

# Oral Antimicrobial Susceptibility Patterns of Urinary Tract Infection (UTI) Isolates from Hospitalized Patients in Europe (EU), Latin America (LA), and North America (NA): Report from the SENTRY Antimicrobial Surveillance Program (2000)

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## ABSTRACT

**Background:** UTIs remain a worldwide nosocomial infection problem. The most common pathogens involve enteric bacilli, *P. aeruginosa* (PSA) and *Enterococcus* spp. (ESP). Geographic variations in pathogen occurrence and susceptibility (S) profiles require monitoring to provide information to guide therapeutic options.  
**Methods:** 2,780 UTI isolates from EU (n=783), LA (n=531), and NA (n=1,466) were tested at a central laboratory against 44 agents (8 presented) by NCCLS methods. Seven pathogens accounted for 90% of all isolates. The rank order for all regions combined was: *E. coli* (EC; 1,316; 47%), ESP (351; 13%), *Klebsiella* spp. (KSP; 306; 11%), PSA (210; 8%), *P. mirabilis* (145; 5%), *Enterobacter* spp. (97; 4%), and *Citrobacter* spp. (78; 3%).  
**Results:** Pathogen rank order was similar among regions except for rarer occurrence of ESP (rank #6, 4%) in LA, and more indole-positive Proteae isolated in LA and EU (rank #7, 2-3%). EC ampicillin (AMP) resistance R was highest in EU and LA (51-55%). AMP resistance (37% R), ciprofloxacin (CIP; 4%), BMS284756 (BMSQ; 4%), and trim/sulfa (T/S; 23%) R was lowest in NA. Nitrofurantoin (NIT) S in EC ranged from 91-96% across all regions. Regional CIP-R rank order in PSA was: LA (55%) > EU (41%) > NA (29%). AMP, amox/clav (A/C), T/S and NIT were not effective oral agents vs. PSA. VRE were only detected in NA (7%) and beta-lactam (AMP, A/C) S was (84-100%) across all regions. BMSQ possessed a 34-44% wider spectrum of activity than CIP vs. ESP UTI isolates. Phenotypic ESBL rates for EC and KSP were 4% and 19%, respectively.  
**Conclusion:** UTI pathogen frequency was similar among EU, LA, and NA regions with significantly lower ESP rates in LA. VRE were only observed in NA (USA > Canada). Quinolone (CIP)-R among PSA and EC was greatest in LA (55% and 18%), and overall CIP-R rates in PSA are approaching 40% worldwide.

## INTRODUCTION

Urinary tract infections (UTIs) remain a worldwide problem causing nosocomial and community acquired infections and are most commonly caused by *E. coli*, other Gram-negative bacilli, and *Enterococcus* spp. An estimated 3-5 million physician visits, of which approximately 100,000 result in hospitalization, are due to UTIs in the United States annually. UTIs are also among the most common hospital-acquired and nursing home infections. UTIs occur more frequently in females and some estimates suggest that approximately 50% of all women have had at least one UTI episode during their lifetime. UTIs pose a significant health problem because they can lead to urosepsis with high associated mortality rates, morbidity, and economic loss.

In the "pre-antibiotic era", control of recurring UTIs was aided by long term prophylaxis using a formaldehyde-producing compound (methanamine) or cranberry juice to alter the acidity of urine. In more recent years, antimicrobials have been used to treat UTIs, including numerous drug classes. Due to the increased and sometimes inappropriate use of antimicrobials, organisms have been developing resistances to multiple classes of antimicrobial agents. Multidrug resistant organisms present a serious challenge in chemotherapeutic treatment and in some instances are becoming a serious public health risk.

Among newer agents, the fluoroquinolones have broad potency against a variety of Gram-negative and -positive pathogens, including those commonly implicated in UTIs. These antimicrobial qualities have prompted over a decade of increasing use, spawning rising resistance rates world-wide. Global surveillance studies such as The SENTRY Antimicrobial Surveillance Study have shown *E. coli* strains isolated from UTIs have increased resistance rates to ciprofloxacin in Latin American countries and this trend is becoming evident in other countries as well. The purpose of this study was to compare the antimicrobial susceptibility patterns of orally administered agents used in the treatment of UTIs from patients in Europe, Latin America and North America.

**Table 2.** Susceptibility to commonly prescribed oral antimicrobial agents among all UTI pathogens isolated in the SENTRY Program (2000).

Antimicrobial agent	% susceptible/resistant for:		
	<i>E. coli</i> (1/1,316) <sup>a</sup>	<i>P. aeruginosa</i> (4/210) <sup>a</sup>	Enterococci (2/351) <sup>a</sup>
Ampicillin	54/45	0/100	88/12
Amoxicillin/Clavulanate	83/5	1/99	88/12
Cefuroxime	78/4	0/100	NT <sup>b</sup>
Ciprofloxacin	89/11	59/37	44/47
BMS284756	89/11	56/44	85/15
Nitrofurantoin	94/3	0/100	91/1
Trimethoprim/Sulfamethoxazole	69/31	1/99	65/35
Vancomycin	NT <sup>b</sup>	NT <sup>b</sup>	95/5

a. Rank order of pathogen occurrence/number of strains tested.  
b. NT = not tested.

