

Resistance of Nosocomial Pathogens to Fluoroquinolones, 1995-2003: Results of the Antimicrobial Resistance Management (ARM) Program

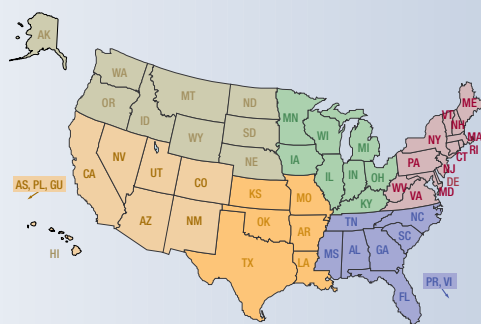
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What is the Antimicrobial Resistance Management (ARM) Program?

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 336 institutions have enrolled as of September 14, 2004
 - 270 (80%) nonteaching
 - 66 (20%) teaching
- For the purposes of comparison, US hospitals are grouped in 6 geographic regions (see map, below)



- The number of hospitals included from each region is as follows:
 - North Central: 52 (15%)
 - South Central: 57 (17%)
 - Northeast: 88 (26%)
 - Southeast: 103 (31%)
 - Northwest: 8 (2%)
 - Southwest: 27 (8%)

DATA COLLECTION

- Each hospital provides a minimum of 3 years of antibiogram or sensitivity report data
- To date, 25.7 million isolates are represented in the database
- Individual antibiotics and organisms captured include
 - 48 antibiotics
 - 19 organisms
- www.armprogram.com is a Web-based analysis tool that 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 documents trends in antimicrobial susceptibility. The ARM surveillance database contains data on 24.1 million inpatient/outpatient isolates (19 organisms/48 antibiotics) collected from 314 US institutions in 6 US regions.

METHODS: Antibiograms/sensitivity reports for *E coli*, *K pneumoniae*, and *P mirabilis* were reviewed from 1995-2003 for resistance to ciprofloxacin and levofloxacin. To determine MRSA, *S aureus* isolates were reviewed for resistance to nafcillin/oxacillin. National and regional resistance rates were compared to those in the Southeast, which comprise 52% of isolates in the database, and to Florida.

RESULTS: Between 1995 and 2003, resistance increased nationally.

	Increase in resistance (%)			
	<i>E coli</i> (n=971,061)	<i>K pneumoniae</i> (n=284,748)	<i>P mirabilis</i> (n=173,422)	<i>S aureus</i> (n=484,717)
Ciprofloxacin	11.6	3.4	25.2	10.9
Levofloxacin*	11.2	3.3	24.2	21.3
Nafcillin/oxacillin				26.5

*1997-2003

Isolate susceptibility to levofloxacin was suppressed in the context of preexisting ciprofloxacin resistance, suggesting a class effect. Regionally, *E coli*, *K pneumoniae*, *P mirabilis*, and *S aureus* isolates remained most susceptible to fluoroquinolones in the Northwest, although rates have declined. Resistance trends for the Southeast region were similar to national. In Florida, increase in ciprofloxacin resistance of *E coli* (14.6%) and *K pneumoniae* (4.4%) isolates were greater than that seen nationally; levofloxacin rates were higher (*E coli*, 12.9%) and lower (*K pneumoniae*, 2.6%). For *P mirabilis*, resistance rates were greater for levofloxacin (28.4%) than for ciprofloxacin (26.1%), both of which were higher than observed nationally.

CONCLUSION: Resistance of nosocomial pathogens, particularly *P mirabilis*, to fluoroquinolones has increased. *S aureus* isolates showed similar resistance trends to fluoroquinolones and nafcillin/oxacillin, with MRSA increasing as sensitivity to ciprofloxacin has decreased. Trending resistance at the regional and state level (eg, www.armprogram.com) allows benchmarking for appropriate intervention.

BACKGROUND

- The Infectious Diseases Society of America (IDSA), among other organizations, is working to call attention to the impending crisis with respect to the decline in availability of antimicrobials, including resistance to existing agents¹
- The ARM Program was established in 1997 to document national and regional antimicrobial susceptibility trends among inpatient and outpatient isolates
- At the time this study was conducted, the ARM surveillance database contained data on 24.1 million inpatient/outpatient isolates (19 organisms/48 antibiotics) collected from 314 US institutions in 6 US regions

METHODS

- To determine whether resistance to the fluoroquinolones ciprofloxacin and levofloxacin increased between 1995 and 2003, antibiograms/sensitivity reports for *E coli*, *K pneumoniae*, and *P mirabilis* were reviewed
- Methicillin-resistant *S aureus* (MRSA) was determined by reviewing *S aureus* isolates for resistance to nafcillin/oxacillin
- Resistance rates were compared both nationally and regionally
 - Southeast comprises 52% of the isolates in the database
 - Florida was selected as a representative state in the Southeast region

