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Trends in Gram-Negative Isolate Resistance to Imipenem: Results of the Antimicrobial Resistance Management (ARM) Program, 1999-2005

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ABSTRACT

BACKGROUND: Resistance to carbapenems, specifically imipenem, is increasing due to use of a broad-spectrum agent in cases where more directed therapy is warranted. The ARM Program, an ongoing project of the University of Florida, is an antibiogram-based surveillance system that can benchmark local antibiotic use and resistance rates.

METHODS: Institutions (n=364) participating in ARM provide a minimum of 3 years of antibiogram/sensitivity report data in a HIPAA-compliant nonidentifying format, which comprise a national aggregate database (www.armprogram.com) containing 29.6 million drug/isolate comparisons. The database was interrogated to determine national/regional resistance patterns for Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, *and* Serratia marcescens *to imipenem from 1999-2005.*

RESULTS: For E coli *(n=417,087 isolates), national susceptibility to imipenem remained consistent from 1999 (99.4%) to 2005 (99.9%). North Central, Northeast, and South Central regions demonstrated 100% susceptibility in 2005. Nationally,* K pneumoniae *(n=114,755) susceptibility remained high, 99.5% in 1999 and 98.7% in 2005; it declined in Northeast from 99.3% (1999) to 98% (2005).* P mirabilis *(n=99,677) susceptibility decreased nationally, from 97.5% (1999) to 93.5% (2005), likely due to a decline in Northeast from 96.7% (1999) to 91% (2005). Nationally,* P aeruginosa *(n=185,614) susceptibility decreased from 82.8% (1999) to 77.2% (2003), when susceptibility was 65.3% in Southwest, then increased to 84.2% in 2005. Similar trends were observed across regions.* S marcescens *(n=20,419) susceptibility increased nationally from 96.8% (1999) to 99.5% (2005); this trend was observed in all regions except the Southwest, where it declined from 94.9% (1999) to 86.3% (2002) before increasing to 96.6% (2003).*

CONCLUSION: These data suggest resistance to imipenem is increasing annually among P mirabilis *isolates, specifically in the Northeast, as well as among* P aeruginosa *isolates, particularly in the Southwest.*

BACKGROUND

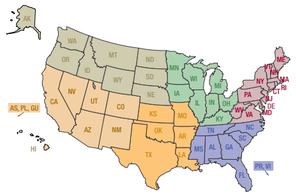
- The Centers for Disease Control and Prevention (CDC) has identified reversing antimicrobial resistance as one of its top 8 priority health goals for the 21st century
- The Antimicrobial Resistance Management (ARM) Program was established at the University of Florida in 1997 to document trends in antimicrobial susceptibility patterns in inpatient/outpatient isolates using an antibiogram-based surveillance system
- Use of a broad-spectrum agent is increasing resistance to carbapenems; specifically, imipenem
- By benchmarking local antibiotic use and resistance rates, the ARM Program can help hospitals fulfill CDC recommendations to target the pathogen, leading to more effective use of antimicrobial agents

METHODS

GENERAL DATA COLLECTION

- Each hospital is enrolled in the ARM Program at no cost and provides a minimum of 3 years of antibiogram or sensitivity report data in a HIPAA-compliant, nonidentifying format
- All data are entered into a national aggregate database
- Susceptibility data on nearly 30 million drug/isolate comparisons have been captured in the database
  - 48 antibiotics
  - 19 organisms
- A total of 364 US institutions have enrolled to date
  - 77 teaching
  - 287 nonteaching
- For the purposes of comparison, the US hospitals enrolled in the ARM Program are grouped into 6 geographic regions
- The number of hospitals enrolled in each region are as follows:
  - Northeast: 111 (30%)
  - Southeast: 106 (29%)
  - North Central: 53 (15%)
  - South Central: 58 (16%)
  - Northwest: 8 (2%)
  - Southwest: 28 (8%)

Figure 1. Institutions in the ARM Program Comprise 6 Geographic Regions



SPECIFIC DATA ANALYSES

- The aggregate database, available at www.armprogram.com, was interrogated to determine national and regional imipenem resistance patterns from 1999-2005 for the following gram-negative organisms:
  - *Escherichia coli*
  - *Klebsiella pneumoniae*
  - *Proteus mirabilis*
  - *Pseudomonas aeruginosa*
  - *Serratia marcescens*

RESULTS

E COLI

- For *E coli*, national susceptibility to imipenem remained consistent from 1999 (99.4%) to 2005 (99.9%) (Table 1)
- North Central, Northeast, and South Central regions demonstrated 100% susceptibility in 2005
- In the Southeast, susceptibility decreased slightly from 2003-2005

Table 1. National and Regional E coli *Isolate (n=417,087) Susceptibility to Imipenem by Year, 1999-2005*

% susceptible isolates	1999-2005 n=417,087	1999 n=80,554	2000 n=88,372	2001 n=97,311	2002 n=78,858	2003 n=45,797	2004 n=16,507	2005 n=9688
National	99.7	99.4	99.7	99.6	99.8	99.9	99.7	99.9
Northeast	99.7	99.5	99.3	99.9	99.9	99.8	99.7	100
Southeast	99.6	99.2	99.7	99.7	99.9	99.9	99.6	99.4
North Central	99.3	99.7	99.7	98.3	100	100	100	100
South Central	99.9	99.8	99.9	100	99.7	100	100	100
Northwest	99.8	100	100	99.8	99.6	—	—	—
Southwest	99.8	99.8	99.6	99.9	99.9	100	—	—

K PNEUMONIAE

- Nationally, *K pneumoniae* susceptibility remained high, ranging from 99.5% in 1999 to 98.7% in 2005 (Table 2)
- Susceptibility declined in Northeast from 99.3% (1999) to 98% (2005), and from 100% in 1999 to 99.6% in 2003 in the Southwest

