44.014
Longitudinal Analysis of Tigecycline Activity against US Isolates of Staphylococcus aureus Based on Patient Location and Specimen Source

D.C. Draghi1, N.P. Brown1, M.K. Torres1, C.M. Pillar1, M.J. Dowzicky2, D.F. Sahm1
1 Eurofins Medinet, Inc., Herndon, VA, USA
2 Wyeth Pharmaceuticals, Collegeville, PA, USA

Background: Tigecycline (TIG) is a novel glycylcycline that was approved in 2005 in the US for treatment of complicated skin and skin structure infections and complicated intra-abdominal infections. S. aureus (SA), including methicillin-resistant S. aureus (MRSA), is a leading cause of skin and skin structure infections. This study examines the in vitro activity of TIG against SA, including MRSA, over the last five years. Additionally, data were stratified according to patient location (PL) and specimen source (SS) to determine if any variation in TIG activity against SA was apparent among these subpopulations.

Methods: SA isolates were collected from multiple locations across all nine US Bureau of Census regions during '03–'04 (N=1,796), '05 (N=1,802), and '06–'07 (N=1,800) and centrally tested using broth microdilution according to current CLSI standards. TIG activity was analyzed by patient locations (PL; outpatient [OP], intensive-care unit [ICU], and inpatient non-ICU [IP]) and by specimen source (SS; blood [BL], respiratory [RP], and skin and skin structure [SST]). FDA breakpoints were used to interpret all TIG MIC results.

Results: Against SA overall, TIG had an MIC50/90 of 0.12/0.12 mg/L in '03–'04 and an MIC50/90 of 0.12/0.25 mg/L in both '05 and '06–'07. Throughout the study periods, percent susceptibility (%) of TIG remained ≥99.5%. TIG activity by MIC90 was largely unaffected by methicillin susceptibility status of the isolate (MIC90: 0.12 mg/L for MSSA and 0.25 mg/L for MRSA in '03–'04, 0.25 mg/L for MSSA and MRSA in '05, and '06–'07). In each study period, the activity of TIG by MIC90 was identical among all PL (OP, ICU, and IP) and SS (BL, RP, SST) evaluated relative to TIG activity against SA overall. In the most recent study period ('06–'07), SA isolates were ≥99% S to TIG regardless of PL or SS.

Conclusion: By MIC90, TIG in vitro activity was stable against SA over the past five years spanning both its development and introduction to use and the %S of SA isolates to TIG remained unaltered and high >99.5%. TIG activity by MIC90 was not notably affected by the methicillin susceptibility status of the isolate and was consistent across all PL and SS evaluated.

doi:10.1016/j.ijid.2008.05.704

44.015
Activity of Telavancin Against Contemporary Streptococcus spp. Pathogens: Recent Results from a European Surveillance Program (2007)

T. Fritsche*, H. Sader, R. Jones
JMI Laboratories, North Liberty, IA, USA

Background: β-haemolytic streptococci (BHS), viridans group streptococci (VGS) and Streptococcus pneumoniae (SPN) are commonly occurring Gram-positive pathogens responsible for a variety of local and systemic infections. We evaluated potency of telavancin and comparators against isolates belonging to these species/groups as part of a global surveillance protocol for 2007. Telavancin is an investigational, intravenous, semi-synthetic, rapidly bactericidal lipoglycopeptide broadly active against both aerobic and anaerobic Gram-positive bacteria and has been evaluated in two Phase 3 complicated skin and skin structure infection trials.

Methods: Non-duplicate clinical isolates (1087 total) of BHS (339), VGS (100) and SPN (648) were submitted from medical centres in Europe (23), Turkey (2) and Israel (1) participating in surveillance for 2007. Identiﬁcations were conﬁrmed by the central monitor and isolates were tested using CLSI broth microdilution.

Results: Against BHS, SPN and VGS, telavancin potency was most similar to penicillin (MIC50 values, 0.03 vs ≤0.015–0.06 mg/L, respectively) and superior to other comparators; all tested isolates were inhibited by ≤0.25 mg/L of telavancin. Telavancin inhibited all VGS and SPN at ≤0.12 mg/L, including penicillin-non-susceptible strains (27.0% and 30.2%, respectively), and BHS at ≤0.25 mg/L. Telavancin was most active against Group A BHS (MIC90, 0.03 mg/L) compared with Groups B and G (0.06 and 0.12 mg/L, respectively). All streptococci were susceptible to vancomycin and linezolid, and BHS and VGS were susceptible to daptomycin. While most strains were susceptible to levofloxacin (95.0–99.4%), resistance to erythromycin/penicillin were variable (41.0/4.0%, 13.6/0.0% and 33.6/19.3% for VGS, BHS and SPN, respectively).

Conclusions: Telavancin was broadly active against 2007 European streptococcal isolates. Based on MIC90 values, telavancin was most similar to penicillin in ‘by weight’ activity against SPN, BHS and VGS (all MICs, ≤0.25 mg/L). Continued monitoring for resistance among Gram-positive cocci will be critical in assessing long-term efficacy of this potent agent.

doi:10.1016/j.ijid.2008.05.705

44.016
Emergence of Optochin Resistant Streptococcus pneumoniae in Bangladesh

N. Mawla1,∗, M. Rahman1, A.B. Lutfor2, S.M. Shamsuzzaman2, D. Ahmed1, H. Rashid1, M.A. Hossain1
1 ICDDR,B, Dhaka, Bangladesh
2 Department of Microbiology, Sir Saimullah Medical College, Dhaka, Bangladesh

Background: The optochin susceptibility test remains the primary and in some cases the only method in clini-
cal laboratories to differentiate *Streptococcus pneumoniae* (Pneumococci) from other α-haemolytic streptococci. However, presence of optochin resistant pneumococci may lead to misidentification that will cause a compromise with treatment and prevention of pneumococcal diseases. The typical optochin susceptibility of Pneumococci resides in the Fo complex of its FoF1 H+-ATPase, an ion transport enzyme that is essential for the viability of this organism. Mechanism of optochin resistance has been attributed to a single point mutation in amino acid residues of the H+-ATPase c-subunit (atpC).

