

Activity of Antimicrobial Agents Recommended for Empiric Therapy of Complicated Intra-abdominal Infections in North America 2007-2008

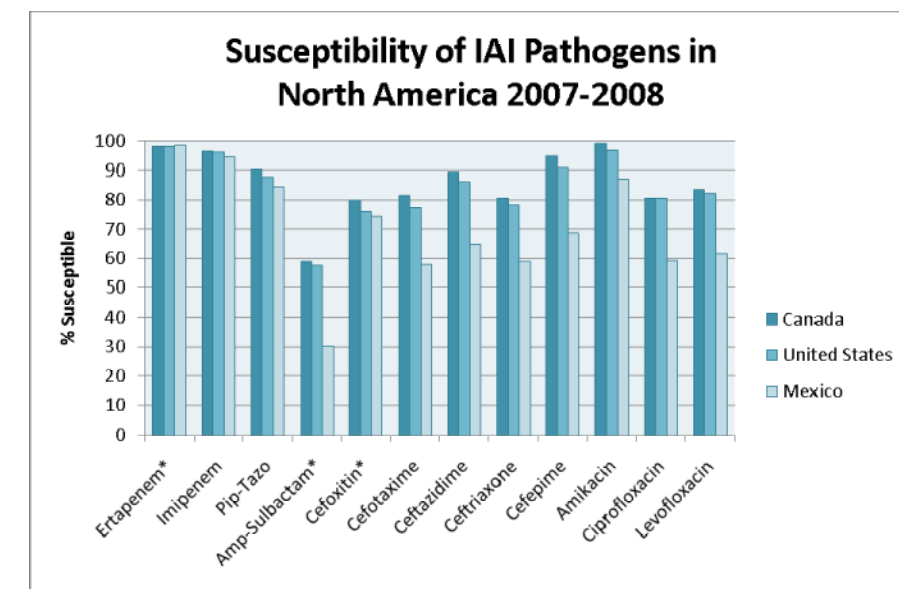
#814

R. Badal¹, S. Bouchillon¹, S. Hawser², M. Hackel¹, D. Hoban¹, A. Johnson¹
¹International Health Management Associates, Inc., Schaumburg, IL, USA
²IHMA Europe Sàrl, Epalinges, Switzerland

IHMA, Inc.
 2122 Palmer Dr.
 Schaumburg, IL 60173
 Tel: 847.303.5003
 Fax: 847.303.5601
 www.ihmainc.com

Revised Abstract

Background: The IDSA provides recommendations for empiric therapy of both community- and healthcare-associated intra-abdominal infections (IAI). Local resistance data are necessary to determine appropriate empiric therapy for IAI. The Study for Monitoring Antimicrobial Resistance Trends (SMART) has been tracking susceptibility of aerobic gram-negative IAI pathogens around the world since 2002, and can help alert physicians to changes in *in vitro* activity of recommended drugs. This report presents 2007-2008 susceptibility data of gram-negative aerobic or facultatively anaerobic IAI pathogens from Canada, the U.S., and Mexico versus many of the drugs recommended in the IDSA guidelines. **Methods:** 14 hospitals (3 Canada, 3 Mexico, 8 U.S.) collected and identified 1,459 gram-negative pathogens from IAI in 2007-2008. Susceptibility testing, quality control, and detection of extended spectrum beta-lactamase (ESBL) were performed following Clinical and Laboratory Standards Institute methods at each hospital laboratory in 2007 and at a central laboratory in 2008. **Results:** Susceptibility of all aerobic gram-negative IAI pathogens from Canada, the U.S., and Mexico is shown in the following chart.



*% susceptibility was calculated for isolates having CLSI interpretive breakpoints for a given drug; therefore %S calculations for ertapenem, cefoxitin, and ampicillin/sulbactam do not include *P. aeruginosa*, for which no CLSI breakpoints exist.

ESBL-positive rates among *E. coli*, *K. pneumoniae*, and *K. oxytoca* in 2007-2008 for Canada, the U.S., and Mexico were 3.8, 8.4, and 38.5%, respectively. **Conclusions:** ESBL rates were dramatically higher in Mexico than in the US or Canada. Several drugs had much lower activity against IAI pathogens from Mexico than in the U.S. and Canada, due in large part to the much higher ESBL rates in Mexico. Ertapenem and imipenem were the only study drugs listed in the IDSA guidelines to achieve >90% susceptibility among *Enterobacteriaceae* in all 3 countries. No drug achieved >80% susceptibility against non-*Enterobacteriaceae* in all 3 countries. SMART continues to provide important information about levels of resistance and pathogen prevalence that may be useful in the development of guidelines for empiric therapy of complicated IAIs.

