# Significant Increases in the Rate of Fluoroquinolone Resistance Among Gram-Negative Bacilli: Six-Year (1999-2004) Report from the USA MYSTIC Programme

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MYSTIC
Meropenem Yearly Susceptibility Test Information Collection

## ABSTRACT

**Objective**: To utilize the Meropenem (MEM) Yearly Susceptibility Test Information Collection (MYSTIC) Programme, a global longitudinal surveillance network of >100 medical centers, to monitor the activity of broad-spectrum agents in hospitals actively using carbapenems. Between 1999 and 2004, 10-16 USA medical centers referred 200 consecutive, non-duplicate isolates from clinical infections to a central laboratory.

**Methods**: 15,990 strains were submitted over six years. Enterobacteriaceae (ENT; 7,229), *P. aeruginosa* (PSA; 2,254) and *Acinetobacter* spp. (ASP; 489) strains were tested for susceptibility (S) using current NCCLS reference methods and interpretative criteria (M100-S15; 2005). Antimicrobials tested included: MEM, imipenem (IMP), ceftriaxone, cefazidime, cefepime, aztreonam, gentamicin (GENT), tobramycin (TOB), piperacillin/tazobactam, ciprofloxacin (CIPRO), and levofloxacin (LEVO). Strains demonstrating multi-drug R (MDR) from the same site were further characterized by automated ribotyping and PFGE to determine clonality.

**Results**: The rates of CIPRO R within ENT increased from 3.7% in 1999 to 12.9% in 2004 (range, 0.0 - 4.3%; average 1.8% increase/year). The greatest increases in CIPRO-R were noted among indole-positive Proteae (IPP; +24.0%), *E. coli* (EC; +16.6%), *Enterobacter* spp. (EBS; +8.8%) and *P. mirabilis* (+4.9%). Between 2003 and 2004, an 89.9% increase in CIPRO-R was observed for EC. During the same period, the % R for the comparators against ENT remained stable (range, -0.3 to +0.7%) except for GENT (+4.1%) and TOB (+2.3%). Among PSA, the CIPRO-R rate increased from 11.9% in 1999 to 25.3% in 2003, but decreased in 2004 to 21.2%. Percent R for IMP and MEM also decreased 13.6% and 10.3%, respectively. The CIPRO-R rate among ASP strains increased from 25.0% to 44.4% (average 3.9% increase/year). LEVO-R rate (2003 - 2004) was consistently lower than the CIPRO-R rate for all ENT and ASP, but slightly higher against PSA. In 2004, clonal spread of MDR (including fluoroquinolone [FQ]-R) strains was detected in 12 of the 15 hospitals (EC and ASP clusters in 6 sites each).

**Conclusions**: During the monitored period (1999-2004), the rate of FQ-R in ENT tested within the MYSTIC Programme has increased most dramatically for IPP and EC strains. FQ-R has emerged to an even greater degree amongst ASP and PSA. Continued surveillance within the MYSTIC Programme participant sites is warranted to monitor the escalating loss of FQ activity against Gram-negative pathogens.

## INTRODUCTION

Surveillance studies have documented the emergence and continued increase in fluoroquinolone resistance within nearly all important clinical bacterial genus groups over the past decade. Fluoroquinolone resistance (FQR) is mediated by the accumulation of single-base pair mutations in the topoisomerase genes *gyrA, gyrB, parC* and *parE*. The emergence of FQR in oxacillin- (methicillin-) resistant *Staphylococcus aureus* has increased dramatically following the introduction of ciprofloxacin (1988) for the treatment of staphylococcal infections.

The Meropenem Yearly Susceptibility Test Information Collection (MYSTIC) Programme is a longitudinal resistance surveillance project with greater than 125 participant sites worldwide in Europe, North America, Latin America and Asia that monitors the in vitro activity of meropenem and other broad-spectrum antimicrobial agents. Medical centers have been monitored in the United States (USA) since 1999 by a central processing laboratory (JMI Laboratories, North Liberty, Iowa, USA) using reference susceptibility testing methods to detect resistance rate changes to carbapenems and comparator antimicrobial agents. The purpose of this study component was to assess the change in fluoroquinolone resistance rates among both Enterobacteriaceae and Gram-negative non-fermentative bacilli over the six year period of the MYSTIC Programme (USA; 1999 - 2004) and determine the role clonal spread of multidrug-resistant (MDR) strains has on FQR observed rates.

