ORIGINAL STUDIES

Antimicrobial resistance in 11 hospitals in Puerto Rico: results of an antimicrobial resistance management (ARM) program

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Purpose: **The Antimicrobial Resistance Management Program (ARMP) was established in 1997 at the University of Florida as an ongoing project to document trends in antimicrobial susceptibility patterns in inpatient/outpatient isolates and track resistance that may occur with specific antibiotic use.**

Methods: **Institutions are enrolled at no charge and provide a minimum of 3 years of antibiogram/ sensitivity report data, which are reviewed to create a customized analysis of antimicrobial susceptibility trends benchmarked against national/regional comparators. The data, in a HIPAA-compliant non-identifying format, comprise a national aggregate database of 28.4 million isolates from 358 institutions. This database was interrogated to determine resistance rates for eleven hospitals in Puerto Rico from 1998-2003 and, as comparators, those in the database from the State of Florida and all U.S. institutions.**

Results: **Between 1996-2003, data on 328,837 isolates collected from 11 hospitals throughout Puerto Rico, 5,388,897 isolates from 46 institutions in Florida, and 24,951,098 isolates from 358 U.S. institutions for the following organisms (number of antibiotics tested against) were reviewed for susceptibility: coagulase-negative staphylococci (14)/*Staphylococcus epidermidis* (18), *Enterococcus faecalis* (7), *Enterococcus faecium* (5), Enterococcus species (4), *Escherichia coli* (24), *Klebsiella pneumoniae* (24), *Proteus mirabilis* (22), *Pseudomonas aeruginosa* (14), *Serratia marcescens* (22), *Staphylococcus aureus* (23), and *Streptococcus pneumoniae* (9). Antimicrobial resistance in Puerto Rico varied organism to organism from that observed in Florida and nationally.**

Conclusions: **This first broad analysis of antimicrobial resistance in Puerto Rico provides important baseline data, both for sentinel surveillance programs and for determining strategies for intervention.**

Key words: Antibiotics, Drug resistance, Microbial, Surveillance, Sentinel.

Growing concern about microbial drug resistance and patient safety has led to the promotion of good antimicrobial stewardship (1). The Antimicrobial Resistance Management Program (ARM Program) was established in 1997 at the University of Florida as an ongoing project to document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates.

This broad analysis represents the first summary of antimicrobial resistance among hospitals in Puerto Rico from 1996-2003.

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Methods

Institutions are enrolled in the ARM Program at no charge. Each institution provides a minimum of 3 years of antimicrobial susceptibility data in a HIPAA-compliant non-identifying format. These data are reviewed to create a customized analysis of antimicrobial susceptibility trends within an institution, benchmarked against national/ regional comparators.

To date, the ARM Program has enrolled 358 institutions. The national aggregate database includes 28.3 million isolates, categorized by 48 antibiotics and 19 organisms. By interrogating this national aggregate database, susceptibility patterns for antibiotics and infectious disease organisms can be detected, allowing modification of use of antibacterial therapy as needed.

The database was interrogated to determine resistance rates for hospitals in Puerto Rico from 1996-2003, which were then compared with rates for the State of Florida as well as the United States.

Results

Between 1996-2003, data on 328,837 isolates were collected from 11 hospitals throughout Puerto Rico. For comparative purposes, aggregate data on 5,388,897 isolates from 46 institutions in the State of Florida and 24,951,098 isolates from 358 U.S. institutions nationally were also reviewed.

The following organisms were reviewed for susceptibility to commonly prescribed antibiotics: *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus mirabilis*, *Serratia marcescens*, *Staphylococcus aureus*, Coagulase-negative staphy-lococci/*Staphylococcus epidermidis*, Entero-coccus species, and *Streptococcus pneumoniae*.

Escherichia coli

Ampicillin susceptibility among 80,227 isolate comparisons is 52.4%, or approximately 48% resistance (Table 1). This level of resistance is slightly higher than that documented in Florida (42% resistance) or throughout the US nationally (38% resistance). There is a strong correlation between susceptibilities to ampicillin and susceptibilities to ampicillin/sulbactam within Puerto Rico. This provides surrogate evidence that the majority of ampicillin resistant *E coli* isolates in Puerto Rico are hyperproducing beta lactamase. Through hyperproduction, *E coli* can create exponentially large concentrations of the enzyme that render suicidal agents such as sulbactam ineffective. This phenomenon is also in place in Florida as well as the rest of the nation.