Introduction

The Infectious Disease Society of America (IDSA) publishes therapy guidelines for the treatment of a wide variety of infections, including community- and hospital-associated intra-abdominal infections (IAI) (1). These guidelines are periodically updated, with a new set of guidelines for IAI due to be published 4th quarter of 2009. However, with resistance rates varying greatly by geographical region as well as over time, it is important to take such guidelines into consideration with national or more local antibiograms in mind.

The Study for Monitoring Antimicrobial Resistance Trends (SMART) program has been monitoring the activity of ertapenem, imipenem, amikacin, cefepime, cefotaxime, cefoxitin, ceftazidime, ceftriaxone, ciprofloxacin, levofloxacin, ampicillin-sulbactam, and piperacillin-tazobactam against gram-negative aerobic bacteria from IAI around the world since 2002. The present report summarizes the activity of the study drugs, all of which are included in the IDSA guidelines, against recent (2007-2008) isolates causing IAI in North America (Canada, the United States, and Mexico).

Materials and Methods

- All isolates were non-repeat isolates derived from IAIs. Only one isolate per species per patient was accepted into the study. Each participating laboratory collected up to 100 consecutive non-selected gram-negative pathogens each year of the study. Isolates from 2007 were identified to the species level and tested at each site. Those from 2008 were identified and tested at a central laboratory (Laboratories International for Microbiology Studies, a subsidiary of International Health Management Associates, Inc., Schaumburg, IL, USA).
- Minimum inhibitory concentrations (MICs) were determined using MicroScan dehydrated broth microdilution panels manufactured by Siemens Medical Solutions Diagnostics (West Sacramento, California, USA), following Clinical and Laboratory Standards Institute (CLSI) guidelines [2]. All antimicrobial agents were supplied by the panel manufacturer. The following antimicrobial agents were included on the panels with their dilution ranges (expressed in mcg/ml): ertapenem 0.03-4, imipenem 0.06-8, cefepime 0.5-32, ceftazidime 0.5-128, ceftazidime-clavulanic acid 0.12-16, cefoxitin 2-16, ciprofloxacin 0.25-2, amikacin 4-32, levofloxacin 0.5-4, cefotaxime 0.5-128, cefotaxime-clavulanic acid 0.12-16, piperacillin-tazobactam 2/4-64/4, ampicillin-sulbactam 2/2-16/2, and ceftriaxone 1-32.
- MIC interpretive criteria followed guidelines established by CLSI [3].
- Escherichia coli*, *Klebsiella pneumoniae*, and *K. oxytoca* isolates were classified in line with CLSI guidelines as extended spectrum beta-lactamase (ESBL) producers if there was at least an eight-fold reduction of MIC for ceftazidime or cefotaxime tested in combination with clavulanic acid versus their MICs when tested alone [3].
- Quality control testing (QC) was done on each day of testing using the CLSI-recommended QC strains: *E. coli* ATCC 25922, *K. pneumoniae* ATCC 700603 (positive ESBL control), and *Pseudomonas aeruginosa* ATCC 27853. Results were included in the analysis only when corresponding QC isolates tested within the acceptable range according to CLSI guidelines [3].
- Development of a centralized database of study results was managed by International Health Management Associates, Inc. located in Schaumburg, IL, USA.

References

- Solomkin, J. S. Mazuski, J. E., et al. Guidelines for the Selection of Anti-infective Agents for Complicated Intra-abdominal Infections. Clin Infect Dis. 2003;37: 997-1005.
- CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard—Seventh Edition, in Document M7-A7. 2006: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.
- CLSI. Performance Standards for Antimicrobial Susceptibility Testing, Document M100-S19. 2009: Clinical Laboratory Standards Institute (CLSI), 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA.

Acknowledgements

The contributions of all the SMART investigators and laboratories in Canada, the U.S., and Mexico are greatly appreciated. This study was funded by a grant from Merck & Co., Inc.

Results

Distribution of isolates by species, ESBL incidence rates among *E. coli*, *K. pneumoniae*, and *K. oxytoca*, and overall susceptibility of *Enterobacteriaceae* and non-*Enterobacteriaceae* in the three countries are summarized in Figures 1-5.

Figure 1.