## MATERIALS AND METHODS

Bacterial strains. The MYSTIC Programme in 2004 utilized 15 medical centers geographically dispersed across the USA. The study protocol outlined specific quotas within Gram-negative species (200 isolates from serious infections). Only *Stenotrophomonas maltophilia* and *Chryseobacterium* spp. were excluded from collection due to their intrinsic mechanisms of resistance to carbapenems. A total of 2,799 isolates (93.3% compliance) were submitted to the central processing laboratory from the participant sites (range 64 to 214 isolates per site). Organism identifications were performed locally with identification confirmation achieved by colony morphology, biochemical tests (Remel, Kansas, USA) and/or the Vitek System identification cards (bioMerieux, Missouri, USA) at the monitoring laboratory when required.

Susceptibility testing. Susceptibility testing was performed for all bacterial strains utilizing Clinical Laboratory Standards Institute (formerly National Committee for Clinical Laboratory Standards [NCCLS]) reference methods to determine minimum inhibitory concentrations (MICs). The antimicrobial agents tested were: meropenem, imipenem, aztreonam, cefepime, ceftazidime, ceftriaxone, piperacillin/tazobactam, amikacin, gentamicin, tobramycin, ciprofloxacin and levofloxacin. NCCLS M100-S15 (2005) criteria were applied for interpretation of susceptibility and resistance. Quality control of the susceptibility tests methods was assured utilizing concurrent testing with American Type Culture Collection (ATCC) strains *Escherichia coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212 and *S. aureus* ATCC 29213.

## MATERIALS AND METHODS CONTINUED

Additional testing. The NCCLS (2005) ESBL screening criteria (MIC, ≥ 2 mg/L for ceftazidime or ceftriaxone or aztreonam) were applied to *E. coli, Klebsiella* spp. and *Proteus mirabilis*. All screen-positive isolates were tested by the disk approximation method to demonstrate an enhanced ceftazidime, cefotaxime or aztreonam activity in the presence of clavulanate. In addition, all isolates resistant to meropenem, imipenem and cefazidime were screened for the production of metallo-ß-lactamase using a disk approximation method to demonstrate EDTA or 2-mercaptopropionic acid inhibition of meropenem or imipenem hydrolysis.

Epidemiologic typing. All Gram-negative isolates within a bacterial species or genus group from each medical center were analyzed by antimicrobial resistance antibiogram pattern. Multidrug-resistant isolates were typed for molecular similarity using automated ribotyping (RiboPrinter™ Microbial Characterization System, Qualicon, DE, USA) and further discriminated using CHEF-DRII pulsed-field gel electrophoresis (PFGE; BioRad Laboratories, CA, USA) when necessary.

