344

Ongoing National Surveillance of Antimicrobial Resistance: www.armprogram.com

John G. Gums, PharmD, University of Florida, Gainesville, FL

John G. Gums, PharmD
625 SW Fourth Avenue
University of Florida, Gainesville, FL 32601 USA
Tel: +1.352-392-4541 Fax: +1.352-392-7766
E-mail: gums@chfm.ufl.edu

UPDATED ABSTRACT

PURPOSE: The emergence of antimicrobial resistance has intensified the need to select the most appropriate antibacterial therapy. The Antimicrobial Resistance Management (ARM) Program, an ongoing project of the University of Florida, was established in 1997 with two principal goals: (1) to document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates; and (2) to identify relationships between specific antibiotic use and rates of resistance.

METHODS: Qualifying hospitals or systems may participate in the ARM Program at no cost. At enrollment, each hospital or system provides a minimum of 3 years of antibiogram or sensitivity report data. These data are used to create a confidential customized analysis of antimicrobial susceptibility trends on an organism-by-organism basis, benchmarked against national, regional, and state comparators. Where possible, the analysis attempts to identify the etiology of the problem and whether it occurred at one point in time or developed over time. Potential solutions that should lead to improved patient care and reduced health care costs are suggested; eg, determine degree of community-acquired vs nosocomial resistance. The data, in a HIPAA-compliant non-identifying format, become part of a national aggregate resistance database.

RESULTS: The ARM Program has enrolled 353 institutions as of November 16, 2004, 281 (80%) nonteaching and 72 (20%) teaching. For comparative purposes, the institutions are grouped regionally: Northeast, North Central, Northwest, Southeast, South Central, and Southwest. The database includes 27.7 million isolates with details on 48 commonly used antibiotics and 19 organisms; the most significant are Escherichia coli *(11,277,077 isolates),* Staphylococcus aureus *(4,777,965),* Pseudomonas aeruginosa *(2,663,502), and* Proteus mirabilis *(1,718,441). At the ARM Program Web site, www.armprogram.com, users can access the database to view trending data nationally and regionally for each of the above organisms and four others (*Enterococcus faecalis, Enterococcus faecium, Streptococcus pneumoniae, *and* Haemophilus influenzae*). For example, for* E coli, *4 figures with antibiotics grouped by class and a table show trends for 1997-2003. Users can also create custom aggregate reports; eg, compare state to regional and national data by individual years or a range of years.*

CONCLUSION: Hospitals or systems enrolled in the ARM Program are provided with a predictive analysis whereby they can identify resistance rates for specific organisms before they become significant, allowing pharmacists to select or modify appropriate antibacterial agents. In addition, by providing an interface with the national aggregate database, pharmacists can benchmark institutional susceptibility patterns against regional and national trending data.

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

	Acinetobacter species	Coagulase negative staphylococci	Enterobacter aerogenes	Enterobacter cloacae	Enterococcus faecalis	Enterococcus faecium	Enterococcus species	Escherichia coli	Haemophilus influenzae	Klebsiella pneumoniae	MRSA	MSSE	Proteus mirabilis	Pseudomonas aeruginosa	Serratia marcescens	Staphylococcus aureus	Staphylococcus epidermidis	Streptococcus pneumoniae	VRE
amikacin		•	•	•	•	•	•	•		•	•	•	•	•	•	•	•	•	
amoxicillin		•						•	•	•			•			•	•	•	
amoxicillin/clavulanate		•						•	•	•			•			•	•	•	
ampicillin		•			•	•	•	•	•	•			•			•	•	•	
ampicillin/sulbactam		•	•	•				•	•	•			•			•	•	•	
azithromycin		•						•	•	•			•			•	•	•	
aztreonam	•		•	•				•	•	•			•	•	•				
cefaclor		•						•	•	•			•			•	•	•	
cefazolin		•	•	•				•	•	•			•			•	•	•	
cefepime		•	•	•				•	•	•			•	•	•	•	•	•	
cefoxime		•	•	•				•	•	•			•			•	•	•	
cefoperazone		•	•	•				•	•	•			•	•	•	•	•	•	
cefotaxime	•	•						•	•	•			•			•	•	•	
cefotetan								•		•			•						
cefoxitin								•		•			•						
cefpodoxime		•						•	•	•			•			•	•	•	
ceftazidime		•	•	•				•	•	•			•	•	•	•	•	•	
ceftriaxone	•	•	•	•				•	•	•			•			•	•	•	
cefuroxime		•						•	•	•			•			•	•	•	
cephalothin		•	•	•				•	•	•			•			•	•	•	
chloramphenicol					•	•	•		•	•	•	•						•	
ciprofloxacin		•	•	•				•	•	•	•	•	•	•	•	•	•	•	
clarithromycin		•						•	•	•			•			•	•	•	
clindamycin		•						•	•	•			•			•	•	•	
dalfopristin/quinupristin			•	•	•	•	•	•		•	•	•	•	•	•				•
doxycycline	•	•			•	•	•	•		•	•	•	•						•
erythromycin		•						•	•	•			•			•	•	•	
gatifloxacin		•						•	•	•	•	•	•	•	•	•	•	•	
gemifloxacin		•						•	•	•	•	•	•	•	•	•	•	•	
gentamicin		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
imipenem		•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	•	
levofloxacin		•			•			•	•	•	•	•	•	•	•	•	•	•	•
meropenem		•	•	•	•	•	•		•				•	•	•	•	•	•	
moxifloxacin		•						•	•	•	•	•	•	•	•	•	•	•	•
nafcillin/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