Table 1. *Escherichia coli*

	Susceptibility (%)		
Antibiotic	***Puerto Rico (n=80,227)***	***Florida (n=1,921,284)***	***National (n=10,581,097)***
ampicillin	52.4	58.5	62.4
ampicillin/sulbactam	54.1	62.1	66.8
cefazolin	86.5	89.5	91.1
cephalothin	86.7	48.9	73.2
cefuroxime	91.3	92.3	94.4
cefotetan	99.9	98.8	99.3
cefoxitin	94.4	97.6	96.8
cefotaxime	95.7	98.7	99.1
ceftriaxone	94.5	98.5	99.0
ceftazidime	95.4	91.5	97.3
cefepime	94.4	98.9	99.1
ciprofloxacin	83.1	91.0	94.3
ofloxacin	74.4	95.4	96.7
levofloxacin	81.9	89.6	92.8
gatifloxacin	62.6	81.8	88.6
TMP/SMX	72.7	76.0	83.4
gentamicin	90.2	94.8	96.3
tobramycin	93.6	96.2	97.3
amikacin	99.7	99.1	99.6
imipenem	99.8	99.5	99.9
piperacillin	59.1	64.6	68.3
pip/taz	93.6	96.2	96.0
ticarcillin	59.5	68.6	66.9
ticarcillin/clavulanate	81.2	86.0	87.8

The presence of extended-spectrum beta lactamase (ESBL) activity within Puerto Rico was evaluated by comparing cephalosporin susceptibilities across generations. Third-generation and fourth-generation cephalosporins routinely demonstrate higher susceptibilities to second or first-generation cephalosporins. This provides surrogate evidence to Puerto Rico that no significant ESBL activity is present among *E coli* pathogens. This finding is consistent with data from Florida as well as the rest of the United States.

Fluoroquinolone resistance is present within Puerto Rico to *E coli* pathogens. Ciprofloxacin at 17% resistance; ofloxacin at 26% resistance; levofloxacin at 18% resistance; and gatifloxacin at 37% resistance are all higher than that demonstrated in Florida or the rest of the United States. The close similarities in resistance patterns among the fluoroquinolones suggest that fluoroquinolone resistance to *E coli* within Puerto Rico is class-mediated. Attempts to resolve this issue clinically through adjustments from one fluoroquinolone to another would not be expected to have long-term success.

Suppressed activity is documented to both piperacillin and ticarcillin compared to the combination agents piperacillin/tazobactam and ticarcillin/clavulanate, respectively. This provides surrogate evidence that the majority of resistance mediated by *E coli* to either piperacillin or ticarcillin is mediated via beta lactamase production. As hyperproduction of beta lactamase increases, the potential for other suicidal agents such as tazobactam and clavulanate to be affected increases.

Other broad-spectrum agents, including the aminoglycosides and imipenem, exhibit good-to-excellent activity against *E coli* isolates within Puerto Rico.

Klebsiella pneumoniae

The presence of extended-spectrum cephalosporinase activity was evaluated within Puerto Rico using surrogate markers of cephalosporin susceptibilities across generations (Table 2). Third-generation and fourth-generation cephalosporins routinely exhibit enhanced susceptibility percentages compared to first-generation or second-generation cephalosporins. This provides surrogate evidence that no significant extended-spectrum cephalosporinase activity is present within the island. The significance of longitudinal evaluation around this phenomenon is based on increasing extended-spectrum cephalosporinase activity documented against this gram-

Table 2. *Klebsiella pneumoniae*

Antibiotic	*Susceptibility (%)*		
	Puerto Rico (n=38,028)	*Florida (n=565,758)*	*National (n=2,468,468)*
ampicillin	1.7	2.4	2.5
ampicillin/sulbactam	68.9	76.6	79.1
cefazolin	76.6	89.1	91.0
cephalothin	83.8	87.5	87.0
cefuroxime	83.4	87.7	90.4
cefotetan	98.8	97.4	98.0
cefoxitin	88.7	96.5	93.0
cefotaxime	95.9	97.6	97.4
ceftriaxone	90.3	96.0	97.0
ceftazidime	93.1	88.3	93.2
cefepime	94.1	96.9	96.3
ciprofloxacin	90.6	94.2	94.8
ofloxacin	91.2	92.6	94.3
levofloxacin	90.0	94.1	93.7
gatifloxacin	80.0	91.7	92.7
TMP/SMX	69.7	94.0	92.6
gentamicin	88.2	93.8	95.4
tobramycin	89.6	94.1	95.5
amikacin	100	98.9	98.5
imipenem	97.8	99.6	99.6
piperacillin	68.6	74.0	76.7
pip/taz	85.5	91.9	92.7
ticarcillin	2.9	5.7	5.7
ticarcillin/clavulanate	74.5	87.6	90.9

negative respiratory pathogen. National incidences of extended spectrum cephalosporinase activity from *K pneumoniae* range from 10% to 15%.