## RESULTS

- The rate of ciprofloxacin resistance against all Enterobacteriaceae isolates within the USA MYSTIC Programme increased an average of 1.8% per year from 3.7% in 1999 to 12.9% in 2004 (Table 1).
- The greatest increases in ciprofloxacin resistance rates from the 1999 baseline level were observed among the indole-positive *Proteae* (24.0%), *E. coli* (16.6%), *Enterobacter* spp. (8.8%) and *P. mirabilis* (4.9%). A significant increase in ciprofloxacin resistance among *E. coli* isolates was observed from 2003 to 2004 (10.9 to 20.7% resistant).
- Among Enterobacteriaceae, the percent resistance rate for all comparator agents remained stable in the same time period (1999 -2004) with a change ranging from only a 0.3% decrease to a 0.7% increase, except for gentamicin (4.1%) and tobramycin (2.3%).
- Among *P. aeruginosa* isolates, the ciprofloxacin resistance rate increased from 11.9% in 1999 to 25.3% in 2003, but decreased slightly to 21.2% in 2004 (Table 2).
- Over the monitored time period (1999 - 2004), the rate of carbapenem resistance in *P. aeruginosa* isolates decreased 13.6% for imipenem and 10.3% for meropenem.
- The ciprofloxacin resistance rate among *Acinetobacter* spp. strains increased from 25.0% in 1999 up to 44.4% in 2004, an average of 3.9% increase per year.
- Levofloxacin MIC results generated in 2003 and 2004 demonstrated an increase in resistance similar to that of ciprofloxacin. The rate of resistance to levofloxacin was consistently lower than to ciprofloxacin for all Enterobacteriaceae and *Acinetobacter* spp. The trend was reversed for *P. aeruginosa* isolates with levofloxacin resistance rates being greater than ciprofloxacin (23.2% and 21.2%, respectively).
- A total of 16 genotypically identical epidemic clusters were observed among the multidrug-resistant Enterobacteriaceae isolates submitted in the 2004 MYSTIC Programme from nine medical centers (Table 3).
- Thirty-eight FQR *E. coli* isolates from seven medical centers clustered into four distinct ribogroups. The ribogroup 105.243.2 was the most common, representing *E. coli* isolates from sites 1, 2, 14, 16, 18 and 23 (Table 3). PFGE further descriminated the 105.243.2 ribogroup into four similar band patterns (A, A1, A2 and A3) including pattern A observed in all six medical centers.
- Molecular typing results indicated the occurrence of clonal dissemination of ESBL-producing *E. cloacae* and *K. pneumoniae* (site 4; Table 3).
- Eleven clonally related MDR *Acinetobacter baumannii* clusters were identified within six medical centers submitting isolates in the 2004 MYSTIC Programme. Between 1999 and 2004, the ribotype 105.931.7 was observed in six sites but demonstrated persistence over several years within three sites. PFGE results for ribotype 105.931.7 showed multiple types and subtypes with only pattern B noted in all three hospitals (Table 4).
- Molecular typing results suggestive of clonal dissemination of MDR *P. aeruginosa* were observed only in one medical center in 2004, where 10 isolates showed only three distinct ribotypes.

**Table 1.** Antimicrobial activity of meropenem and selected broad-spectrum comparator agents against Enterobacteriaceae isolates from the USA MYSTIC Programme (1999-2004).

