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National and Regional Susceptibility Patterns of Staphylococcus aureus and Methicillin-Sensitive and Methicillin-Resistant Staphylococci: Results of the Antimicrobial Resistance Management (ARM) Program

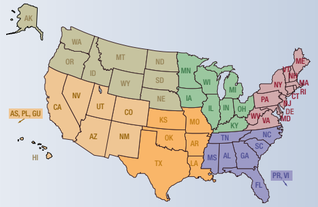
Gums JG. University of Florida, Gainesville, FL, USA

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@fpmg.health.ufl.edu

What is the Antimicrobial Resistance Management (ARM) Program?

Purpose

- The Antimicrobial Resistance Management (ARM) Program is an ongoing study to document trends in antimicrobial susceptibility patterns in inpatient and outpatient isolates and to identify relationships between antibiotic use and resistance rates
- Hospitals can delineate if and when antimicrobial resistance occurs
  - Allows strategic intervention
  - Provides data for local, regional, national benchmarks
  - Has potential to reduce costs of antibiotics associated with inappropriate use
- A total of 112 hospitals have enrolled to date
  - 83 (74%) nonteaching
  - 29 (26%) teaching
- For the purposes of comparison, US hospitals are grouped in 6 geographic regions (see map, below)
- The number of hospitals included from each region is as follows:
  - North Central: 18 (16%)
  - South Central: 9 (8%)
  - Southwest: 5 (5%)
  - Northeast: 25 (22%)
  - Southeast: 55 (49%)



Data Collection

- Each hospital provides a minimum of 3 years of antibiogram or sensitivity report data
- Individual antibiotics and organisms are captured in the database
  - 41 antibiotics
  - 16 organisms
- A Web-based analysis tool allows comparisons between antibiotic use and resistance rates for any number of parameters
  - One year with another year
  - Groups of years to other groups of years
  - Hospital to hospital
  - Hospital to hospital system
  - Hospital to state
  - Within a state
  - Hospital to region
  - Hospital to national
  - State to state
  - State to region
  - State to national
  - Region to national

Abstract

Background: The ongoing ARM program was developed to document susceptibility patterns, including for *S aureus*, methicillin-sensitive *S aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA) in inpatient and outpatient isolates. Since 1987, more than 10 million isolates have been collected on 19 organisms and 46 antibiotics from 105 US hospitals in 5 regions (Northeast, North Central, Southeast, South Central, Southwest).

Methods: Antibiograms and sensitivity reports of *S aureus*, MSSA, and MRSA isolates were reviewed for susceptibility to fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin, trovafloxacin) and other antibiotics (vancomycin, clindamycin, erythromycin, and nafcillin/oxacillin).

Results: Total number of isolates and percentage of isolates susceptible to each antibiotic were determined both nationally and regionally. Nationally, *S aureus* isolates were as susceptible to ciprofloxacin (62.3%, n=194,937) as to levofloxacin (62.2%, n=78925), with a greater sensitivity to ciprofloxacin seen in North Central (60.9% vs 58.7%), Southeast (62.7% vs 62.2%), and Northeast (60.7% vs 52.8%). These data suggest cross-resistance between ciprofloxacin and levofloxacin. Susceptibility to levofloxacin was greater than to ciprofloxacin in South Central (82.9% vs 72.4%) and Southwest (80.4% vs 54.3%). *S aureus* isolate susceptibility to erythromycin nationally was 32.5% (n=272,184), accounted for primarily in Southeast (22.9%); it was higher in all other regions: North Central (53.4%), Northeast (54.3%), South Central (61.1%), Southwest (67.1%). Compared with erythromycin, *S aureus* isolates had a much greater susceptibility to clindamycin (75.9%, n=33180). This difference was seen in every region, with the smallest comparative difference noted in South Central (61.1% vs 70.3%). Susceptibility to nafcillin/oxacillin nationally was 64.9% (n=256,121); this ranged from 63.2% in North Central to 78.0% in South Central. The majority of change in susceptibility to nafcillin/oxacillin and ciprofloxacin nationally over the past decade has occurred in the last 3 years (1998 to 2000), with ciprofloxacin sensitivity declining with increasing levels of MRSA; however, there is a lack of correlation regionally. For example, in Southeast, *S aureus* susceptibility to ciprofloxacin declined 15.8%, while MSSA declined 0.5%. Nationally and regionally, percentages of *S aureus* and MRSA isolates susceptible to vancomycin were similar (*S aureus*, range 99.6% to 99.9%; MRSA, range 99.4% to 100%).

Conclusions: Nationally and regionally, the majority of *S aureus* and MRSA isolates remain sensitive to vancomycin. For *S aureus*, nafcillin/oxacillin, ciprofloxacin, and levofloxacin show similar rates of susceptibility; however, as sensitivity to ciprofloxacin has decreased, MRSA levels have increased nationally.

