100.0
Meropenem	756	≤0.12	0.25	≤0.12–8	99.7	515	≤0.12	0.25	≤0.12-4	100.0
Levofloxacin	1299	0.12	0.50	≤0.06-≥64	95.9	880	0.12	0.50	≤0.06-≥64	94.5
Linezolid	1299	2.00	4.00	≤0.5-4	100.0	880	2.00	4.00	≤0.5-4	100.0
Vancomycin	1299	1.00	1.00	≤0.12-4	99.8	880	1.00	1.00	≤0.12-4	99.9
Minocycline	1299	≤0.25	0.50	≤0.25-≥16	99.2	880	≤0.25	≤0.25	≤0.25-≥16	99.7
Tigecycline	1299	0.12	0.25	0.03-0.5	100.0	880	0.12	0.25	0.015-0.5	100.0
Methicillin-resistant isolates										
Levofloxacin	721	8.00	≥64.00	≤0.06-≥64	17.9	714	16.00	≥64.00	≤0.06-≥64	6.7
Linezolid	721	2.00	4.00	≤0.5-4	100.0	714	2.00	4.00	≤0.5-4	100.0
Vancomycin	721	1.00	1.00	≤0.12-2	100.0	714	1.00	1.00	0.25-4	99.9
Minocycline	721	≤0.25	4.00	≤0.25-≥16	93.5	714	≤0.25	4.00	≤0.25-≥16	95.1
Tigecycline	721	0.12	0.25	0.03-0.5	100.0	714	0.12	0.25	≤0.008-0.5	100.0

With the exception of methicillin resistance, no major differences are evident when comparing susceptibility data of bloodstream isolates of *S. aureus* (MSSA and MRSA) from non-ICU and ICU settings (Table 3).

No major differences in susceptibility are observed when comparing isolates from patients aged 18-64 years and ≥65 years of age with the exception of levofloxacin against MRSA. In the case of this fluoroquinolone, while 17.9% of those isolates from

patients aged 18-64 years are susceptible, only 6.7% among isolates from patients aged ≥65 years are susceptible (Table 4).

DISCUSSION

Bloodstream infection is a serious medical condition associated with high mortality, which can be reduced by initiation of prompt and appropriate empirical antimicrobial therapy (Bates *et al*., 1995; Mylotte *et al*., 2001; Hanon *et al*., 2002). *S. aureus* is a serious cause of bacteremia and successful treatment of this important pathogen is complicated by methicillin and multi-drug resistance, with rates of resistance higher amongst isolates cultured from patients in ICU rather than non-ICU settings and also from the elderly (Safdar and Maki, 2002; Cosgrove *et al*., 2003; Biedenbach *et al*., 2004; Cosgrove, 2006). MRSA bacteraemia has been shown to be more life threatening than MSSA due to the inferior efficacy of vancomycin which remains the standard treatment of serious MRSA infections in many countries (Turnidge *et al*., 2009). Against this background, continuing surveillance of the antimicrobial susceptibility of bacterial pathogens, including *S. aureus* and the development and characterization of new compounds are essential (Zinner, 2005; Zhanel *et al*., 2008).

Most pharmaceutical and biotechnology companies have reduced or ceased development of new antimicrobial agents in recent years, despite the continual threat to public health caused by the increasing prevalence of antibacterial resistance. One key reason is that considerably larger profits can be made through the development and sale of drugs for chronic medical conditions (Infectious Diseases Society of America, 2004; Payne *et al*., 2007). Tigecycline is one of a small number of new antimicrobials to have undergone successful clinical development recently and was licensed by the Food and Drug Administration (FDA) of the USA in 2005 and by the European Medicines Agency (EMEA) in 2006 for use in the treatment of complicated skin and skin structure infections and complicated intra-abdominal infections caused by a variety of susceptible bacterial pathogens including MSSA and MRSA (European Medicines Agency, 2009; Wyeth Pharmaceuticals Inc, 2009a; 2009b). Tigecycline is unaffected by the majority of clinically important resistance mechanisms, including those two key in the expression of tetracycline resistance-ribosomal protection and efflux pumps-and methicillin resistance in staphylococci. TEST was established in 2004 as a global surveillance programme designed to monitor the *in vitro* activity of tigecycline and to compare it with that of other antimicrobials in common clinical use against a wide range of bacterial species, including antimicrobial-resistant strains (Wyeth Pharmaceuticals Inc, 2009a; 2009b).

In this study, we have reported on the susceptibility of bloodstream isolates of *S. aureus* to tigecycline and a range of comparator compounds, collected by centers worldwide and submitted to the TEST programme during the period 2004-2008. All of the isolates of *Staphylococcus aureus* included in the study, whether MSSA or MRSA strains, were inhibited by tigecycline at a concentration of 0.5 mg L^{-1} or less, indicating clinical susceptibility regardless of the activity of comparators.

Antimicrobial resistance is more likely to be encountered among bacterial isolates cultured from patients treated on ICUs and those considered elderly (Safdar and Maki, 2002; Biedenbach *et al*., 2004). There is some evidence for this in the case of methicillin resistance among the combined isolates (non-ICU Vs ICU isolates, MRSA occurrence = 38.2% Vs 45.5%; age 18-64 Vs ≥65 years, MRSA occurrence = 37.0% Vs 44.8%). However, since no representatives of the aminglycosides, the macrolides or inhibitors of folate synthesis were tested, coupled with the fact that all isolates were susceptible to linezolid and at least 99.8% to vancomycin, the association between resistance and whether isolates were sourced from ICU and the elderly patients could not be tested robustly in this study.

Staphylococcus aureus susceptibility to the fluoroquinolone levofloxacin increased significantly during the course of this study, with increasing MSSA susceptibility and decreasing MRSA susceptibility reported between 2004 and 2008. One possible explanation for this is real change in *S. aureus* susceptibility brought on by more judicious use of beta-lactam antibiotics in recent years. As awareness of the risks of MRSA increases, current treatment regimens may exert less selective pressure on the mecA genes which cause methicillin resistance. Continued observation of MRSA susceptibility rates via surveillance studies such as TEST will reveal if this trend continues.

The development of new antimicrobials unaffected by current, commonly occurring mechanisms of resistance is of critical importance if the advantages of infection control, made possible by antimicrobial therapy and prophylaxis during the past 50 years, are to be maintained.

CONCLUSION

Tigecycline is indicated in the treatment of cSSSIs, cIAIs and CABP caused by penicillin-

susceptible *S. pneumoniae* or β-lactamase negative *H. influenzae*. Although tigecycline is not indicated for the treatment of bloodstream infections, the results of this analysis of bloodstream isolates of *S. aureus* submitted to the TEST programme during the period 2004-2008 clearly demonstrate the potent activity of tigecycline and indicate its potential in the treatment of this challenging pathogen.

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Daniel Amsterdam is on the Speakers Bureau of Astellas Pharmaceuticals. Michael J Dowzicky is an employee of Wyeth Pharmaceuticals.

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