Fluoroquinolone activity is marginally suppressed for ciprofloxacin, ofloxacin, and levofloxacin, with resistance rates ranging from 9% to 10% among 38,028 isolate comparisons. This represents a marginal increase in resistance compared to resistance rates to the same fluoroquinolones documented in both Florida and the United States. The close similarity in the percent resistance among the documented fluoroquinolones provides surrogate evidence that this resistance phenomenon is class-mediated. The gatifloxacin resistance at 20% is considered an outlier, since it represents fewer total *K pneumoniae* isolate comparisons and therefore has larger standards of deviation associated with the percent susceptibility.

There is significant suppression of activity against tobramycin and gentamicin compared to amikacin. This phenomenon is not consistent with what has been previously documented in Florida or the United States as a whole. In addition, susceptibility to piperacillin as well as piperacillin/tazobactam is suppressed in Puerto Rico compared to Florida and the United States nationally. It is highly recommended that sentinel surveillance systems be established within Puerto Rico for the purpose of longitudinal evaluation of this phenomenon and to determine if different regions of Puerto Rico exhibit different levels of resistance.

Pseudomonas aeruginosa

Predictably, gentamicin susceptibilities in Puerto Rico are suppressed compared to those of tobramycin or amikacin (Table 3). This is expected since it is assumed that, throughout the island, gentamicin is the preferred-use aminoglycoside. This preferential use status associated with gentamicin increases the likelihood of selective use pressure against gentamicin. Selective use pressure will be maintained as long as gentamicin is the preferentially used aminoglycoside. This selective use pressure against gentamicin is consistent with previous reports from both Florida and the United States as a whole. Institutions throughout Puerto Rico must continue to monitor selective use pressure against gentamicin in an effort to determine when or if it would be reasonable to consider therapeutic substitution.

The 31% resistance within Puerto Rico among 60,047 isolate comparisons to ceftazidime is significantly higher

Table 3. *Pseudomonas aeruginosa*

Antibiotic	*Susceptibility (%)*		
	Puerto Rico (n=60,047)	*Florida (n=683,632)*	*National (n=2,395,327)*
ceftazidime	69.6	81.4	84.1
cefepime	59.5	75.3	74.5
ciprofloxacin	60.3	67.6	67.6
ofloxacin	21.4	59.9	59.8
levofloxacin	59.0	65.4	63.1
gatifloxacin	53.3	31.5	48.0
gentamicin	64.2	71.6	73.9
tobramycin	77.6	89.6	89.4
amikacin	84.5	91.2	91.8
imipenem	67.2	83.5	82.7
piperacillin	68.7	87.3	87.2
pip/taz	74.2	89.0	88.9
ticarcillin	69.0	84.7	81.5
ticarcillin/clavulanate	64.1	77.1	77.6

than resistance patterns documented in both Florida and the United States nationally. In addition, the 40% to 41% resistance to cefepime within Puerto Rico is also higher than that seen in both Florida and the rest of the United States. Cefepime resistance patterns within the island remain higher than those seen to ceftazidime, which is consistent with reports from the ARM database from the rest of the United States. The fact that the fourth-generation agent cefepime exhibits higher levels of resistance than the third-generation agent ceftazidime suggests that *P aeruginosa* resistance to the anti-pseudomonal

cephalosporins is horizontal in nature. This implies that established resistance to either ceftazidime or cefepime would not be effectively dealt with by simply switching to the alternative anti-pseudomonal cephalosporin.

The 40% resistance to ciprofloxacin is slightly higher than the 32% resistance seen in Florida or the rest of the United States. However, a 40% resistance documented among 60,047 isolate comparisons within Puerto Rico is consistent with the peer-reviewed literature suggesting increasing prevalence of ciprofloxacin resistance from this gram-negative nosocomial pathogen. Similarities in resistance patterns between ciprofloxacin, levofloxacin, and gatifloxacin suggest a class-mediated resistance that would not be addressed therapeutically by switching from one fluoroquinolone to another.

Imipenem resistance is currently documented at approximately 33% within Puerto Rico. This represents a significant increase in the level of resistance to this carbapenem compared to that documented in either Florida (16.5%) or the United States as a whole (17.3%). Recent recognition of a plasmid-encoded enzyme, imipenemase, is thought to have increased the pressures for imipenem resistance from *P aeruginosa*. Individual institutions throughout Puerto Rico are encouraged to employ longitudinal surveillance around imipenem resistance and to look for possible reasons for decreasing empiric utilization of imipenem as a mechanism to decrease further pressures for imipenem resistance.