| | | 2004 | | 1999 | 2000 | 2001 | 2002 | 2003 |
|---|---|---|---|---|---|---|---|---|
| Organism (no. tested)/antimicrobial agent | $MIC_{50}$ | $MIC_{90}$ | % S/R[a] | % S/R | % S/R | % S/R | % S/R | % S/R |
| *Citrobacter* spp. (no. tested)[b] | | (141) | | (46) | (68) | (80) | (85) | (141) |
| Meropenem | 0.03 | 0.03 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 |
| Ceftazidime | 0.25 | >16 | 89.4/10.6 | 84.8/6.5 | 75.0/23.5 | 90.0/8.8 | 87.1/11.8 | 84.4/14.2 |
| Piperacillin/Tazobactam | 2 | 16 | 91.5/2.8 | 97.8/2.2 | 88.2/10.3 | 92.5/1.3 | 87.1/3.5 | 90.8/5.0 |
| Gentamicin | ≤1 | 2 | 91.5/7.8 | 97.8/2.2 | 92.6/7.4 | 93.8/6.3 | 91.8/8.2 | 90.8/8.5 |
| Ciprofloxacin | ≤0.25 | ≤0.25 | 95.0/4.3 | 93.5/6.5 | 95.6/4.4 | 95.0/2.5 | 92.9/5.9 | 91.5/7.1 |
| Levofloxacin | ≤0.06 | 0.5 | 95.0/2.8 | - | - | - | - | 92.2/4.3 |
| *Enterobacter* spp. (no. tested)[c] | | (160) | | (97) | (158) | (145) | (152) | (158) |
| Meropenem | 0.03 | 0.06 | 100.0/0.0 | 100.0/0.0 | 99.4/0.6 | 98.6/0.7 | 99.3/0.7 | 100.0/0.0 |
| Ceftazidime | 0.25 | >16 | 80.6/16.3 | 83.5/13.4 | 84.2/11.4 | 75.9/19.3 | 82.2/15.1 | 77.2/15.2 |
| Piperacillin/Tazobactam | 2 | 32 | 86.9/5.6 | 85.6/6.2 | 88.0/5.1 | 77.9/11.0 | 84.9/6.6 | 84.8/6.3 |
| Gentamicin | ≤1 | ≤1 | 90.0/9.4 | 97.9/2.1 | 98.1/1.3 | 95.2/4.1 | 94.7/3.9 | 90.5/7.6 |
| Ciprofloxacin | ≤0.25 | ≤0.25 | 90.0/8.8 | 100.0/0.0 | 97.5/1.9 | 89.7/9.7 | 92.1/6.6 | 88.0/9.5 |
| Levofloxacin | ≤0.06 | 0.5 | 90.6/7.5 | - | - | - | - | 89.2/5.7 |
| *E. coli* (no. tested) | | (742) | | (197) | (312) | (306) | (323) | (469) |
| Meropenem | ≤0.016 | 0.03 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 |
| Ceftazidime | ≤0.12 | 0.25 | 97.5/1.5 | 97.0/2.5 | 98.4/1.6 | 97.1/2.3 | 99.4/0.3 | 99.6/0.4 |
| Piperacillin/Tazobactam | 2 | 4 | 98.5/1.1 | 97.5/1.5 | 98.1/1.3 | 97.7/1.3 | 98.1/1.5 | 98.3/1.3 |
| Gentamicin | ≤1 | 8 | 89.8/9.4 | 96.4/3.0 | 97.8/1.9 | 95.1/4.2 | 95.4/4.0 | 96.6/2.8 |
| Ciprofloxacin | ≤0.25 | >2 | 78.9/20.7 | 95.9/4.1 | 96.8/2.9 | 90.5/9.2 | 92.9/7.1 | 89.1/10.9 |
| Levofloxacin | ≤0.06 | >8 | 79.0/20.2 | - | - | - | - | 89.1/10.2 |
| *Klebsiella* spp. (no. tested)[d] | | (433) | | (152) | (233) | (225) | (248) | (303) |
| Meropenem | 0.03 | 0.03 | 99.5/0.5 | 100.0/0.0 | 97.9/2.1 | 100.0/0.0 | 100.0/0.0 | 99.7/0.0 |
| Ceftazidime | ≤0.12 | 0.5 | 94.7/4.6 | 96.1/3.3 | 94.4/5.2 | 93.8/5.4 | 97.6/2.4 | 95.4/4.0 |
| Piperacillin/Tazobactam | 2 | 8 | 95.6/3.5 | 93.4/3.9 | 95.7/3.0 | 96.4/2.2 | 94.4/4.4 | 94.4/3.0 |
| Gentamicin | ≤1 | ≤1 | 94.9/3.9 | 96.1/2.6 | 94.8/4.3 | 95.6/2.7 | 96.0/3.2 | 93.7/4.3 |
| Ciprofloxacin | ≤0.25 | ≤0.25 | 94.7/4.8 | 94.7/3.3 | 94.0/4.3 | 94.7/3.6 | 96.8/2.0 | 95.0/4.6 |