**Table 3.** Susceptibility to commonly prescribed oral antimicrobial agents among UTI pathogens isolated in North America (SENTRY Program, 2000).

Antimicrobial agent	% susceptible/resistant for:		
	<i>E. coli</i> (1/635) <sup>a</sup>	<i>P. aeruginosa</i> (4/106) <sup>a</sup>	Enterococci (2/232) <sup>a</sup>
Ampicillin	62/37	0/100	88/12
Amoxicillin/Clavulanate	86/5	0/100	88/12
Cefuroxime	80/2	0/100	NT <sup>b</sup>
Ciprofloxacin	95/4	66/29	41/50
BMS284756	96/4	62/38	85/15
Nitrofurantoin	96/1	0/100	92/1
Trimethoprim/Sulfamethoxazole	77/23	0/100	63/37
Vancomycin	NT <sup>b</sup>	NT <sup>b</sup>	93/7

a. Rank order of pathogen occurrence/number of strains tested.  
b. NT = not tested.

**Table 4.** Susceptibility to commonly prescribed oral antimicrobial agents among UTI pathogens isolated in Europe (SENTRY Program, 2000).

Antimicrobial agent	% susceptible/resistant for:		
	<i>E. coli</i> (1/361) <sup>a</sup>	<i>P. aeruginosa</i> (3/71) <sup>a</sup>	Enterococci (2/100) <sup>a</sup>
Ampicillin	48/51	0/100	84/16
Amoxicillin/Clavulanate	81/6	1/99	86/14
Cefuroxime	73/7	0/100	NT <sup>b</sup>
Ciprofloxacin	85/15	55/41	47/43
BMS284756	85/15	52/48	81/19
Nitrofurantoin	91/3	0/100	87/2
Trimethoprim/Sulfamethoxazole	67/33	1/99	68/32
Vancomycin	NT <sup>b</sup>	NT <sup>b</sup>	100/0

a. Rank order of pathogen occurrence/number of strains tested.  
b. NT = not tested.

**Table 5.** Susceptibility to commonly prescribed oral antimicrobial agents among UTI pathogens isolated in Latin America (SENTRY Program, 2000).

Antimicrobial agent	% susceptible/resistant for:		
	<i>E. coli</i> (1/320) <sup>a</sup>	<i>P. aeruginosa</i> (3/33) <sup>a</sup>	Enterococci (6/19) <sup>a</sup>
Ampicillin	45/55	0/100	100/0
Amoxicillin/Clavulanate	79/4	0/100	100/0
Cefuroxime	81/6	0/100	NT <sup>b</sup>
Ciprofloxacin	82/18	42/55	63/21
BMS284756	82/18	42/58	100/0
Nitrofurantoin	93/5	0/100	100/0
Trimethoprim/Sulfamethoxazole	55/45	0/100	79/21
Vancomycin	NT <sup>b</sup>	NT <sup>b</sup>	100/0

a. Rank order of pathogen occurrence/number of strains tested.  
b. NT = not tested.

**Table 1.** Pathogen rank order of strains causing UTIs during the SENTRY Antimicrobial Surveillance Program (2000).

Rank	Pathogen	No. of strains by region:			
		EU	LA	NA	All (%)
1	<i>E. coli</i>	361	320	635	1,316 (47.3)
2	Enterococci	100	19	232	351 (12.6)
3	<i>Klebsiella</i> spp.	69	61	176	306 (11.0)
4	<i>P. aeruginosa</i>	71	33	106	210 (7.6)
5	<i>P. mirabilis</i>	56	27	62	145 (5.2)
6	<i>Enterobacter</i> spp.	33	20	44	97 (3.5)
7	<i>Citrobacter</i> spp.	17	9	52	78 (2.8)
8	<i>S. aureus</i>	13	10	47	70 (2.5)
9	Indole positive Proteae	24	11	28	63 (2.3)
10	CoNS	9	6	44	59 (2.1)
11	<i>Serratia</i> spp.	8	5	18	31 (1.1)
12	<i>Acinetobacter</i> spp.	15	4	11	30 (1.1)
13	Other	7	6	11	24 (0.9)
	Total	783	531	1,466	2,780 (-)

## MATERIALS AND METHODS

**Bacterial collection.** Each medical center was to collect 50 consecutive clinically significant urinary tract infection isolates (one per patient episode). Pure cultures of isolates were forwarded to the SENTRY Program monitors in a semisolid transport medium by recruited laboratories which provided species identification. If questionable colony morphology or an unusual antimicrobial susceptibility pattern was of concern, further identification confirmation was ruled necessary.