Antiobiogram 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%

Ampicillin susceptibilities have fluctuated between 63% and 68%. The current level of 37% resistance among 1,109 isolates is consistent with national and regional averages of 30%-40% resistance. Susceptibilities to ampicillin/sulbactam have mirrored those of ampicillin. This suggests that the majority of *E coli* pathogens are hyperproducing beta-lactamase. Through hyperproduction, resistant *E coli* pathogens create exponentially large concentrations of the enzyme. This renders suicidal agents such as sulbactam ineffective, resulting in combination therapy being no more active than single-agent therapy. The institution and the laboratory are encouraged to continue to follow the relationship between ampicillin and ampicillin/sulbactam as a surrogate marker for hyperproduction of beta-lactamase.

The presence of extended-spectrum beta-lactamase (ESBL) activity is evaluated via surrogate markers of comparative cephalosporin susceptibilities across generations. Third-generation cephalosporins continue to exhibit enhanced activity over first or second-generation cephalosporins. This provides surrogate evidence to Hospital X that no significant ESBL activity is present within the institution.

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.

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 *Streptococcus pneumoniae* (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 *Streptococcus pneumoniae* isolates in Hospital X is different than national averages which suggests that approximately 60%-70% of pneumococcal resistance is efflux mediated.

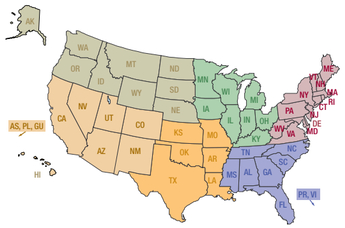
The institution is congratulated for incorporating an anti-pneumococcal fluoroquinolone to its reporting structure. Recent information from the PROTEKT US database shows *Streptococcus pneumoniae* increasing in resistance to the fluoroquinolones. Recent evidence from *Antimicrobial Agents and Chemotherapy* 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 (*Antimicrobial Agents and Chemotherapy* 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.

RESULTS

- As of November 16, 2004, the ARM Program has enrolled 353 institutions
  - 281 (80%) nonteaching
  - 72 (20%) teaching
- For the purposes of comparison, institutions are grouped in 6 geographic regions (Figure 1)

Figure 1. Geographic Distribution of Institutions



- The number of institutions from each region are:
  - North Central: 52 (15%)
  - Northeast: 104 (29%)
  - Northwest: 8 (2%)
  - South Central: 57 (16%)
  - Southeast: 104 (29%)
  - Southwest: 28 (8%)
- 27.7 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)
Escherichia coli	11,277,077
Staphylococcus aureus	4,777,965
Pseudomonas aeruginosa	2,663,502
Klebsiella pneumoniae	2,676,684
Proteus mirabilis	1,718,441

*as of November 16, 2004

- 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
- In addition, a Custom Report can be created with up to 7 national, regional, and/or state comparators specified by individual years or a collective number of years
- For example, Figure 2 summarizes a Custom Report run for 1997-2002 that compared *S aureus* susceptibility to a number of commonly used antibiotics nationally vs the states of Florida and Georgia

Figure 2A-D. Sample Custom Report of S aureus Isolate Susceptibility (%), 1997-2002, by Antibiotic

Figure 2A. Erythromycin, 1997-2002 (n=383,948)

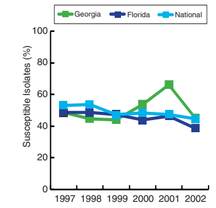


Figure 2B. Clindamycin, 1997-2002 (n=311,433)

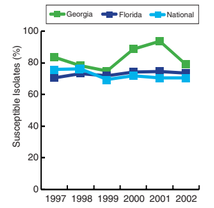
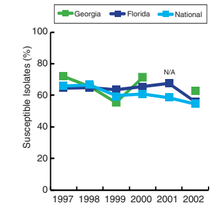
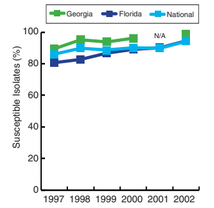


Figure 2C. Nafcillin/Oxacillin, 1997-2002 (n=448,961)



N/A=Data not available

Figure 2D. Gentamicin, 1997-2002 (n=242,808)



N/A=Data not available

CONCLUSION

- Through benchmarking at a variety of levels, the ARM Program can work with institutions/systems to delineate occurrence and extent of antimicrobial resistance before they become significant
  - Allows 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 the aggregate database that compare national to regional and state data

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www.armprogram.com
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