As expected, no significant increase in susceptibility to *P aeruginosa* is seen between piperacillin/tazobactam and piperacillin. This is expected, since it is assumed that piperacillin is the ingredient in piperacillin/tazobactam that contributes the bulk of anti-pseudomonal activity. It is also expected because production of beta lactamase is not a common mechanism used by *P aeruginosa*. Resistance patterns to both piperacillin and piperacillin/tazobactam within Puerto Rico are significantly higher than those seen in either Florida or the rest of the United States. Similar relationships between Puerto Rico and the rest of the United States are present with ticarcillin and ticarcillin/clavulanate, respectively. Increased empiric utilization of piperacillin/tazobactam will increase pressures for piperacillin resistance from Pseudomonas aeruginosa. While increased utilization of piperacillin/tazobactam and/or ticarcillin/clavulanate can not fully explain this resistance pattern within Puerto Rico, it is assumed that it is a major contributor to the problem. Institutions throughout Puerto Rico are encouraged to look for opportunities to increase the appropriate use of these combination broad-spectrum agents.

Proteus mirabilis

As a general observation, *P mirabilis* resistance to a wide spectrum of antibiotics within Puerto Rico is significantly less than that seen in either Florida or the US as a whole (Table 4). While ampicillin/sulbactam susceptibilities are consistent between Puerto Rico and the rest of the United States, ampicillin susceptibilities remain higher than that which is documented in Florida alone. In addition, fluoroquinolone susceptibilities including that of ciprofloxacin, ofloxacin, and levofloxacin are elevated compared to previously documented susceptibilities from *P mirabilis* within Florida or the rest of the United States.

There does not appear to be a significant resistance problem within Puerto Rico to *P mirabilis*; however, continued longitudinal surveillance is recommended among institutions on the island, since *P mirabilis* resistance can be class-mediated among certain classes of antibiotics and appears to be generally increasing within the United States.

Table 4. *Proteus mirabilis*

	Susceptibility (%)		
Antibiotic	***Puerto Rico (n=13,530)***	***Florida (n=417,510)***	***National (n=1,589,906)***
ampicillin	84.7	78.6	83.5
ampicillin/sulbactam	90.8	90.3	91.9
cefazolin	90.9	89.5	91.3
cephalothin	94.4	51.1	85.6
cefuroxime	88.9	95.7	97.1
cefotetan	98.1	99.2	98.8
cefoxitin	88.9	98.9	98.0
cefotaxime	99.0	98.7	99.2
ceftriaxone	96.5	99.2	99.3
ceftazidime	98.2	93.5	97.8
cefepime	92.5	98.9	97.9
ciprofloxacin	94.2	72.9	80.3
ofloxacin	100	88.1	86.7
levofloxacin	95.4	75.6	80.5
gentamicin	94.1	90.1	92.1
tobramycin	95.3	92.7	94.1
amikacin	100	98.8	99.3
imipenem	98.2	95.7	97.3
piperacillin	88.5	90.1	90.1
pip/taz	95.1	97.3	97.0
ticarcillin	85.5	86.4	87.9
ticarcillin/clavulanate	94.9	98.8	98.9

Serratia marcescens

While the isolate comparison numbers (8,323) are significantly smaller for this gram-negative nosocomial pathogen compared to other organisms tracked by the ARM Program in Puerto Rico, important resistance patterns can still be identified (Table 5).

There appears to be a suppression of susceptibility

Table 5. *Serratia marcescens*

Antibiotic	*Susceptibility (%)*		
	Puerto Rico (n=8323)	*Florida (n=107,146*	*National (n=409,382)*
ampicillin	5.7	4.7	6.3
ampicillin/sulbactam	6.8	7.5	11.0
cefazolin	6.9	0.3	0.5
cefuroxime	0	0.9	3.2
cefotetan	100	98.8	97.7
cefoxitin	44.4	46.5	50.2
cefotaxime	91.6	91.7	90.0
ceftriaxone	59.2	88.2	91.6
ceftazidime	72.0	81.2	87.3
cefepime	90.8	95.6	95.9
ciprofloxacin	76.1	89.1	89.3
ofloxacin	60.0	86.9	85.1
levofloxacin	81.9	94.2	92.4
gatifloxacin	76.6	86.2	91.0
gentamicin	69.2	90.7	94.1
tobramycin	71.5	85.5	90.1
amikacin	86.1	95.7	97.4
imipenem	81.6	97.6	96.6
piperacillin	68.5	79.7	85.8
pip/taz	87.2	84.6	86.3
ticarcillin	68.3	80.2	80.8
ticarcillin/clavulanate	47.7	83.2	86.6

within Puerto Rico to both ceftriaxone and ceftazidime compared to either Florida or the US as a whole. Before this observation is validated, isolate numbers from *S marcescens* tested against both ceftriaxone and ceftazidime would require evaluation. If isolate numbers tested against these third-generation cephalosporins are significantly suppressed compared to the total isolates recorded, the true value of resistance within the island to these third-generation cephalosporins would remain undetermined.

There also appears to be a suppression of activity from *S marcescens* against the fluoroquinolones including ciprofloxacin, ofloxacin, levofloxacin, and gatifloxacin as compared to either the Florida data or that reported from the US as a whole. This class-based resistance documented to the fluoroquinolones is consistent with patterns of resistance documented to the fluoroquinolones from other gram-negative pathogens within Puerto Rico.