A total of 2,780 UTI isolates (Table 1) were collected from January through December 2000 as part of the SENTRY Program from participating laboratories in North America (n=1,466 isolates), Europe (n=783), and Latin America (n=531). The top seven pathogens in all regions combined accounted for 90% of the isolates and the rank order of all pathogens was: *E. coli* (1,316, 47.3%), *Enterococcus* spp. (351, 12.6%), *Klebsiella* spp. (306, 11%), *P. aeruginosa* (210, 7.6%), *P. mirabilis* (145, 5.2%), *Enterobacter* spp. (97, 3.5%), *Citrobacter* spp. (78, 2.8%), *S. aureus* (70, 2.5%), indole-positive Proteae (63, 2.3%), CoNS (59, 2.1%), *Serratia* spp. (31, 1.1%), *Acinetobacter* spp. (30, 1.1%), and other (24, 0.9%).

**Susceptibility test methods.** Susceptibility testing for all isolates was performed utilizing NCCLS reference broth microdilution methods and common reagent lots in all geographic regions. Each strain was tested against a panel of 44 Gram-positive/negative focused and broad spectrum antimicrobial agents including ampicillin, amoxicillin/clavulanate, BMS284756, cefuroxime, ciprofloxacin, nitrofurantoin, trimethoprim/sulfamethoxazole, and vancomycin. Enteric Gram-negative bacilli suspected of harboring extended spectrum  $\beta$ -lactamase enzymes (ESBL) by phenotypic criteria established by NCCLS were further screened using Etest strips containing various cephalosporin substrates with and without clavulanate (AB BIODISK, Solna, Sweden). MIC values were interpreted using NCCLS M100-S12 guidelines. Quality control was performed using American Type Culture Collection (ATCC) strains.

## RESULTS

- The top seven pathogens in all regions combined accounted for 90% of all infections. *E. coli* was isolated most frequently (n = 1,316, 47.3%) followed by *Enterococcus* spp. (n = 351, 12.6%), *Klebsiella* spp. (n = 306, 11%), *P. aeruginosa* (n = 210, 7.6%), *P. mirabilis* (n = 145, 5.2%), *Enterobacter* spp. (n = 97, 3.5%), and *Citrobacter* spp. (n = 78, 2.8%).
- Pathogen rank order was similar among all regions except for lower isolation rates of *Enterococcus* spp., (rank #6, 4%) in Latin America, and higher isolation rates of indole-positive Proteae in Latin America and Europe (rank #7, 2-3%) compared to North America.
- Phenotypic ESBL rates for *E. coli* and *Klebsiella* spp. were 4% and 19%, respectively (data not shown).
- Among *E. coli*, susceptibility to ampicillin (62%), ciprofloxacin (95%), BMS284756 (96%), and trimethoprim/sulfamethoxazole (77%) was highest in North America. Nitrofurantoin susceptibility among *E. coli* ranged from 91-96% across regions. Overall, resistance to amoxicillin/clavulanate and cefuroxime remained under 5% for *E. coli* in all regions combined (Table 2).
- Marginal sustained activity of trimethoprim/sulfamethoxazole against *E. coli* was determined with susceptibility rates of 55, 67, and 77% in Latin America, Europe, and North America, respectively.
- Ciprofloxacin-resistant *P. aeruginosa* was highest in Latin America (55%) > Europe (41%) > North America (29%).
- Susceptibility to the  $\beta$ -lactams (ampicillin, amoxicillin/clavulanate) among *Enterococcus* spp. was acceptable across all regions with 84-86, 88, and 100% susceptibility in Europe, North America, and Latin America, respectively.
- The enterococcal susceptibility rates were higher for BMS284756 (ciprofloxacin) in Europe, North America, and Latin America at 81% (47%), 85% (41%), and 100% (63%) respectively.
- Susceptibility of *Enterococcus* spp. to nitrofurantoin was 87%, 92%, and 100% of the bacterial isolates in Europe, North America, and Latin America, respectively. Trimethoprim/sulfamethoxazole susceptibility against the enterococci ranged from 63% in North America, 68% in Europe, and 79% in Latin America.
- Vancomycin-resistant enterococci (VRE) were detected only in North America (7%).

## CONCLUSIONS

- E. coli* was the number one causative pathogen of UTIs (47.3%) among all regions tested.
- Enterococcus* spp. ranked as the second most common UTI isolates in both Europe (12.7%) and North America (15.8%) while ranked sixth in Latin America (3.5%) accounting for only 19 out of a total 531 organisms submitted. Vancomycin resistant enterococci from UTIs were observed only in the United States and Canada (7%).
- Quinolone (ciprofloxacin) resistance among *P. aeruginosa* (55%) and *E. coli* (18%) was greatest in Latin America. *E. coli* demonstrated 11% resistance to both ciprofloxacin/BMS284756 overall, while *P. aeruginosa* demonstrated resistance at 37/44% to these same agents.
- Trimethoprim/sulfamethoxazole had marginal activity with 55% susceptibility rates in Latin America, 67% in Europe, and 77% in North America against *E. coli* isolates causing UTIs.
- The increasing resistance rates, cross-resistant patterns, and multi-drug resistant pathogens causing UTIs is increasing. This information strengthens the need for surveillance studies, such as the SENTRY Program directed toward infection site specific analyses.

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