

Increased Fluoroquinolone Resistance of Gram-Negative and *Staphylococcus aureus* Isolates Between 1994-2001: Results of the Antimicrobial Resistance Management (ARM) Program

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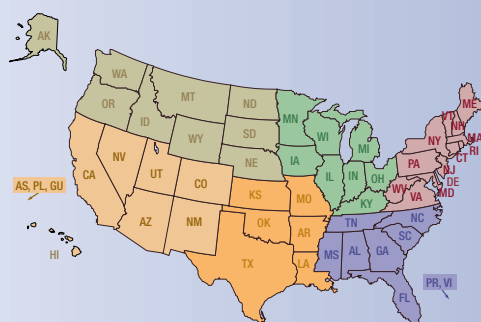


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What is the Antimicrobial Resistance Management (ARM) Program?

PURPOSE

- The Antimicrobial Resistance Management (ARM) Program is an ongoing study to document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates and to identify relationships between antibiotic use and resistance rates
- Hospitals can delineate if and when antimicrobial resistance occurs
 - Allows strategic intervention
 - Provides data for local, regional, national benchmarks
 - Has potential to reduce costs of antibiotics associated with inappropriate use
- A total of 251 institutions have enrolled as of April 22, 2003
 - 199 (79.3%) nonteaching
 - 52 (20.7%) teaching
- For the purposes of comparison, US hospitals are grouped in 6 geographic regions (see map, below); one non-US state is also included (Puerto Rico), which is grouped with the Southeast



- The number of hospitals included from each region is as follows:
 - North Central: 46 (18.3%)
 - South Central: 46 (18.3%)
 - Northeast: 68 (27.1%)
 - Southeast: 74 (29.5%)
 - Northwest: 5 (2.0%)
 - Southwest: 12 (4.8%)

DATA COLLECTION

- Each hospital provides a minimum of 3 years of antibiogram or sensitivity report data
- Individual antibiotics and organisms are captured in the database
 - 44 antibiotics
 - 16 organisms
- A Web-based analysis tool allows comparisons between antibiotic use and resistance rates for any number of parameters
 - One year with another year
 - Groups of years to other groups of years
 - Hospital to hospital
 - Hospital to hospital system
 - Hospital to state
 - Within a state
 - Hospital to region
 - Hospital to national
 - State to state
 - State to region
 - State to national
 - Region to national

ABSTRACT

BACKGROUND: The ARM Program, established in 1997, documents trends in antimicrobial susceptibility patterns. Data on 17.4 million inpatient/outpatient isolates (19 organisms/46 antibiotics) have been collected from 245 US institutions.

METHODS: Antibiograms and sensitivity reports from 1994-2001 for *E coli* (n=770,105), *P mirabilis* (n=66,807), *P aeruginosa* (n=307,513) and *S aureus* isolates (n=398,467) were reviewed for resistance to fluoroquinolones (ciprofloxacin, levofloxacin, and ofloxacin). *S aureus* isolates (n=333,211) were reviewed for resistance to nafcillin/oxacillin to determine MRSA.

RESULTS: Nationally, resistance to fluoroquinolones increased (Table):

	Increase in resistance (%)		
	<i>E coli</i>	<i>P mirabilis</i>	<i>P aeruginosa</i>
Ciprofloxacin	6.9%	19.1%	12.9%
Levofloxacin*	3.5%	7.9%	4.5%
Ofloxacin	6.0%	21.8%	11.7%

*1997-2001

Isolate susceptibility to levofloxacin was suppressed in the context of preexisting ciprofloxacin resistance, suggesting a class effect. In 1997, 76.5% of *P aeruginosa* isolates were susceptible to ciprofloxacin and 66.5% to levofloxacin; by 2001, ciprofloxacin susceptibility was 64.2% and levofloxacin, 62.0%. Regionally, *P mirabilis* isolates were least susceptible to fluoroquinolones in South Central; few differences were seen for *E coli*. Nationally, *S aureus* resistance also increased to ciprofloxacin (15.4%), levofloxacin (16.0%), and ofloxacin (5.3%), while resistance to nafcillin/oxacillin (MRSA) increased 6.9%.