In addition, the aminoglycosides, including amikacin, demonstrate suppressed activity within Puerto Rico compared to the rest of the United States. These differences appear to be most dramatic with gentamicin and tobramycin. Institutions throughout Puerto Rico are encouraged to establish longitudinal surveillance around this phenomenon as a first step in identifying possible triggers for why activity against this gram-negative pathogen is suppressed to the aminoglycosides.

Activity is also suppressed to imipenem within Puerto Rico as compared to the rest of the United States. Institutions throughout the island are encouraged to reevaluate imipenem use and, where possible, to decrease empiric use of imipenem as a mechanism to decrease pressures for continuing resistance to this carbapenem.

Staphylococcus aureus

Under the assumption that the reciprocal to the susceptibility numbers associated with nafcillin/oxacillin is the accepted methicillin-resistant *S aureus* (MRSA) activity, the MRSA level throughout Puerto Rico among 85,014 isolate comparisons is 42.6% of all *S aureus* isolate comparisons (Table 6). This level of MRSA is higher than the level of MRSA reported in Florida at 37.2% or that reported for the US as a whole at 39.7%. This level of MRSA breeds cross-resistance to other classes of antibiotics including the macrolides, the lincosamides, and the fluoroquinolones.

Table 6. *Staphylococcus aureus*

Antibiotic	*Susceptibility (%)*		
	Puerto Rico (n=85,014)	*Florida (n=1,113,813)*	*National (n=4,421,014)*
penicillin	7.4	8.3	8.3
ampicillin	7.4	9.5	9.0
ampicillin/sulbactam	57.7	71.1	64.8
nafcillin/oxacillin	57.4	62.8	60.3
vancomycin	98.9	100	99.9
cefazolin	56.3	65.5	64.0
cephalothin	67.2	99.0	66.8
cefuroxime	44.1	84.3	63.7
cefotetan	40.0	—	40.0
cefoxitin	20.0	—	98.4
cefotaxime	57.0	77.7	65.4
ceftriaxone	50.9	71.6	66.1
cefepime	53.7	60.2	58.8
clindamycin	69.6	72.2	71.2
erythromycin	46.0	44.7	48.4
ciprofloxacin	66.7	58.4	59.2
ofloxacin	60.5	64.6	65.4
levofloxacin	68.8	57.9	55.5
gatifloxacin	61.5	48.1	57.6
TMP/SMX	100	97.3	95.2
gentamicin	84.2	88.6	90.5
tobramycin	100	—	69.4
imipenem	55.3	61.8	61.7

The 54% resistance documented to erythromycin is consistent with the current level of MRSA throughout Puerto Rico. Contrasting erythromycin, a macrolide, to clindamycin, a lincosamide, allows inferences to be drawn regarding the mechanism of *S aureus* resistance to the macrolides. It is assumed that a *S aureus* isolate

resistant to erythromycin but sensitive to clindamycin is resistant via efflux pump mechanisms (mef). However, an isolate resistant to both the macrolide and the lincosamide is assumed to be resistant via methylation induced mechanisms (erm). Using aggregate data among 85,014 *S aureus* isolate comparisons, the calculated total macrolide resistance is 54% with an efflux level of 23.6% and a methylation induced level of 30.4%. Longitudinal evaluation of each of these parameters remains important to institutions throughout Puerto Rico because it allows them to track not only total frequency of macrolide resistance but also severity, methylation induced resistance being considered uniformly more severe than efflux mediated resistance.

As expected, fluoroquinolone resistance is present. Resistance patterns to ciprofloxacin, levofloxacin, and gatifloxacin are slightly lower than those documented previously in either Florida or the US as a whole. However, the approximate 33% resistance to ciprofloxacin and 31% resistance to levofloxacin suggest that these agents are not reasonable empiric selections for patients presenting with skin or skin structure infections. Additionally, recent peer-reviewed literature has implicated fluoroquinolones in an institutional environment as a possible trigger for increasing MRSA activity. Institutions throughout Puerto Rico are encouraged to evaluate their fluoroquinolone usage patterns in an attempt to determine if there is any correlation between increasing level of fluoroquinolone use and rising MRSA rates. The similarity in resistance patterns among the fluoroquinolones throughout the island of Puerto Rico also suggests that this resistance phenomenon is class-mediated among all agents. This is consistent with the peer-reviewed literature, which has suggested that fluoroquinolone resistance from *S aureus* may be mediated through single-gene mutation.

Imipenem resistance patterns are elevated compared to those documented in either Florida or the US as a whole. The nearly 45% resistance to imipenem from *S aureus* is consistent with the elevated MRSA level. Unfortunately, this decreases the clinical utility of this broad-spectrum carbapenem as an empiric choice in patients suspected of being infected with *S aureus*.