| Levofloxacin | ≤0.06 | 0.5 | 94.9/4.2 | - | - | - | - | 95.4/3.6 |
| *P. mirabilis* (no. tested) | | (128) | | (95) | (143) | (142) | (148) | (154) |
| Meropenem | 0.03 | 0.06 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 |
| Ceftazidime | ≤0.12 | ≤0.12 | 100.0/0.0 | 98.9/1.1 | 97.3/2.1 | 98.6/1.4 | 100.0/0.0 | 100.0/0.0 |
| Piperacillin/Tazobactam | ≤1 | ≤1 | 100.0/0.0 | 100.0/0.0 | 99.3/0.7 | 99.3/0.0 | 100.0/0.0 | 100.0/0.0 |
| Gentamicin | ≤1 | ≤1 | 97.7/0.8 | 98.9/1.1 | 92.3/7.7 | 93.7/4.2 | 93.9/5.4 | 93.5/5.8 |
| Ciprofloxacin | ≤0.25 | 2 | 89.8/7.0 | 96.8/2.1 | 90.9/7.0 | 92.3/7.0 | 90.5/6.8 | 85.1/10.4 |
| Levofloxacin | ≤0.06 | 2 | 93.8/6.3 | - | - | - | - | 89.6/7.8 |
| Indole-positive *Proteae* (no. tested)[e] | | (90) | | (33) | (38) | (39) | (58) | (52) |
| Meropenem | 0.06 | 0.12 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 |
| Ceftazidime | 0.25 | 4 | 92.2/5.6 | 93.9/3.0 | 92.1/5.3 | 97.4/0.0 | 94.8/1.7 | 98.1/0.0 |
| Piperacillin/Tazobactam | ≤1 | 4 | 95.6/1.1 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 | 100.0/0.0 |
| Gentamicin | ≤1 | 8 | 87.8/7.8 | 87.9/12.1 | 86.8/13.2 | 87.2/5.1 | 81.0/6.9 | 84.6/11.5 |
| Ciprofloxacin | ≤0.25 | >2 | 56.7/42.2 | 78.8/18.2 | 84.2/13.2 | 92.3/5.1 | 58.6/34.5 | 69.2/23.1 |
| Levofloxacin | 0.25 | >8 | 58.9/34.4 | - | - | - | - | 73.1/19.2 |
| *Serratia* spp. (no. tested)[f] | | (149) | | (53) | (74) | (74) | (82) | (133) |
| Meropenem | 0.03 | 0.06 | 100.0/0.0 | 96.2/3.8 | 100.0/0.0 | 100.0/0.0 | 98.8/0.0 | 100.0/0.0 |
| Ceftazidime | 0.25 | 0.5 | 96.6/2.7 | 100.0/0.0 | 95.9/2.7 | 97.3/1.4 | 96.3/2.4 | 99.2/0.8 |
| Piperacillin/Tazobactam | 2 | 8 | 95.3/0.0 | 98.1/0.0 | 95.9/0.0 | 94.6/0.0 | 98.8/1.2 | 97.7/0.0 |
| Gentamicin | ≤1 | ≤1 | 93.3/4.7 | 98.1/1.9 | 95.9/2.7 | 93.2/1.4 | 95.1/3.7 | 99.2/0.8 |
| Ciprofloxacin | ≤0.25 | 1 | 94.6/1.3 | 92.5/3.8 | 90.5/8.1 | 89.2/8.1 | 95.1/2.4 | 93.2/3.8 |
| Levofloxacin | 0.12 | 1 | 98.0/0.0 | - | - | - | - | 95.5/3.0 |
| All Enterobacteriaceae (no. tested) | | (1,865) | | (708) | (1,048) | (1,037) | (1,131) | (1,439) |
| Meropenem | 0.03 | 0.06 | 99.9/0.1 | 99.7/0.3 | 99.4/0.6 | 99.8/0.1 | 99.8/0.1 | 99.9/0.0 |
| Ceftazidime | ≤0.12 | 0.5 | 94.7/4.3 | 94.6/4.0 | 93.2/5.6 | 93.1/5.5 | 95.3/3.9 | 94.7/4.1 |
| Piperacillin/Tazobactam | 2 | 4 | 96.0/2.0 | 95.6/2.3 | 95.4/2.7 | 94.3/2.5 | 95.1/2.7 | 95.5/2.2 |
| Gentamicin | ≤1 | 2 | 92.1/6.8 | 96.9/2.7 | 95.5/4.0 | 94.6/3.8 | 94.2/4.5 | 94.3/4.6 |
| Ciprofloxacin | ≤0.25 | >2 | 86.1/12.9 | 95.3/3.7 | 94.6/4.4 | 92.1/6.8 | 91.7/6.8 | 89.9/8.6 |
| Levofloxacin | ≤0.06 | 8 | 86.9/11.7 | - | - | - | - | 91.0/7.0 |

