Variability of Resistance Rates Among *Streptococcus* spp. Isolated from Different Regions and Sources of Infection (TEST 2008-2012)

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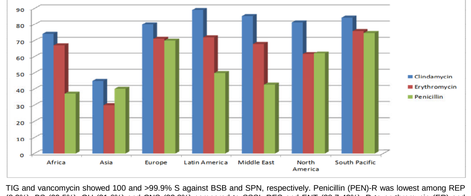
Revised Abstract

Objectives: *Streptococcus pneumoniae* (SPN) and *S. agalactiae* (BSB) can cause serious infections, particularly among neonates, the elderly and patients that are immunocompromised. These species are associated with various infections in several anatomic organ systems, including reproductive (REP), genitourinary (GU), bone and joint (BJ), respiratory (RES), bloodstream (BS), skin and skin structure (SSSI), ear-nose-throat (ENT) and central nervous system (CNS). This study documents the susceptibility (S) rates observed for several antimicrobial agents tested over a five year surveillance study (TEST) comparing susceptibility (S)% for each source of infection. **Methods:** Isolates were collected from multiple countries in 7 geographic regions and tested locally by broth microdilution using CLSI guidelines and S% is reported using CLSI and FDA breakpoints for tigecycline (TIG). S and resistance (R) rates were analyzed for tigecycline (TIG) and appropriate comparator agents for SPN and BSB in these regions. **Results:** Selected S rates for SPN by region for three antimicrobial agents:



TIG and vancomycin showed 100 and >99.9% S against BSB and SPN, respectively. Penicillin (PEN)-R was lowest among REP (8.3%), BS (29.5%), GU (31.6%) and CNS (33.8%) compared to SSSI, RES and ENT (38.7-42%). R to erythromycin (ER) and clindamycin (CL) was highest among these three sources. Only 1-2% of these streptococcal species were non-S to levofloxacin.

Conclusions: Regional variation was observed for PEN, ER and CL, generally higher in Asia and Africa. This data also shows S differences based upon the source of infection for some tested agents with higher R rates observed among RES, ENT and SSSI isolates. TIG had activity against nearly 100% of the strains regardless of infection source.

Introduction

Antimicrobial treatment of infections caused by streptococci can be problematic due to the diverse and invasive diseases that these pathogens can cause. *Streptococcus agalactiae* is commonly associated with invasive neonatal disease due to the passage from maternal colonization from the urogenital or gastrointestinal tract during delivery. This species is also culpable for skin and skin structure infections. *Streptococcus pneumoniae* is a major respiratory tract pathogen, particularly related to community-acquired infections, but can also cause serious invasive disease such as sepsis and meningitis. These two streptococcal species along with *Streptococcus pyogenes* are the most common pathogens in this genus involved in human infections. Monitoring the susceptibility of these species against antimicrobial agents remains important.

The Tigecycline Evaluation Surveillance Trial (TEST) program has provided significant data on the antimicrobial susceptibility rates associated with numerous pathogens, including streptococci, on a global scale. This report provides susceptibility data from a worldwide collection of *S. agalactiae* and *S. pneumoniae* isolates isolated from clinically relevant infections during 2008-2012.

Materials & Methods

- A total of 14,577 clinical isolates of *S. pneumoniae* and *S. agalactiae* from a variety of infection sites from a variety of locations both in hospital and community were collected and tested between January 2008 and December 2012. Isolates were identified to the species level and tested at each site by the participating laboratory using supplied dried broth microdilution panels.
- Organism collection, transport, confirmation of organism identification, and development and management of a centralized database were coordinated by Laboratories International for Microbiology Studies (LIMS), a division of International Health Management Associates, Inc. located in Schaumburg, IL, USA.
- Minimum inhibitory concentrations (MICs) were determined by the Clinical and Laboratory Standards Institute (CLSI) recommended broth microdilution testing method [1]. MIC interpretive criteria followed published guidelines established by the CLSI [2], where available. FDA interpretive guidelines were used for tigecycline [3].
- Quality controls (QC) were performed by each testing site on each day of testing using appropriate ATCC control strains. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI guidelines [2].

