

Trends in Antimicrobial Resistance Documented at www.armprogram.com

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UPDATED ABSTRACT

PURPOSE: This study documents institution participation in the Antimicrobial Resistance Management Program (ARMP), begun in 1997 to compare antibiotic use and resistance rates, and demonstrates how the data collected from these institutions, available on www.armprogram.com, can be used to create custom reports on susceptibility of specific organisms to antibiotics over time.

METHODS: Institutions are enrolled in ARMP at no cost. Each provides a minimum of 3 years of antibiogram/sensitivity report data which, in a HIPAA-compliant non-identifying format, comprise a national aggregate database.

RESULTS: As of March 25, 2005, ARMP has enrolled 356 institutions, 282 (79%) nonteaching and 74 (21%) teaching, and collected 28.1 million isolates detailing 48 antibiotics and 19 organisms, including on *Escherichia coli* (11,424,793 isolates), *Staphylococcus aureus* (4,852,625), *Pseudomonas aeruginosa* (2,687,251) *Klebsiella pneumoniae* (2,717,761), and *Proteus mirabilis* (1,741,301). Institutions receive an analysis of antimicrobial susceptibility trends on an organism-by-organism basis, benchmarked against national, regional, and state comparators. At the ARMP Web site, the database was interrogated to determine whether an association existed between fluoroquinolone resistance and ESBL production. Nationally, between 1997 and 2003, *E. coli* isolates became less susceptible to fluoroquinolones with the introduction of each new agent: susceptibility to ciprofloxacin declined from 98.1% to 86.5%; ofloxacin, 97.6% to 84.4%; levofloxacin, 96.5% to 87.2%; gatifloxacin from 90% (2000) to 88.8%; moxifloxacin was 79.9% for 2003.

Susceptibility to extended-spectrum cephalosporin antibiotics also decreased slightly: cefotaxime, 99.2% to 98.9%; ceftriaxone, 99.6% to 97.9%; and cefepime, 100% to 98.9%. Similar results were noted for *K pneumoniae* and *P mirabilis*.

CONCLUSIONS: ARMP allows institutions to document trends in antimicrobial susceptibility before they become significant, allowing selection/modification of antibacterial agents. The Web-based aggregate database enables users to create custom reports demonstrating, as in the example above, low level ESBL activity is occurring, indicating fluoroquinolone resistance should be monitored.

BACKGROUND

- ARMP is an ongoing study to
 - Document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates
 - Identify relationships between antibiotic use and resistance rates

METHODS

DATA COLLECTION

- Qualifying hospitals/systems participate in ARMP at no cost
- Each provides ≥ 3 years of antibiogram or sensitivity report data
- The data, in a HIPAA-compliant non-identifying format, become part of the ARMP national aggregate surveillance resistance database
- Individual antibiotics and organisms collected include 48 antibiotics and 19 organisms (Table 1)

Table 1. Organism/Drug Matrix

	<i>Acinetobacter</i> species	Cocci, negative staphylococci	Enterobacter aerogenes	Enterobacter cloacae	Enterobacter faecalis	Enterobacter faecium	Enterobacter species	<i>Escherichia coli</i>	Haemophilus influenzae	<i>Klebsiella pneumoniae</i>	MSSA	MRSE	<i>Proteus mirabilis</i>	<i>Pseudomonas aeruginosa</i>	<i>Serratia marcescens</i>	<i>Staphylococcus aureus</i>	<i>Staphylococcus epidermidis</i>	<i>Streptococcus pneumoniae</i>	VRE	
amikacin																				
amoxicillin																				
amoxicillin/clavulanate																				
ampicillin																				
ampicillin/sulbactam																				
azithromycin																				
aztreonam																				
cefalor																				
cefazolin																				
cefepime																				
cefixime																				
cefoperazone																				
cefotaxime																				
cefotetan																				
cefotixin																				
cefprozime																				
ceftazidime																				
ceftriaxone																				
cefuroxime																				
cephalothin																				
chloramphenicol																				
ciprofloxacin																				
clarithromycin																				
clindamycin																				
dalfopristin/quinuipristin																				
doxycycline																				
erythromycin																				
gatifloxacin																				
gemifloxacin																				
gentamicin																				
imipenem																				
levofloxacin																				
meropenem																				
moxifloxacin																				
naicillin/oxacillin																				
nitrofurantoin																				
ofloxacin																				
penicillin																				
piperacillin/tazobactam																				
piperacillin																				
rifampin																				
tetracycline																				
ticarcillin																				
ticarcillin/clavulanate																				
tmp/smx																				
tobramycin																				
trovafloxacin																				
vancomycin																				