CONCLUSIONS: *P mirabilis* and *P aeruginosa* isolate resistance to fluoroquinolones increased across the class. For *S aureus*, the fluoroquinolones and nafcillin/oxacillin showed similar resistance trends; however, as sensitivity to ciprofloxacin has decreased, MRSA levels have increased.

BACKGROUND

- The emergence of antimicrobial resistance is a complex problem driven by many interconnected factors; in particular, the use and misuse of antimicrobial agents¹
- The ongoing ARM program was established in 1997 to document national and regional antimicrobial susceptibility trends among inpatient and outpatient isolates
- ARM program surveillance data are anticipated to complement existing and emerging consensus guidelines for the treatment of a number of disease states, including those for which the fluoroquinolone class of agents are most often prescribed

METHODS

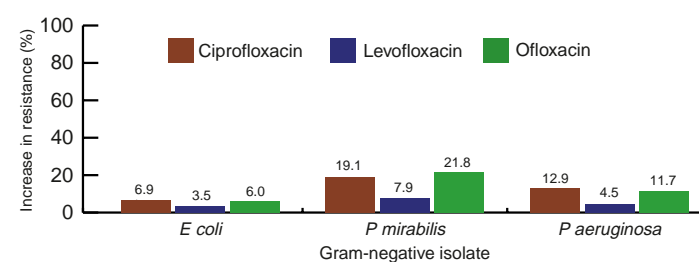
- Using a Web-based analysis tool, *E coli* (n=770,105), *P mirabilis* (n=66,807), *P aeruginosa* (n=307,513), and *S aureus* isolate (n=398,467) antibiograms and sensitivity reports from 1994-2001 were reviewed for resistance to the fluoroquinolones ciprofloxacin, levofloxacin, and ofloxacin both nationally and by region: North Central, Northeast, South Central, Southeast, and Southwest*
- MRSA isolates were identified as *S aureus* isolates (n=333,211) resistant to nafcillin/oxacillin

*Isolates not available in Northwest

RESULTS

- Nationally, resistance to fluoroquinolones increased among the gram-negative isolates *E coli*, *P mirabilis*, and *P aeruginosa* between 1994 and 2001 for ciprofloxacin and ofloxacin and between 1997 and 2001 for levofloxacin (Figure 1)
- A class effect is suggested by reduced isolate susceptibility to levofloxacin at its introduction; ie, in the context of preexisting ciprofloxacin and ofloxacin resistance

Figure 1. Increase in Fluoroquinolone Resistance Among Gram-Negative Isolates, 1994*-2001

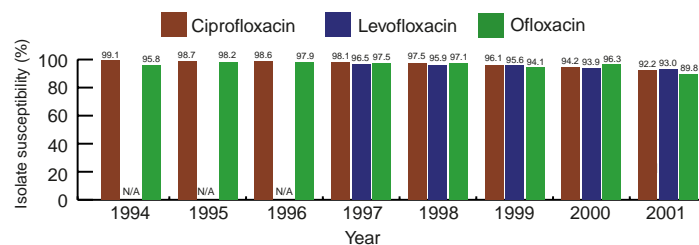


*1997-2001 for levofloxacin

E COLI

- For *E coli*, susceptibility was reduced between 1994 and 2001 for ciprofloxacin and ofloxacin and between 1997 and 2001 for levofloxacin (Figure 2)
- Regionally, few differences were seen for *E coli*

Figure 2. Reduced *E coli* Susceptibility to the Fluoroquinolones, 1994*-2001

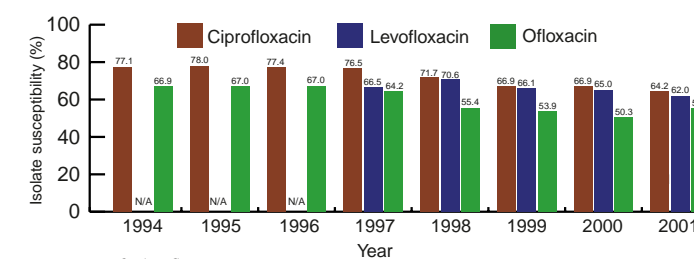


*1997-2001 for levofloxacin
N/A = not available

P AERUGINOSA

- In 1997, 76.5% of *P aeruginosa* isolates were susceptible to ciprofloxacin and 66.5% to levofloxacin; by 2001, ciprofloxacin susceptibility was 64.2% and levofloxacin, 62.0% (Figure 3)