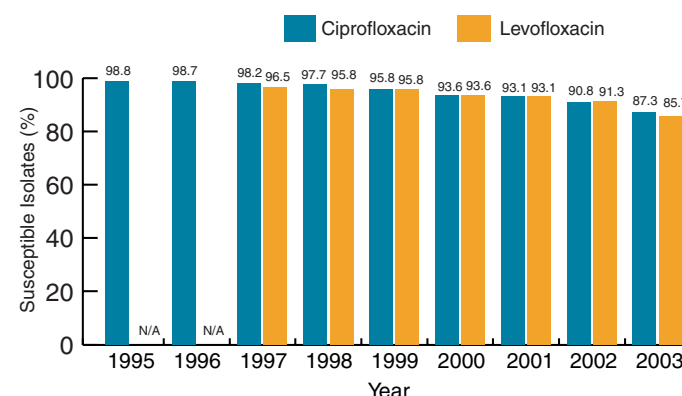
RESULTS

- Between 1995 and 2003, resistance to each of the organisms increased nationally, as seen by declining susceptibility to the antibiotics studied
- Isolate susceptibility to levofloxacin was suppressed in the context of preexisting ciprofloxacin resistance, suggesting a class effect

E COLI

- For *E coli* (n=971,061), the decline in susceptibility was similar for both ciprofloxacin (11.6%) and levofloxacin (11.2%) (Figure 1)

Figure 1. National Decline in *E coli* Susceptibility to Fluoroquinolones, 1995-2003

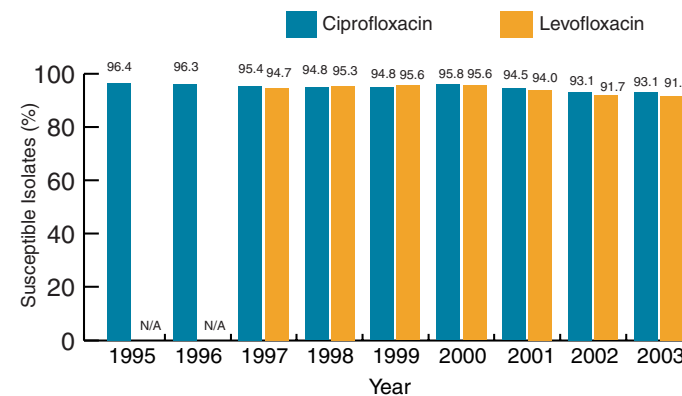


N/A=not available

K PNEUMONIAE

- A similar trend was seen for *K pneumoniae* (n=284,748) although resistance to ciprofloxacin (3.4%) and levofloxacin (3.3%) did not increase to the same extent as either *E coli* or *P mirabilis*

Figure 2. National Decline in *K pneumoniae* Susceptibility to Fluoroquinolones, 1995-2003

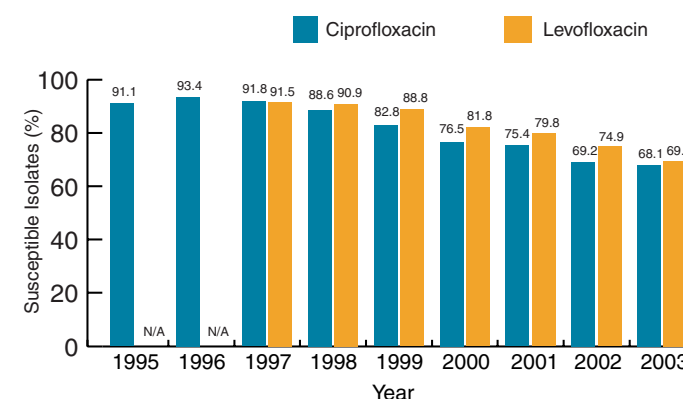


N/A=not available

P MIRABILIS

- For *P mirabilis* (n=173,422), resistance rates to ciprofloxacin increased 25.2%, with a similar increase observed for levofloxacin (24.2%), higher than for the other organisms (Figure 3)

Figure 3. National Decline in *P mirabilis* Susceptibility to Fluoroquinolones, 1995-2003