- Hospitals/systems receive a customized Antibiogram Report and Analysis detailing antimicrobial susceptibility trends benchmarked

- against national, regional, and state comparators
- Table 2 is a representative de-identified sample report

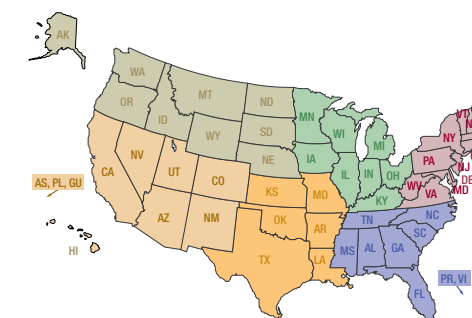
Table 2. Abridged Institutional Report

Hospital X			
Anytown, USA			
Antibiogram Report and Analysis			
Notes: includes outpatient isolates; includes urinary isolates			
I. Escherichia coli			
Antibiotic	Year-2001	Year-2002	Year-2003
ampicillin	n=569 68%	n=1111 68%	n=1109 63%
ampicillin/sulbactam	n=252 71%	n=327 69%	n=186 56%
cefazolin	n=569 96%	n=1109 95%	n=1109 94%
cefuroxime	n=321 95%	n=771 94%	n=882 93%
cefotaxime	n=253 100%	n=328 99%	n=186 98%
ceftriaxone	n=568 100%	n=1111 99%	n=1111 98%
ceftazidime	n=254 99%	n=332 98%	n=201 96%
ciprofloxacin	n=569 95%	n=1101 93%	n=1112 89%
levofloxacin	n=567 96%	n=1110 93%	n=1109 89%
imipenem	n=255 100%	n=334 100%	n=238 100%
piperacillin	n=251 71%	n=327 72%	n=186 60%
pip/taz		n=5 80%	n=36 92%
Sections II. - XII. omitted due to space limitations			
XIII. Streptococcus pneumoniae			
Antibiotic	Year-2001	Year-2002	Year-2003
cefuroxime	n=18 83%	n=60 70%	n=55 76%
cefotaxime	n=18 94%	n=60 90%	n=58 97%
ceftriaxone	n=18 94%	n=60 92%	n=58 95%
clindamycin	n=18 89%	n=60 83%	
erythromycin	n=18 78%	n=60 67%	n=58 78%
levofloxacin	n=17 100%	n=46 100%	n=58 98%
penicillin	n=18 72%	n=61 57%	n=59 68%
vancomycin	n=18 100%	n=61 98%	n=59 100%
The clinical laboratory is congratulated for spending the time and effort to record this offline community-based organism. The penicillin resistant <i>Streptococcus pneumoniae</i> (PRSP) rate within the isolates tested at Hospital X has ranged from 28% in 2001 to 43% in 2002. The current rate of 32% PRSP among 59 isolates is consistent with national and regional averages of 30%-40% PRSP.			
Consistent with the PRSP rate over the last three years, the macrolide resistance rate has also fluctuated. For 2001 and 2002, a comparison of erythromycin to clindamycin susceptibilities is possible. Making this comparison allows the institution to draw inference regarding the mechanism of resistance. For 2001, out of a total 22% macrolide resistance it is assumed that half (11%) is mediated through efflux mechanisms while the remaining 11% is methylation induced. For 2002, among the 33% total macrolide resistance, 17% is assumed to be methylation-induced, with the remaining 16% efflux mediated. This approximate 1:1 ratio between methylation and efflux mediated resistance among <i>Streptococcus pneumoniae</i> isolates in Hospital X is different than national averages which suggests that approximately 60%-70% of pneumococcal resistance is efflux mediated.			
The institution is congratulated for incorporating an anti-pneumococcal fluoroquinolone to its reporting structure. Recent information from the PROTEKT US database shows <i>Streptococcus pneumoniae</i> increasing in resistance to the fluoroquinolones. Recent evidence from <i>Antimicrobial Agents and Chemotherapy</i> 2004 also suggests that this resistance may be class-mediated. Continued surveillance around this resistance is recommended.			
The laboratory is congratulated for reporting both cefotaxime and ceftriaxone. Data from the ARM Program as well as the peer-reviewed literature (<i>Antimicrobial Agents and Chemotherapy</i> 2003) has previously suggested that these two third-generation cephalosporins are not interchangeable even though they share the same resistant breakpoint. While susceptibility differences within Hospital X between these two third-generation cephalosporins are minimal, differences have been noted in other hospitals throughout the country. Continued surveillance around both third-generation cephalosporins is recommended.			
Fluoroquinolone activity continues to leak. The 11% resistance to ciprofloxacin and levofloxacin is consistent with national averages, as well as peer-reviewed literature indicating that gram-negative bacilli resistance to the fluoroquinolones is increasing. The similarities in susceptibility patterns between the two fluoroquinolones indicate a class-mediated effect within Hospital X.			