The current vancomycin resistance throughout the island of Puerto Rico is recorded at 1.1%. While not significantly different than resistance patterns recorded from either Florida (0%) or the nation (0.1%), it actually represents a significant number of pathogens that are no longer responding to vancomycin. Of the 85,014 total *S aureus* isolate comparisons, approximately 935 were considered vancomycin resistant. Institutions across Puerto Rico are encouraged to implement sentinel and longitudinal surveillance around this phenomenon, especially if total cultured isolates of *S aureus* are also increasing. It is also recommended that institutions within Puerto Rico establish more sensitive screening parameters for vancomycin resistance from this opportunistic gram-positive pathogen; ie, performing minimum inhibitory concentration (MIC) testing against randomly selected MRSA isolates on a quarterly basis. The mean and median MIC against vancomycin can then be compared by quarter to determine the magnitude of MIC leakage to vancomycin. This more specific strategy will allow institutions to better develop interventional strategies to curb the eventual emergence of both vancomycin intermediate *S aureus* (VISA) and vancomycin resistant *S aureus* (VRSA).

Coagulase-negative staphylococci

Staphylococcus epidermidis

Coagulase-negative staphylococci are among the most commonly isolated bacteria in clinical microbiology laboratories (Table 7A) and, without question, *Staphylococcus epidermidis* is one of the leading nosocomial pathogens in United States hospitals. However, because of its high propensity to be present in contaminant cultures, it is difficult to assess truly the resistance patterns from this organism (Table 7B). If desired, the institution is advised to perform a random analysis of selected isolates with evaluation of their correlation to true infectious disease processes. Once identified, extrapolation to the total isolate pool will provide the institution with a more accurate indicator of true resistance patterns.

Table 7A. Coagulase negative *staphylococci*

Antibiotic	*Susceptibility (%)*		
	Puerto Rico (n=4179)	*Florida (n=81,092)*	*National (n=997,513)*
ampicillin	13.8	13.9	12.3
nafcillin/oxacillin	2.7	37.4	33.47
vancomycin	100.0	99.2	99.8
cefazolin	3.0	37.2	37.3
cefotetan	25.0	—	59.5
ceftriaxone	14.7	50.0	31.6
cefepime	15.4	—	25.8
clindamycin	25.0	68.5	66.7
ciprofloxacin	43.1	54.5	50.1
ofloxacin	25.0	61.4	55.6
levofloxacin	53.0	51.6	45.8
gatifloxacin	73.3	65.3	68.7
gentamicin	55.6	72.9	72.1
imipenem	3.1	26.2	33.5

Enterococcus

Data on isolates throughout Puerto Rico was available

Table 7B. *Staphylococcus epidermidis*

Antibiotic	Susceptibility (%)		
	Puerto Rico (n=21,178)	Florida (n=214,884)	National (n=786,511)
penicillin	6.9	6.3	6.0
ampicillin	5.3	5.9	8.0
ampicillin/sulbactam	27.1	26.7	30.6
nafcillin/oxacillin	24.2	27.1	27.4
vancomycin	98.1	100	99.6
cefazolin	23.8	27.2	31.1
cephalothin	21.7	—	24.3
cefuroxime	10.0	46.7	29.2
cefotaxime	0	36.5	25.9
ceftriaxone	10.0	19.0	38.6
cefepime	22.2	—	32.2
clindamycin	54.7	61.7	61.8
erythromycin	26.3	25.6	28.2
ciprofloxacin	56.0	41.0	41.0
ofloxacin	61.2	46.8	44.1
levofloxacin	55.1	35.1	36.6
gentamicin	62.4	59.9	66.5
imipenem	19.6	26.0	24.3

for both *Enterococcus faecalis* (Table 8) and *Enterococcus faecium* (Table 9). While the isolate comparison numbers (1,199) for *E faecium* were less than the isolate comparison numbers (15,507) for *E faecalis*, it remains important for institutions within Puerto Rico to track both *E faecium* and *E faecalis*. Historically, less than 5% of the total enterococcal isolate pool was represented by *E faecium*. More recently, however, as much as 20% of the total enterococcal isolate pool can now be represented by the more virulent form of the species. If institutions track *E faecalis* and *E faecium* separately, they allow themselves the ability to track not only total frequency of enterococcal resistance but also severity.