References

1. Clinical Laboratory Standards Institute. 2012. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standards – Ninth Edition*. CLSI document M07-A9. Wayne, PA.
2. Clinical and Laboratory Standards Institute (CLSI). 2013. *Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Third Informational Supplement.* CLSI Document M100-S23. Wayne, PA. USA.
3. Tygacil®, 2010. *Tigecycline FDA prescribing information*. Pfizer, Inc., Collegeville, PA.

Acknowledgments

We gratefully acknowledge the contributions of the investigators, laboratory personnel, and all members of the Tigecycline Evaluation Study Trials program group. This study was sponsored by a grant from Pfizer, Inc.

Results

Figure 1. Distribution of 2,793 penicillin non-susceptible *S. pneumoniae* isolates collected from seven countries (TEST program 2008-2012).

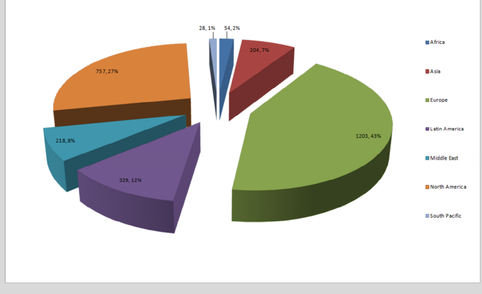


Figure 2. Percentage of penicillin resistance in *S. pneumoniae* from a global collection of isolates (TEST program 2008-2012, n= 1,122).

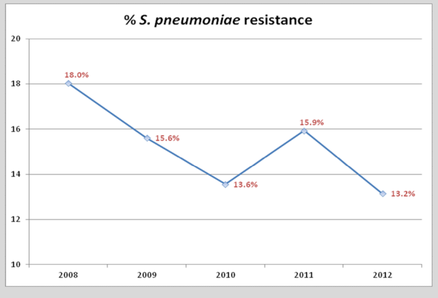


Figure 3. Percent of erythromycin and clindamycin resistance observed by country and penicillin susceptibility among *S. pneumoniae* collected from the TEST program (2008-2012).

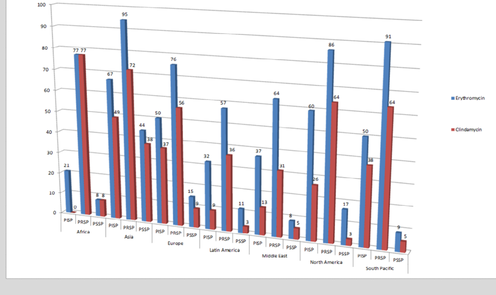
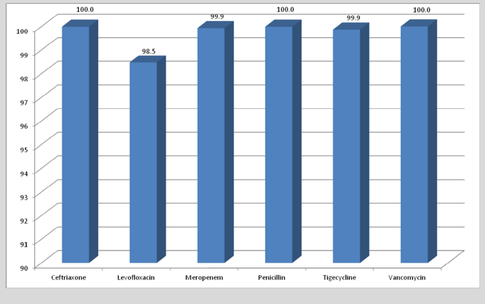


Figure 4. Antimicrobial susceptibility (%) of 6,985 *S. agalactiae* collected during 2008-2012 from the TEST program worldwide.



Conclusions

- Susceptibility among *Streptococcus* spp. varies depending upon the species. *S. agalactiae* remain susceptible to most of the antimicrobial agents that are used for prophylaxis and directed therapies, with some reduced susceptibility to levofloxacin (Figure 4). However, *S. pneumoniae* are often more difficult to treat using empiric therapy due to resistance mechanisms that this species can produce (Figures 2 and 3).
- Resistance to penicillin declined by nearly 5% among the overall population of *S. pneumoniae* during 2008-2012 which is may be due to the overall reduction in pneumococcal disease and changes in seroepidemiology due to increased use of multivalent *S. pneumoniae* vaccines.
- Macrolide and lincosamide resistance was highest among the penicillin-non-susceptible population of *S. pneumoniae* in all regions. Continued surveillance monitoring is warranted as these agents are commonly used for treatment and prophylactic therapy (Figure 3).
- Tigecycline and vancomycin had susceptibility percentages ≥99.9% against both *S. pneumoniae* and *S. agalactiae* during all tested years.