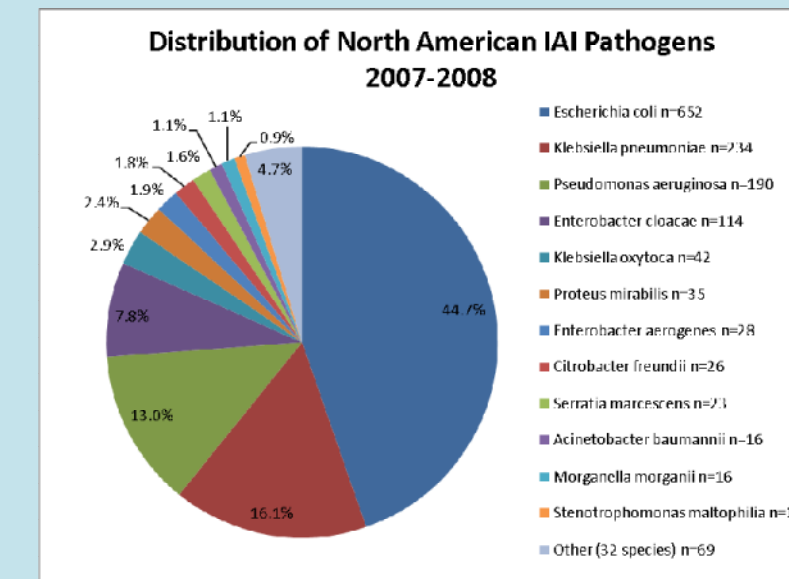


Figure 2.

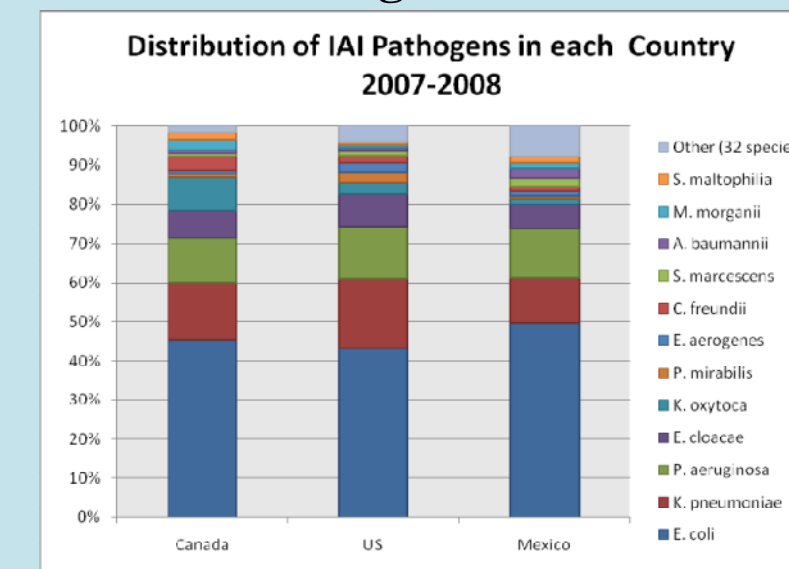


Figure 3.

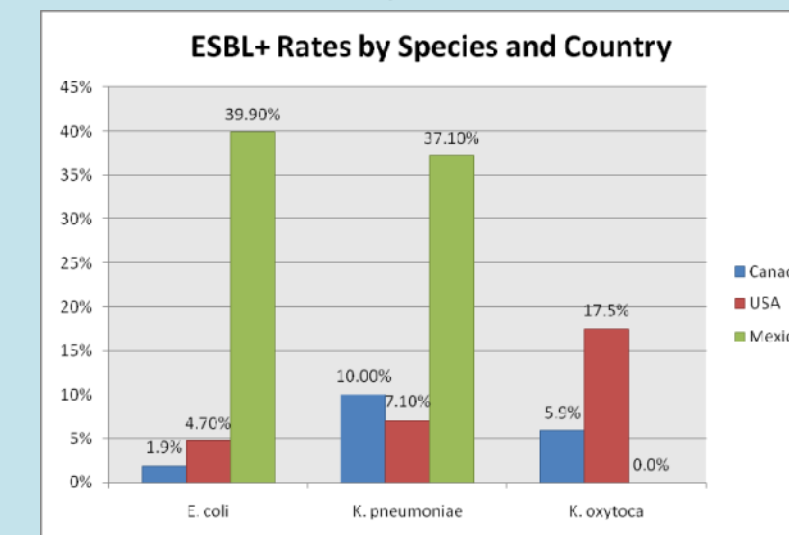


Figure 4.