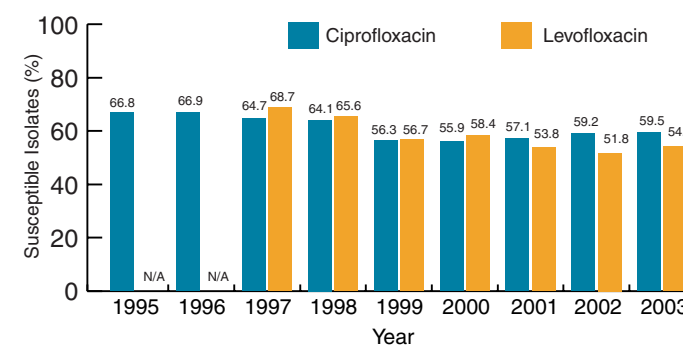


N/A=not available

S AUREUS

- S aureus* (n=484,717) resistance to levofloxacin (21.3%) increased more than twice that seen for ciprofloxacin (10.9%) (Figure 4)
- The increase in *S aureus* resistance to levofloxacin was mirrored by the 26.5% increase in *S aureus* resistance to nafcillin/oxacillin (MRSA)

Figure 4. National Decline in *S aureus* Susceptibility to Fluoroquinolones, 1995-2003



N/A=not available

- When examined in the aggregate, *E coli*, *K pneumoniae*, *P mirabilis*, and *S aureus* isolates remained most susceptible to fluoroquinolones in the Northwest for the range of years studied (Table 1)
- Resistance trends for the Southeast region were similar to national (Table 1)

Table 1. Aggregate National and Regional Susceptibility Rates (%) for *E coli*, *K pneumoniae*, *P mirabilis*, and *S aureus* isolates, 1995-2003

Organism/ Antibiotic	National	North Central	Northeast	Northwest	South Central	Southeast	Southwest
<i>E coli</i>							
Ciprofloxacin	95.2	97.2	95.9	97.6	96.1	93.9	93.6
Levofloxacin	93.4	95.0	93.2	97.0	95.4	92.5	92.9
<i>K pneumoniae</i>							
Ciprofloxacin	95.1	94.7	94.8	98.0	95.3	95.1	94.4
Levofloxacin	94.4	96.0	93.4	97.9	96.2	94.9	91.5
<i>P mirabilis</i>							
Ciprofloxacin	82.3	89.0	87.8	94.4	74.3	79.7	74.9
Levofloxacin	82.0	86.2	86.8	94.5	80.0	81.4	77.4
<i>S aureus</i>							
Ciprofloxacin	60.8	58.7	56.0	72.3	60.2	61.4	72.0
Levofloxacin	57.0	52.5	46.9	70.7	68.9	60.8	50.7

- In Florida, increase in *E coli* (14.6%) and *K pneumoniae* (4.4%) isolate resistance to ciprofloxacin was greater than that seen nationally (Table 2)
- Levofloxacin resistance rates were higher (*E coli*, 12.9%) and lower (*K pneumoniae*, 2.6%) compared with the national rates

Table 2. Decline in Susceptibility (%) to Fluoroquinolones in Florida, 1995-2003

Organism/ Antibiotic	1995	1996	1997	1998	1999	2000	2001	2002	2003
<i>E coli</i>									
Ciprofloxacin	97.1	96.8	97.0	95.1	93.0	88.8	88.7	88.0	82.9
Levofloxacin	N/A	N/A	93.9	92.4	93.9	89.3	88.7	87.6	83.2
<i>K pneumoniae</i>									
Ciprofloxacin	95.8	95.5	94.9	92.5	94.4	95.1	94.3	93.9	91.6
Levofloxacin	N/A	N/A	95.1	92.9	94.2	95.0	94.1	93.3	92.6
<i>P mirabilis</i>									
Ciprofloxacin	80.9	90.7	88.9	88.4	78.2	66.3	68.9	61.6	59.8
Levofloxacin	N/A	N/A	87.4	91.1	85.2	74.2	75.2	68.0	62.6
<i>S aureus</i>									
Ciprofloxacin	66.4	65.2	62.8	56.2	54.4	49.8	62.8	57.8	65.1
Levofloxacin	N/A	N/A	62.8	60.0	58.7	56.6	58.4	58.7	N/A

N/A = not available

CONCLUSION

- Nationally and regionally, nosocomial pathogens, particularly *P mirabilis*, have become increasingly resistant to the fluoroquinolones
- S aureus* isolates showed similar resistance trends to fluoroquinolones and nafcillin/oxacillin, with data suggesting that as sensitivity to ciprofloxacin has decreased, MRSA has increased
- Using data available at www.armprogram.com, institutions can benchmark against national and regional resistance trends, allowing appropriate intervention

REFERENCES

- Bad Bugs, No Drugs. Alexandria, VA: Infectious Diseases Society of America; July 2004.

ACKNOWLEDGMENTS

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www.armprogram.com
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