Table 2. National and Regional K pneumoniae *Isolate (n=114,755) Susceptibility to Imipenem by Year, 1999-2005*

% susceptible isolates	1999-2005 n=114,755	1999 n=23,724	2000 n=24,754	2001 n=25,138	2002 n=20,724	2003 n=13,491	2004 n=4712	2005 n=2212
National	99.5	99.5	99.5	99.4	99.6	99.7	99.2	98.7
Northeast	99.3	99.3	99.2	99.3	99.5	99.5	99.0	98.0
Southeast	99.6	99.6	99.6	99.5	99.6	99.8	99.3	99.5
North Central	99.5	99.5	99.3	99.3	99.8	100	100	100
South Central	99.6	99.7	100	98.9	100	99.4	99.5	100
Northwest	99.8	99.3	99.7	100	99.7	—	—	—
Southwest	99.6	100	99.1	99.9	99.5	99.6	—	—

P MIRABILIS

- Nationally, *P mirabilis* susceptibility decreased from 97.5% in 1999 to 93.5% in 2005 (Table 3)
- Regionally, the greatest declines were observed in:
- Northeast, from 96.7% in 1999 to 91.0%
- Southeast, from 97.7% in 1999 to 93.5% in 2002 and 96.8% in 2005
- South Central, from 97.9% in 1999 to 93.9% in 2004

Table 3. National and Regional P mirabilis *Isolate (n=99,677) Susceptibility to Imipenem by Year, 1999-2005*

% susceptible isolates	1999-2005 n=99,677	1999 n=15,541	2000 n=43,592	2001 n=15,672	2002 n=12,725	2003 n=8484	2004 n=2504	2005 n=1159
National	98.1	97.5	99.3	98.3	96.1	97.0	97.7	93.5
Northeast	97.4	96.7	97.5	98.4	97.9	97.5	97.0	91.0
Southeast	97.2	97.7	98.8	98.6	93.5	95.9	98.5	96.8
North Central	97.2	96.8	93.3	97.6	99.5	100	100	—
South Central	98.4	97.9	98.9	97.9	99.2	98.5	93.9	100
Northwest	100	100	100	100	99.0	—	—	—
Southwest	96.9	99.2	96.5	96.3	96.1	99.2	—	—

P AERUGINOSA

- Nationally, among all the gram-negative organisms, *P aeruginosa* susceptibility was lowest in 1999 and decreased further, from 82.8% to 77.2% in 2003, before increasing to 83% in 2004 and 84.2% in 2005 (Table 4)
- The lowest observed susceptibility was 65.3% in the Southwest in 2003; the Southeast was also low in 2003, 78.6%
- Similar trends of declining susceptibility between 1999 and 2002 or 2003, then increasing in 2005, were observed among most of the regions

Table 4. National and Regional P aeruginosa *Isolate (n=185,614) Susceptibility to Imipenem by Year, 1999-2005*

% susceptible isolates	1999-2005 n=185,614	1999 n=37,303	2000 n=43,394	2001 n=41,161	2002 n=33,559	2003 n=21,730	2004 n=5745	2005 n=2722
National	81.2	82.8	82.1	82.3	79.1	77.2	83.0	84.2
Northeast	89.2	82.9	82.5	83.0	80.4	81.7	82.9	86.0
Southeast	88.3	81.5	82.1	81.8	80.7	78.6	81.7	80.1
North Central	84.9	85.6	82.9	86.4	81.9	85.7	87.4	90.7
South Central	91.4	87.1	87.7	86.1	84.6	87.7	88.1	93.1
Northwest	86.1	86.3	85.9	85.2	87.5	—	—	—
Southwest	72.8	77.9	75.2	77.6	70.7	65.3	—	—

S MARCESCENS

- *S marcescens* susceptibility increased nationally from 96.8% in 1999 to 99.5% (2005) (Table 5)
- This trend was observed in all regions except the Southwest, where it declined from 94.9% in 1999 to 86.3% in 2002 before increasing to 96.6% in 2003
- Susceptibility also declined in the Northwest between 2001 (98.9%) and 2002 (95%)

Table 5. National and Regional S marcescens *Isolate (n=20,419) Susceptibility to Imipenem by Year, 1999-2005*

% susceptible isolates	1999-2005 n=20,419	1999 n=4587	2000 n=4482	2001 n=4471	2002 n=3305	2003 n=2383	2004 n=798	2005 n=393
National	96.7	96.8	97.2	96.1	96.8	95.8	98.1	99.5
Northeast	97.8	96.4	98.0	98.1	98.8	96.9	99.6	100
Southeast	96.2	96.6	96.5	95.1	97.1	94.8	97.0	98.7
North Central	97.8	97.3	95.0	98.5	98.8	100	98.2	100
South Central	97.9	96.4	98.1	98.3	98.5	96.7	100	100
Northwest	98.8	99.6	100	98.9	95	—	—	—
Southwest	90.5	94.9	97.4	85.8	86.3	96.6	—	—

CONCLUSION

- Resistance to imipenem was observed to increase from 1999-2005 among *P mirabilis* and *P aeruginosa* isolates
  - *P mirabilis* resistance was greatest in the Northeast, and *P aeruginosa* resistance greatest in the Southwest
- Knowledge of individual hospital susceptibility, including benchmarking within a specific region, can help denote areas of resistance, allowing better allocation of resources and use of more directed therapy
- The overall national decline in *K pneumoniae* susceptibility to imipenem between 1999 and 2005, albeit slight, suggests low levels of ESBL activity may be occurring
- The increasing resistance observed with ESBL-producing organisms to antibiotic classes such as the carbapenems emphasizes the need for improved ability to detect ESBLs

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www.armprogram.com
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