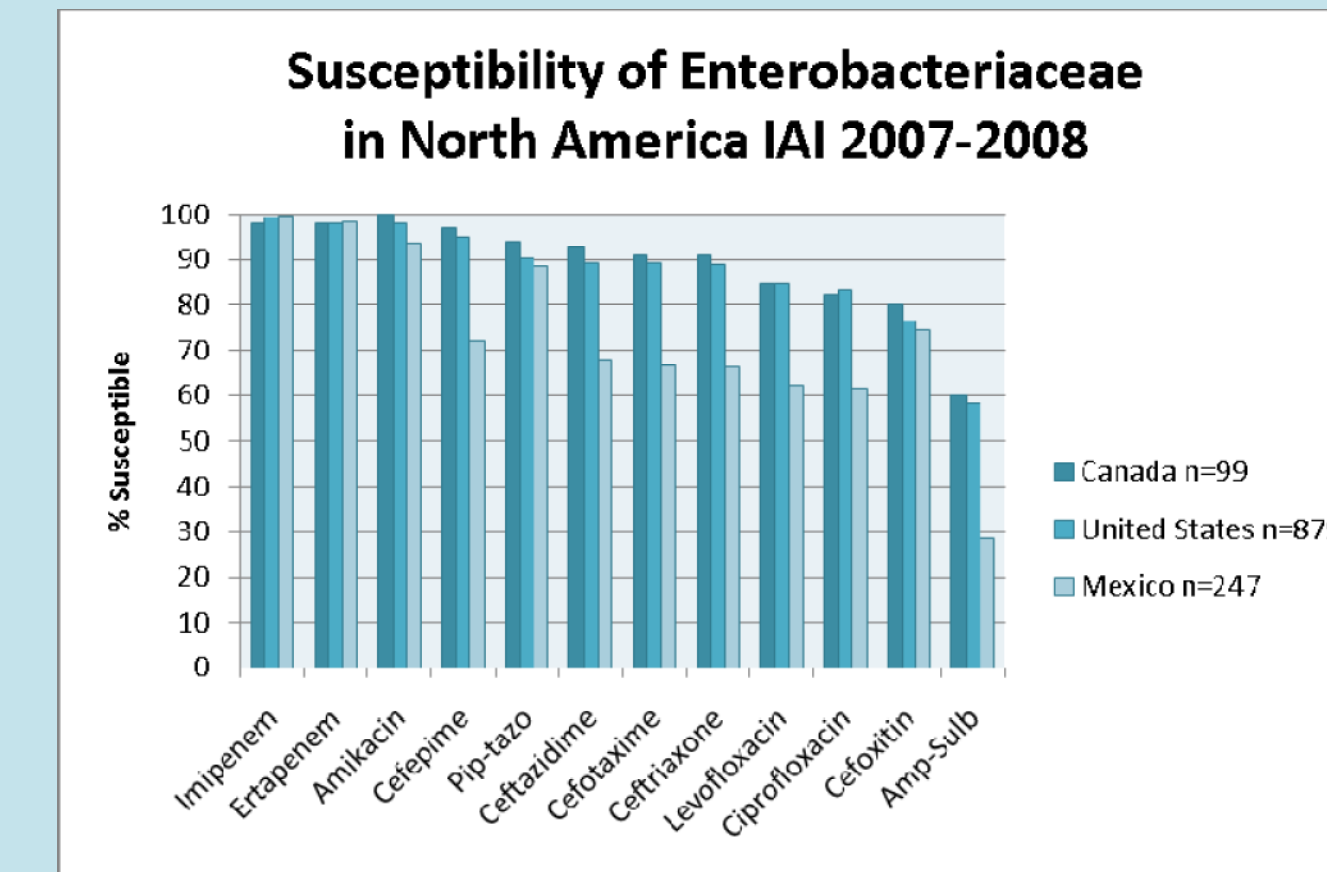
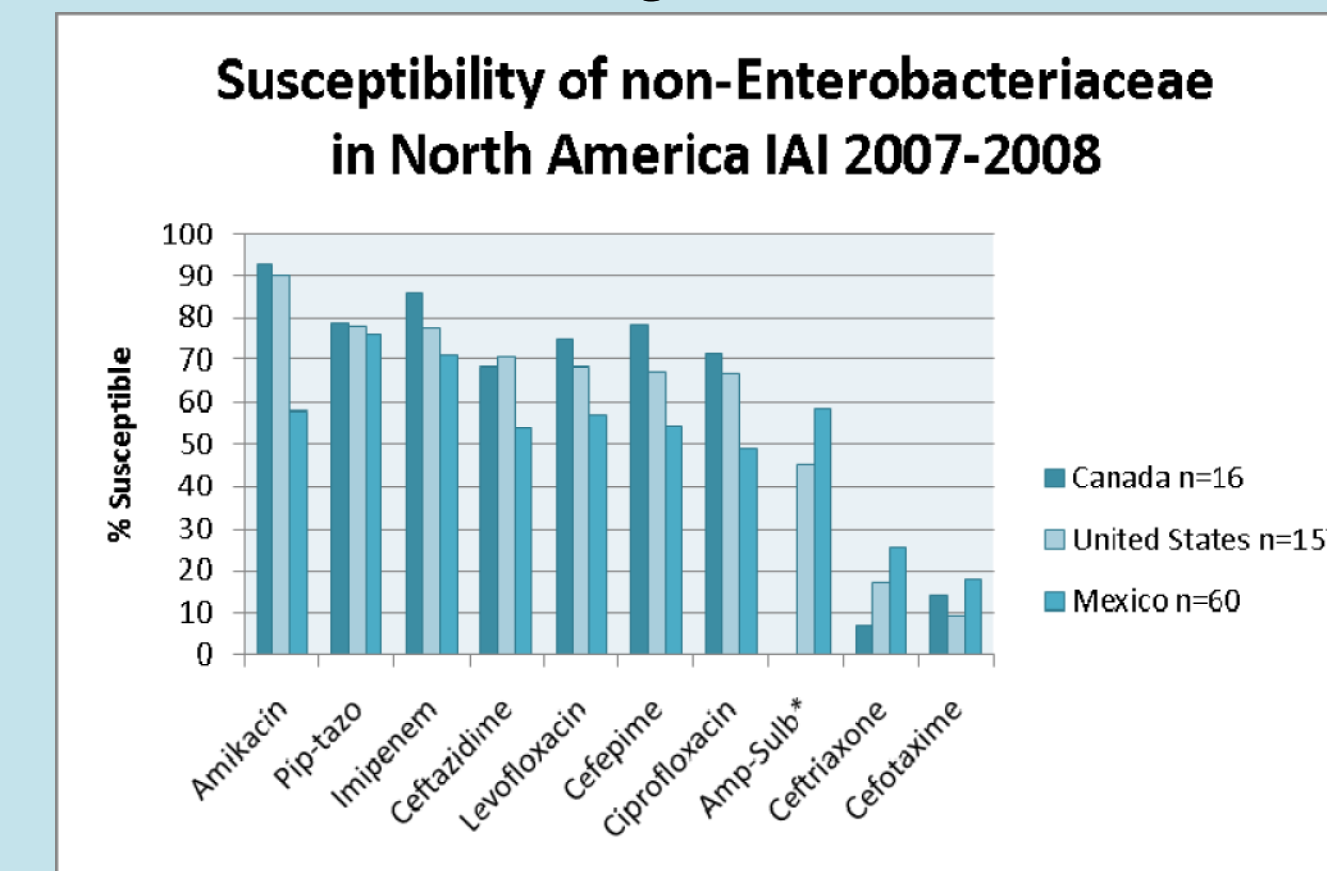


Figure 5.



*Only includes *Acinetobacter* spp., as no breakpoints exist for other non-*Enterobacteriaceae*.

Conclusions

- E. coli* and *K. pneumoniae* accounted for about 60% of the North American aerobic and facultatively anaerobic IAI pathogens, and were present in roughly equivalent proportions in all three countries. However, the incidence of ESBL+ *E. coli* in Mexico was 8- and 21-fold higher than in the US and Canada, respectively, and the *K. pneumoniae* ESBL+ rate in Mexico was 4- and 5-fold higher than in the US and Canada, respectively.
- Several drugs had much lower activity against isolates from Mexico than in the U.S. and Canada, due largely to the much higher ESBL+ rates seen in Mexico.
- Ertapenem and imipenem were the only study drugs listed in the IDSA guidelines to achieve >90% susceptibility among *Enterobacteriaceae* in all 3 countries.
- No drug achieved >80% susceptibility in all 3 countries against non-*Enterobacteriaceae*, which accounted for 13.9-17.5% of IAI pathogens.
- Data from the SMART program can be used to provide current information about levels of resistance and pathogen prevalence, which may be useful in the further development of guidelines for empiric therapy of complicated intra-abdominal infections.