a. Criteria as published by the NCCLS.
b. Includes: *Citrobacter amalonaticus* (four strains), *C. braakii* (one strain), *C. farmeri* (one strain), *C. freundii* (65 strains), *C. koseri* (37 strains) and *Citrobacter* spp. (33 strains).
c. Includes: *Enterobacter aerogenes* (43 strains), *E. cloacae* (92 strains), *E. gergoviae* (one strain) and *Enterobacter* spp. (24 strains).
d. Includes: *Klebsiella ornithinolytica* (three strains), *K. oxytoca* (54 strains), *K. ozaenae* (one strain), *K. pneumoniae* (337 strains) and *Klebsiella* spp. (38 strains).
e. Includes: *Morganella morganii* (43 strains), *Morganella* spp. (three strains), *Proteus* spp. (five strains), *Proteus vulgaris* (six strains), *Providencia alcalifaciens* (one strain), *Providencia rettgeri* (nine strains), *Providencia* spp. (three strains) and *Providencia stuartii* (20 strains).
f. Includes: *Serratia liquifaciens* (four strains), *S. marcescens* (122 strains) and *Serratia* spp. (23 strains).

**Table 2.** Antimicrobial activity of meropenem and selected broad-spectrum comparator agents against *P. aeruginosa* and *Acinetobacter* species isolates from the USA MYSTIC Programme (1999-2004).

| | | 2004 | | 1999 | 2000 | 2001 | 2002 | 2003 |
|---|---|---|---|---|---|---|---|---|
| Organism (no. tested)/antimicrobial agent | $MIC_{50}$ | $MIC_{90}$ | % S/R[a] | % S/R | % S/R | % S/R | % S/R | % S/R |
| *P. aeruginosa* (no. tested) | | (689) | | (193) | (299) | (298) | (321) | (454) |
| Meropenem | 0.5 | 4 | 90.3/5.8 | 78.2/16.1 | 84.3/10.0 | 85.9/8.4 | 93.1/4.4 | 88.3/7.3 |
| Ceftazidime | 2 | >16 | 82.6/13.4 | 82.9/10.9 | 82.6/13.0 | 85.6/10.1 | 85.7/9.7 | 83.7/10.8 |
| Piperacillin/Tazobactam | 4 | 128 | 88.0/12.0 | 89.1/10.9 | 86.3/13.7 | 90.9/9.1 | 91.6/8.4 | 90.3/9.7 |
| Gentamicin | ≤1 | 8 | 86.8/9.9 | 86.5/8.8 | 81.6/9.0 | 82.2/10.1 | 87.9/8.4 | 84.6/11.0 |
| Ciprofloxacin | ≤0.25 | >2 | 73.6/21.2 | 82.9/11.9 | 73.6/20.4 | 74.8/22.1 | 72.3/22.7 | 68.7/25.3 |
| Levofloxacin | 0.5 | >8 | 69.4/23.2 | - | - | - | - | 65.6/26.0 |
| *Acinetobacter* spp. (no. tested)[b] | | (142) | | (32) | (56) | (79) | (69) | (111) |
| Meropenem | 0.5 | 16 | 76.1/16.2 | 78.1/21.9 | 78.6/19.6 | 81.0/19.0 | 84.1/13.0 | 87.4/7.2 |
| Ceftazidime | 16 | >16 | 49.3/41.5 | 68.8/18.8 | 66.1/28.6 | 64.6/29.1 | 58.0/34.8 | 64.0/32.4 |
| Piperacillin/Tazobactam | 16 | >128 | 54.9/37.3 | 71.9/21.9 | 58.9/33.2 | 70.9/21.5 | 62.3/18.8 | 61.3/16.2 |
| Gentamicin | ≤1 | >8 | 63.4/33.8 | 65.6/34.4 | 64.3/33.9 | 62.0/31.6 | 59.4/30.4 | 63.1/32.4 |
| Ciprofloxacin | 0.5 | >2 | 54.2/44.4 | 71.9/25.0 | 62.5/35.7 | 59.5/38.0 | 56.5/40.6 | 58.6/40.5 |
| Levofloxacin | 0.25 | >8 | 59.9/39.4 | - | - | - | - | 60.4/36.0 |

a. Criteria as published by the NCCLS.
b. Includes: *Acinetobacter baumannii* (111 strains), *A. junii* (two strains), *A. lwoffii* (10 strains) and *Acinetobacter* spp. (19 strains).