Table 8. *Enterococcus faecalis*

Antibiotic	Susceptibility (%)		
	Puerto Rico (n=15,507)	Florida (n=192,984)	National (n=645,574)
penicillin	97.5	97.4	96.1
ampicillin	97.4	98.1	98.0
vancomycin	92.3	97.8	97.4
erythromycin	11.1	—	11.8
ciprofloxacin	58.3	48.5	49.2
levofloxacin	60.5	54.4	52.3
imipenem	82.0	86.3	84.5

Table 9. *Enterococcus faecium*

Antibiotic	Susceptibility (%)		
	Puerto Rico (n=1199)	Florida (n=22,152)	National (n=78,756)
penicillin	35.2	17.9	16.3
ampicillin	41.4	22.0	18.9
vancomycin	76.8	49.3	44.0
ciprofloxacin	15.3	12.1	10.9
levofloxacin	24.3	16.0	14.6

The level of vancomycin-resistant Enterococci (VRE) appears to be significantly less in Puerto Rico compared to either Florida or the United States nationally (Table 10). The aggregate VRE for Puerto Rico among 1,199 isolate comparisons of *E faecium* is 23.2%. This is significantly less than the VRE rate in Florida at 50.7% or the United States as a whole at 56% VRE. Caution should be advised in interpreting the VRE percentages for Puerto Rico, since the isolate comparison numbers used to determine the Puerto Rico VRE percentage are significantly less than the isolate comparison numbers used for either Florida or the United States. Continued surveillance around this phenomenon is highly recommended to each institution throughout Puerto Rico.

Table 10. Enterococcus species

Antibiotic	Susceptibility (%)		
	Puerto Rico (n=141)	Florida (n=20,086)	National (n=315,758)
ampicillin	63.2	94.9	89.3
vancomycin	55.3	97.3	93.2
ciprofloxacin	44.7	51.9	53.1
levofloxacin	33.3	36.3	55.2

Streptococcus pneumoniae

The penicillin-resistant *S pneumoniae* (PRSP) rate within Puerto Rico among 1,310 isolate comparisons of *S pneumoniae* is 50.6% (Table 11). This is slightly higher than PRSP rate reported for Florida at 45.2% or the United States nationally at 36.8%. Sentinel surveillance

Table 11. *Streptococcus pneumoniae*

Antibiotic	Susceptibility (%)		
	Puerto Rico (n=1310)	Florida (n=34,160)	National (n=211,597)
penicillin	49.4	54.8	63.2
nafcillin/oxacillin	47.0	67.3	56.1
vancomycin	99.6	100	99.9
cefotaxime	71.4	78.2	79.6
ceftriaxone	100	84.3	85.8
clindamycin	95.0	83.8	89.0
erythromycin	64.6	61.4	68.2
levofloxacin	95.5	98.2	97.7
gatifloxacin	99.1	100	98.7

centers will allow Puerto Rico to determine if the PRSP rate varies according to region. Differences in the PRSP rate within a region and even within a state have been documented by the ARM Program for different parts of the United States.

The macrolide resistance patterns within Puerto Rico are similar to those documented in either Florida or the United States as a whole. Interestingly, however, the clindamycin susceptibility numbers are significantly higher in Puerto Rico compared to either Florida or the rest of the United States. This suggests that while the total macrolide resistance pattern from *S pneumoniae* within Puerto Rico is similar to the rest of the United States, the severity of that macrolide resistance is lower. With only 5% resistance to clindamycin, it is assumed that, of the 35.4% total macrolide resistance, 30.4% is mediated via efflux pump mechanisms. This is significantly higher than the efflux percent contribution in either Florida or the rest of the United States, suggesting that the macrolide resistance within Puerto Rico from *S pneumoniae* is more manageable, with assumed lower MICs.

The 4.5% resistance to levofloxacin is slightly higher than that previously reported in either Florida or the United States as a whole. It remains important for each region throughout the island to track *S pneumoniae* susceptibilities to the fluoroquinolones longitudinally. Recent evidence from a variety of surveillance networks have documented increasing fluoroquinolone resistance; specifically, increasing *S pneumoniae* isolates that contain at least one-step mutation (parC) to the fluoroquinolones. Although a double mutation (parC and jarA) is required for total pneumococcal resistance to the fluoroquinolones, acquisition of the second mutation is much more likely in an isolate that already contains the first-step mutation. It is therefore assumed that resistance rates from *S pneumoniae* to the fluoroquinolones are poised to increase rapidly. Longitudinal sentinel surveillance systems will allow Puerto Rico to identify as early as possible any changes in the susceptibility patterns from *S pneumoniae* to the fluoroquinolones.

There is a significant difference in the percent susceptibility reported from *S pneumoniae* to cefotaxime versus ceftriaxone. This difference is present in Florida as well as the US as a whole; however, the difference between these two third-generation cephalosporins is more pronounced in Puerto Rico. Previous peer-reviewed literature examining this discrepancy concludes that this difference is not a function of laboratory methodology and uniformly represents at least one or greater than one dilutional difference between both drugs. While the exact molecular mechanisms that might better explain this difference in susceptibility have not been determined, the clinical utility of this information remains viable. Institutions throughout Puerto Rico should assume that substitution of ceftriaxone with cefotaxime is not appropriate. In addition, if microbiology laboratories are using ceftriaxone to determine susceptibilities but the hospital is administering cefotaxime to the patient, clinical outcomes may be different than those predicted by the microbiology laboratory.