RESULTS

- As of March 25, 2005 ARMP has enrolled 356 institutions
 - 282 (79%) nonteaching
 - 74 (21%) teaching
- For the purposes of comparison, institutions are grouped in 6 geographic regions (Figure 2)

Figure 2. Geographic Distribution of Institutions



- The number of institutions from each region are:
 - North Central: 52 (15%)
 - South Central: 58 (16%)
 - Northeast: 106 (30%)
 - Southeast: 104 (29%)
 - Northwest: 8 (2%)
 - Southwest: 28 (8%)
- 28.1 million isolates are represented in the ARMP resistance database
- The most significant organisms are summarized in Table 3

Table 3. Significant Organisms in the ARMP Aggregate Resistance Database

Organism	Isolates (n)
<i>Escherichia coli</i>	11,424,793
<i>Staphylococcus aureus</i>	4,852,625
<i>Pseudomonas aeruginosa</i>	2,687,251
<i>Klebsiella pneumoniae</i>	2,717,761
<i>Proteus mirabilis</i>	1,741,301

- www.armprogram.com, the ARMP Web site, allows comparative analysis between antibiotics used and resistance rates
- National and regional trends are available as figures and in tabular format for 1997-2003 for all organism/antibiotic combinations collected in the database
- Custom Reports can be created with up to 7 national, regional, and/or state comparators specified by collective or individual years
- For example, Table 4 summarizes a Custom Report run for 1997-2003 to determine whether there was an association between fluoroquinolone resistance and ESBL production, using comparative cephalosporin susceptibilities across generations as surrogate markers
- Nationally, no significant ESBL activity was detected; however, *E. coli*, *K pneumoniae*, and *P mirabilis* isolates were less susceptible to each new fluoroquinolone as it was introduced

CONCLUSION

- Through benchmarking at a variety of levels, ARMP can work with institutions/systems to delineate occurrence and extent of antimicrobial resistance before they become significant
 - Allows for strategic intervention
 - Provides data for local, regional, national benchmarks
 - Has potential to reduce costs of antibiotics associated with inappropriate use
- At www.armprogram.com, customized reports can be created utilizing

Table 4. Sample Custom Report: National Susceptibility of *E. coli*, *K pneumoniae*, and *P mirabilis* to First through Fourth-Generation Cephalosporins and Fluoroquinolones, by Year, 1997-2003

Organism/Antibiotic	1997	1998	1999	2000	2001	2002	2003
E. coli							
Cefazolin	n=88423 92.8%	n=106105 91.9%	n=106050 91.0%	n=121608 90.4%	n=142882 90.0%	n=110471 90.4%	n=64566 90.2%
Cefuroxime	n=50222 95.6%	n=57202 94.2%	n=63013 95.2%	n=76383 94.9%	n=92105 94.4%	n=64373 92.6%	n=37807 91.9%
Cefotaxime	n=23337 99.2%	n=26238 99.3%	n=18739 98.6%	n=14101 99.3%	n=22186 99.2%	n=14172 98.3%	n=10994 98.9%
Ceftriaxone	n=77460 99.6%	n=92557 99.6%	n=90987 99.4%	n=95887 99.0%	n=110087 98.6%	n=93081 98.1%	n=53737 97.9%
Cefepime	n=48 100%	n=11304 99.3%	n=19273 98.7%	n=39605 99.5%	n=51125 99.1%	n=54062 98.9%	n=39603 98.9%
Ciprofloxacin	n=75810 98.1%	n=88236 97.7%	n=91647 95.7%	n=102831 93.4%	n=116029 93.1%	n=92973 90.4%	n=49093 86.5%
Levofloxacin	n=5534 96.5%	n=36914 95.8%	n=				