Figure 3. Reduced *P aeruginosa* Susceptibility to the Fluoroquinolones, 1994*-2001

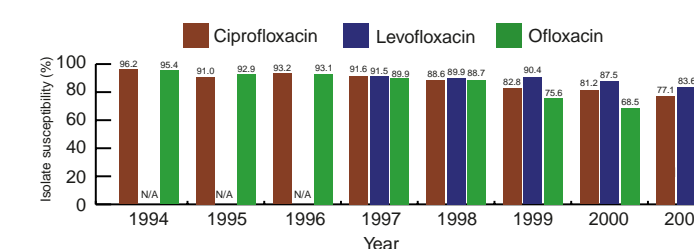


*1997-2001 for levofloxacin
N/A = not available

P MIRABILIS

- Compared with *E coli*, an even greater reduction in isolate susceptibility to the fluoroquinolones was seen for *P mirabilis* (Figure 4)
- P mirabilis* isolates were least susceptible to fluoroquinolones in the South Central region; by 2001, susceptibility was 58.1% for ciprofloxacin, 70.7% for levofloxacin, and 53.8% for ofloxacin

Figure 4. Reduced *P mirabilis* Susceptibility to the Fluoroquinolones, 1994*-2001

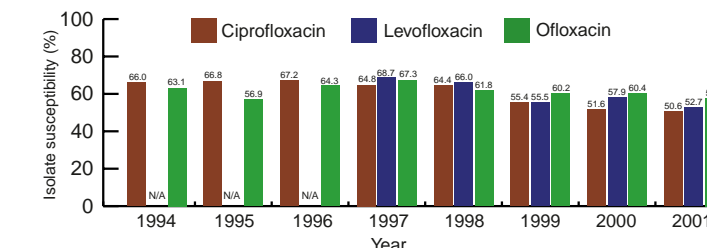


*1997-2001 for levofloxacin
N/A = not available

S AUREUS

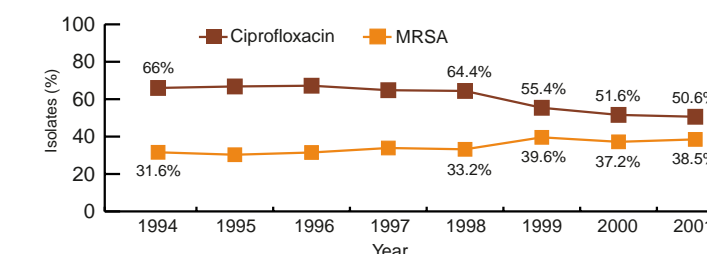
- Nationally, *S aureus* susceptibility decreased to ciprofloxacin, levofloxacin, and ofloxacin (Figure 5), while resistance to nafcillin/oxacillin (MRSA) increased (Figure 6)

Figure 5. Reduced *S aureus* Susceptibility to the Fluoroquinolones, 1994*-2001



*1997-2001 for levofloxacin
N/A = not available

Figure 6. From 1994 to 2001, MRSA Levels Have Increased as Sensitivity to Ciprofloxacin Has Decreased



CONCLUSIONS

- Between 1994 and 2001, gram-negative isolate resistance to fluoroquinolones increased across the class, with a class effect suggested by levofloxacin suppression
- The fluoroquinolones and nafcillin/oxacillin showed similar resistance trends for *S aureus*, with a decline in susceptibility to ciprofloxacin mirrored by an increase in MRSA levels

REFERENCES

- WHO Global Strategy for Containment of Antimicrobial Resistance. WHO/CDS/CSR/DRS/2001. 2a:4.

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