**Objective:** To validate the preserved isolates and identify optochin-resistant pneumococci by bile solubility test and PCR for lytA gene and to determine the mechanism of optochin resistance.

**Methodology:** Alpha hemolytic streptococci isolated from 4,730 nasopharyngeal swabs of children <5 years old. The isolates were validated by colony morphology, optochin susceptibility, bile solubility, PCR for lytA (autolysin) and ATPase c-subunit genes and sequencing to detect any AA mutations.

**Results:** In total, 1618 α-haemolytic isolates were validated; 111 (6.86%) were Optr α-haemolytic strains and only 37 (0.8%) were pneumococcus that were bile soluble and possessed lytA gene. The PCR of atpC from all 37 strains showed the presence of F0 complex in F0F1 H+-ATPase. Sequencing of atpC gene of three strains when compared with reference strain (opts strain R6) revealed the presence of nucleotide change that produces AA substitution in ATPase c-subunit protein.

**Conclusion:** Optochin resistant Streptococcus pneumoniae was first observed in Bangladesh. A single point mutation in H+-ATPase c-subunit gene that contributed for Optr phenotype. Reporting of Optr pneumococci as viridans streptococcus might have significant implications for the treatment and outcome of patients. Therefore, validation of α-haemolytic streptococci as pneumococci by bile solubility test and/or PCR should be made.

doi:10.1016/j.ijid.2008.05.707

**44.017**

**Multisensitive Panton-Valentine Leukocidin-Positive Methicillin-Resistant *Staphylococcus aureus* in Kuala Lumpur, Malaysia**


University Malaya, Kuala Lumpur, Malaysia

**Background:** Recent years have seen the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA) strains often characterised by community acquisition, unusual susceptibility to antimicrobials, and the Panton-Valentine leukocidin (PVL) virulence factor. The epidemiology of these strains varies between geographical locations. This study aimed to determine the occurrence and clinical features of such strains in the University of Malaya Medical Centre, Kuala Lumpur.

**Methods:** Laboratory records were examined for MRSA isolates from 2002—2007. Using CLSI disc diffusion standards, multisensitive MRSA was defined as susceptibility to erythromycin, clindamycin, fusidic acid, rifampicin, gentamicin, ciprofloxacin, cotrimoxazole, and tetracycline. PCR detection of *meca* and PVL genes *lukS-PV-lukF-PV, SCCmec* typing, and MLST were carried out. The PVL product was confirmed by sequencing. Only cases with isolates available for PCR confirmation were included in clinical records review. Centers for Diseases Control and Prevention criteria were used to distinguish between community-associated (CA-MRSA) and healthcare-associated MRSA.

**Results:** Multisensitive MRSA from 13 distinct patient-episodes were identified; 1 in 2003, 2 in 2006, and 10 in 2007 (0.27%, 0.62%, and 3.1% of new MRSA cases, respectively). 9 isolates from 2007 were available for meca confirmation. Of these, only 2 were PVL-positive CA-MRSA; the remaining 7 were healthcare-associated, of which 3 were PVL-positive. All isolates were of SCCmec type IV. There were 3 isolates of each sequence type (ST) ST30 and ST6, 1 ST22 strain, and 2 untypeable isolates. Clinical presentations included skin or soft-tissue infections (6), probable colonisation (2 babies), bacteraemia (1), and no deaths. All 4 isolates unavailable for confirmation were healthcare-associated.

**Conclusion:** We describe the first confirmed clinical infections with multisensitive, SCCmec type IV, PVL-positive MRSA in Malaysia, which were mainly skin or soft-tissue infections. In view of the predominance of healthcare-associated acquisition, and the apparent increase in cases in 2007 (albeit small numbers), further work including multilocus sequence typing is necessary to fully understand the local epidemiology of MRSA.

doi:10.1016/j.ijid.2008.05.707

**44.018**


H. Sader*, T. Fritsche, M. Janechek, R. Jones

JMI Laboratories, North Liberty, IA, USA

**Background:** Daptomycin is a cyclic lipopeptide approved for the treatment of complicated skin and soft tissue infections (cSSTI), right sided infective endocarditis (RIE) due to *Staphylococcus aureus* (SA) and for SA bacteraemia when associated with RIE or with cSSTI. We evaluated the activity of daptomycin and comparator agents tested against multidrug-resistant (MDR) Gram-positive organisms isolated in European hospitals.

**Methods:** 23,269 Gram-positive organisms were collected through the Daptomycin Surveillance Program in the 2003—2007 period, including SA (11,836), coagulase-negative staphylococci (CoNS; 4,445), enterococci (4,464), viridians group streptococci (VGS; 756) and beta-haemolytic streptococci (BHS; 1,768). Isolates were consecutively collected from patients with documented infections in 32 European hospitals (14 countries) and susceptibility tested by CLSI broth microdilution methods against daptomycin and >20 comparators. Mueller-Hinton broth was supplemented to a 50 mg/L calcium concentration for testing daptomycin. MDR was defined as resistance to drugs in 3 or more antimicrobial classes.