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www.armprogram.com – Online US Surveillance of Antimicrobial Resistance

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UPDATED ABSTRACT

BACKGROUND: The Antimicrobial Resistance Management Program (ARMP), an ongoing University of Florida project, documents trends in antimicrobial susceptibility patterns in inpatient/outpatient isolates and identifies relationships between antibiotic use and resistance rates.

METHODS: Qualifying hospitals or systems may participate in ARMP at no cost. Each hospital enrolled provides a minimum of 3 years of antibiogram or sensitivity report data. Individual antibiotics and organisms are captured in the surveillance database. Participants receive a customized analysis of antimicrobial susceptibility trends within their hospital/system. The trends are benchmarked against national, regional, and state comparators. The data, in a HIPAA-compliant non-identifying format, become part of a national aggregate database.

RESULTS: As of October 24, 2004, ARMP has enrolled 352 institutions, 281 (80%) nonteaching, 71 (20%) teaching. Institutions are grouped in 6 geographic regions: Northeast, North Central, Northwest and Southeast, South Central, and Southwest. The database includes 27.5 million isolates representing 48 antibiotics and 19 organisms, with the most significant being Escherichia coli (11,224,978 isolates)*,* Staphylococcus aureus (4,716,828)*,* Pseudomonas aeruginosa (2,644,496)*,* Klebsiella pneumoniae (2,654,265)*, and* Proteus mirabilis (1,703,868)*. The ARMP Web site (www.armprogram.com) hosts the national aggregate database to provide national and regional trend data and serves as an interface for users to create custom aggregate reports comparing, for example, national susceptibility data to regional and state data by individual years or a collective number of years.*

CONCLUSION: *ARMP, through its benchmarking capabilities, provides participating institutions/systems a predictive feature to identify resistance issues before they become significant. The national aggregate database allows users to compare susceptibility patterns for antibiotics and infectious disease organisms, allowing appropriate selection or modification of antibacterial therapy.*

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	MRSE	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		●	●	●				●	●	●			●	●	●	●	●		
cefixime		●	●	●				●	●	●			●	●	●	●	●	●	
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

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%

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.

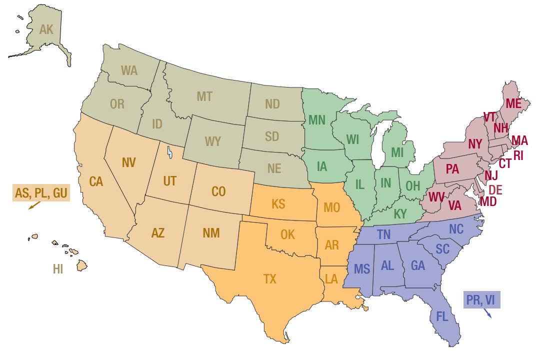
The institution is congratulated for incorporating an anti-pneumococcal fluoroquinolone to its reporting structure. Recent information from the PROTEKT US database on *Streptococcus pneumoniae* shows the fluoroquinolones increasing in resistance. Recent evidence from *Antimicrobial Agents and Chemotherapy* 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 October 24, 2004, the ARM Program has enrolled 352 institutions
  - 281 (80%) nonteaching
  - 71 (20%) 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%)
  - Northeast: 103 (29%)
  - Northwest: 8 (2%)
  - South Central: 57 (16%)
  - Southeast: 104 (30%)
  - Southwest: 28 (8%)
- 27.5 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	11,224,978
Staphylococcus aureus	4,716,828
Pseudomonas aeruginosa	2,644,496
Klebsiella pneumoniae	2,654,265
Proteus mirabilis	1,703,868

*as of October 24, 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, Table 4 summarizes a Custom Report run for 1997-2004 that compared *S pneumoniae* susceptibility to a number of commonly used antibiotics nationally vs the states of Virginia, Maryland, and Florida

Table 4. Sample Custom Report of* S pneumoniae *Susceptibility, 1997-2004*

Drug Name	National	Virginia	Maryland	Florida
penicillin	*n=49710* 62.4%	*n=1478* 65.6%	*n=1268* 69.5%	*n=7943* 54.3%
vancomycin	*n=31240* 99.9%	*n=1313* 99.8%	*n=1149* 99.8%	*n=6160* 100%
cefotaxime	*n=16179* 79.8%	*n=1068* 86.4%	*n=473* 91.3%	*n=3129* 78%
ceftriaxone	*n=34120* 85.8%	*n=1028* 88.2%	*n=824* 89.4%	*n=5137* 83.6%
clindamycin	*n=13434* 89%	*n=925* 87.9%	*n=78* 94.9%	*n=1791* 83.8%
erythromycin	*n=29222* 67.4%	*n=1417* 62.7%	*n=775* 73.9%	*n=4846* 60.5%
levofloxacin	*n=18318* 97.6%	*n=548* 99.3%	*n=832* 93.6%	*n=3003* 98.2%
gatifloxacin	*n=2239* 98.9%	*n=106* 100%	*n=148* 98.6%	*n=198* 100%
tetracycline	*n=2910* 80.7%	*n=328* 81.1%	*n=33* 93.9%	*n=174* 82.8%

*Data included only if available for all 4 comparators

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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