**Table 3.** Molecular typing results for FQR or MDR Enterobacteriaceae tested in MYSTIC Programme 2004 in USA.

| Organism | Site | No. strains | Ribotype | PFGE |
|---|---|---|---|---|
| *C. freundii* | 02 | 2 | 258.238.3 | A |
| *E. coli* | 01 | 5 | 105.243.2 | A |
| | 02 | 3 | 105.243.2 | A/A2 |
| | 14 | 3 | 105.243.2 | A |
| | 16 | 14 | 105.243.2 | A/A1/A2 |
| | 18 | 4 | 105.243.2 | A/A3 |
| | 23 | 2 | 105.243.2 | A |
| | 08 | 2 | 105.254.2 | B/B1 |
| | 16 | 3 | 105.1177.6 | B |
| | 16 | 2 | 258.184.4 | C |
| *E. cloacae* | 04 | 6 | 105.226.3 | A |
| *K. pneumoniae* | 04 | 3 | 105.520.4 | C/C1 |
| *K. oxytoca* | 03 | 2 | 105.890.4 | A |
| *M. morganii* | 04 | 4 | 258.219.5 | A/A1 |
| *P. mirabilis* | 04 | 2 | 258.236.3 | A |
| *P. stuartii* | 16 | 5 | 105.1010.4 | A/A1/A2 |

**Table 4.** Molecular typing results for FQR or MDR non-fermentative bacilli tested in MYSTIC Programme 2004 in USA.

| | | | | | Year | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Organism | Site | No. strains | Ribotype | PFGE | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 |
| *A. baumannii* | 02 | 11 | 105.931.7 | B/B1/C/C1 | | X | X | X | | X |
| | 04 | 26 | 105.931.7 | A/A1/B/B1/C1/C2/D/D2 | X | X | X | X | X | X |
| | 18 | 3 | 105.931.7 | A/B/D1 | | | | X | | X |
| | 17 | 3 | 105.1110.4 | A | | | | | | X |
| | 24 | 7 | 105.1110.4 | A1 | | | | | | X |
| | 02 | 3 | 105.218.3 | A1/A2 | | | | | | X |
| | 18 | 2 | 105.71.2 | C | | | | | | X |
| | 22 | 3 | 105.531.3 | A | | | | | | X |
| | 22 | 5 | 258.243.1 | A | | | | | | X |
| | 22 | 2 | 258.243.3 | B | | | | | | X |
| | 24 | 2 | 105.393.6 | A1 | | | | | | X |
| *P. aeruginosa* | 04 | 6 | 105.566.2 | A/B | | | | | | X |
| | 04 | 2 | 258.149.7 | C | | | | | | X |
| | 04 | 2 | 258.232.7 | D | | | | | | X |

## CONCLUSIONS

- The rate of ciprofloxacin resistance among Gram-negative bacilli within the MYSTIC Programme has increased steadily between 1999 and 2004.
- When compared to ciprofloxacin, levofloxacin demonstrated a consistently lower rate of resistance against all Gram-negative species/groups tested except *P. aeruginosa*.
- The resistance rates for other comparator agents within the USA MYSTIC Programme against Enterobacteriaceae isolates have remained stable (range -0.3% to +0.7%), except for a greater increase in resistance to aminoglycosides.
- The dissemination of MDR clones were most often identified in *E. coli* and *Acinetobacter* spp. isolates leading to an increased rate of resistance to fluoroquinolones among monitored Gram-negative bacilli.
- Continued surveillance of Gram-negative bacilli appears warranted to monitor the activity of broad-spectrum antimicrobial agents, especially the broad-spectrum carbapenems and newer quinolones.

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