Discussion

This is the first broad analysis of antimicrobial resistance conducted from isolates collected from a regional representation of institutions in Puerto Rico. These aggregate baseline data are important for sentinel surveillance programs and for determining strategies for intervention. Previously, surveillance studies conducted in Puerto Rico have focused on broad-spectrum beta-lactam antimicrobial agents, (2) gram-positive cocci, (3) and invasive *S pneumoniae* (4).

It is salutary that institutions throughout Puerto Rico are spending the time and effort to record *S pneumoniae*, considered an offline, community-based respiratory pathogen. It is recommended that sentinel surveillance systems be established throughout the island to allow longitudinal tracking and trending of this common respiratory pathogen. This remains important, since resistance patterns from this gram-positive isolate are increasing to a variety of antibiotics and because it allows institutional laboratories to determine the magnitude of resistance originating within the community versus that resistance which originates within the hospital. Rivera-Matos and Rios-Olivares (4) found a high prevalence of drug-resistant strains of *S pneumoniae* among 38 hospitals island-wide in Puerto Rico, with diabetes, cardiovascular disease, smoking, and bronchial asthma the most common risk factors for invasive pneumococcal disease in adults.

Certain risk factors for patients with Coagulase-negative staphylococcal bacteremia and how they may be differentiated from patients without true infectious disease processes have been identified. Tacconelli et al (5) found the presence of a central venous catheter was an independent risk factor for Coagulase-negative staphylococcal bacteremia. Additionally, patients with bacteremia were more frequently admitted from long-term care facilities; more likely to have had previous *S aureus* infections or colonizations; and more likely to have received antibiotics in the previous 30 days.

Local, provider-level interventions and development of policies to promote careful antibiotic use are recommended, as are ongoing assessment of prescribing

tends and rates of antimicrobial drug resistance (6). Interpretation of antibiogram or sensitivity report data is complicated by the potential for a variety of sources and caveats around individual data reports. We advise that institutions and regions throughout Puerto Rico establish a standardized reporting mechanism in an effort to define resistance trends and compare for any regional differences throughout the island. Ideally, urinary source isolates should be excluded from any report and outpatient isolates should be separated from those that originate within the hospital. Structure for the reporting system as well as consistency throughout the system will allow healthcare providers in Puerto Rico to identify and subsequently manage escalating resistance problems.

Resumen

Objetivo: El programa de manejo de resistencia antimicrobiana fue establecido en 1997 en la Universidad de Florida como parte de un proyecto que documenta las tendencias de los distintos patrones de susceptibilidad antimicrobiana en muestras de pacientes hospitalizados y no hospitalizados, así como también el seguimiento de resistencia que pueda ocurrir con el uso de un antibiótico específico. ***Metodos:*** Las instituciones se inscriben sin costo alguno y proveen por un mínimo de tres años un reporte sobre antibiograma y sensitividad. Este reporte es revisado para crear un análisis personalizado de las tendencias de susceptibilidad antimicrobiana y son comparadas a nivel nacional y regional. La información obtenida es mantenida en anonimato y cumple con los requisitos de HIPPA. La misma esta compuesta por una base de datos nacional de 28.4 millones de muestras de 358 instituciones distintas. Esta base de datos es utilizada para determinar el grado de resistencia que existe en los hospitales de Puerto Rico desde 1998 al 2003 y es comparada con la base de datos obtenida de los distintos hospitales del estado de Florida y de todas las instituciones de Estados Unidos. ***Resultados:*** Entre 1996 y 2003 la información sobre 328.837 muestras colectada de 11 hospitales de Puerto Rico, 5.388.897 muestras de 46 instituciones en Florida y 24.951.098 muestras de 358 instituciones de Estados Unidos fue utilizada para determinar la susceptibilidad de los diferentes organismos (contra distintos tipos de antibióticos): Staphylococcus coagulasa negative (14), Staphylococcus Epidermidis (18), Enterococcus faecalis (7), Enterococcus faecium (5), Enterococcus species (4), Escherichia coli (24), Klebsiella pneumoniae (24), Proteus mirabilis (22), Pseudomona aeruginosa (14), Serratia marcescens (22), Staphylococcus aureus (23) y Streptococcus pneumoniae (9). La resistencia antimicrobiana en Puerto Rico varió de un organismo a otro según lo observado en Florida y a nivel nacional. ***Conclusión:*** Este primer amplio análisis de resistencia antimicrobiana en once hospitales en Puerto Rico prevee importante información de base, no sólo para programas de vigilancia sino también para determinar estrategias para futura intervención.

Acknowledgements

The authors would like to thank the participating institutions in the ARM Program for making data collection possible.

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