Background

- The emergence of antimicrobial resistance is a complex problem driven by many interconnected factors; in particular, use and misuse of antimicrobials[1]
- *Staphylococcus aureus* is a major cause of nosocomial and community-acquired infections, from minor skin infections to life-threatening diseases such as bacteremia, wound infections, endocarditis, septic arthritis, and osteomyelitis[2-4]
- In a study conducted in New York City hospitals in the mid-1990s, death rate, length of stay, and medical costs were twice as high for *S aureus*-associated hospitalizations as for others[5]
- Four deaths attributed to community-acquired methicillin-resistant *S aureus* (MRSA) occurred in children without established risk factors for such infection; when isolated, the MRSA strains appeared to be different from typical nosocomial strains in antimicrobial susceptibility patterns[6]
- An increasing percentage of *S aureus* isolates have been found to be resistant to methicillin[7] and are showing relative resistance to vancomycin[8]

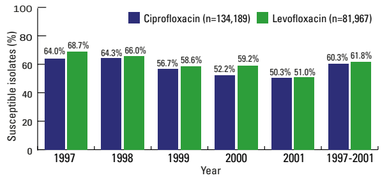
Methods

- Antibiograms and sensitivity reports of *S aureus*, MSSA, and MRSA inpatient and outpatient isolates were reviewed for susceptibility to fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin, trovafloxacin) and other antibiotics (vancomycin, clindamycin, erythromycin, and nafcillin/oxacillin)
- MRSA isolates were identified as being those resistant to nafcillin/oxacillin

Results

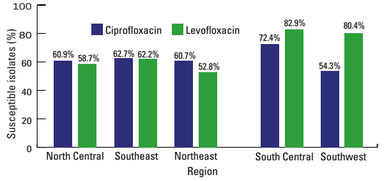
- 112 hospitals have submitted more than 10 million isolates
- Total number of isolates and percentage of isolates susceptible to each antibiotic were determined
- Nationally, *S aureus* isolates decreased in susceptibility to ciprofloxacin and to levofloxacin since its introduction in 1997, suggesting cross-resistance between the two fluoroquinolones (Figure 1)

Figure 1. National S aureus susceptibility to ciprofloxacin and levofloxacin, 1997-2001



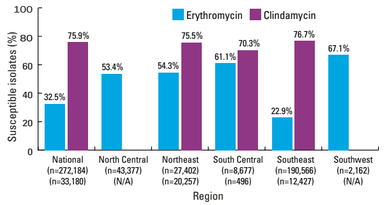
- Regionally, a greater sensitivity to ciprofloxacin was seen in North Central, Southeast, and Northeast (Figure 2)
- However, in the South Central and Southwest regions, susceptibility was greater to levofloxacin than to ciprofloxacin (Figure 2)

Figure 2. S aureus isolates more susceptible to ciprofloxacin, and levofloxacin, by region, 1997-2001



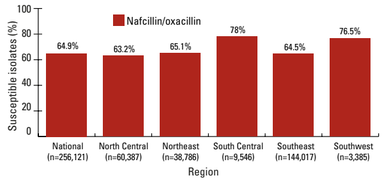
- Nationally, *S aureus* isolate susceptibility to erythromycin was 32.5%
- This was accounted for primarily in Southeast (22.9%), which also represented the greatest percentage of total isolates
- Susceptibility was higher in all other regions (Figure 3)
- Compared with erythromycin, *S aureus* isolates had a much greater susceptibility to clindamycin; the smallest comparative difference was noted in South Central (Figure 3)

Figure 3. S aureus susceptibility to erythromycin and clindamycin, 1987-2001



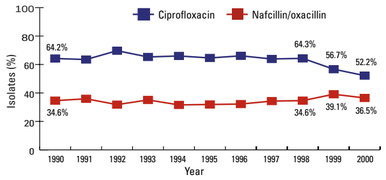
- Susceptibility to nafcillin/oxacillin nationally was 64.9%, with the greatest susceptibility seen in the South Central region (Figure 4)

Figure 4. National and regional S aureus susceptibility to nafcillin/oxacillin, 1987-2001



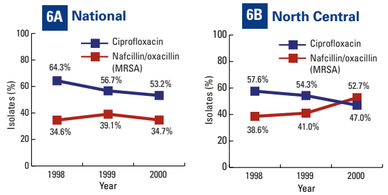
- Nationally, resistance to nafcillin/oxacillin and ciprofloxacin over the past decade has occurred to the greatest extent from 1998 to 2000, with ciprofloxacin sensitivity declining with increasing levels of MRSA (Figure 5)

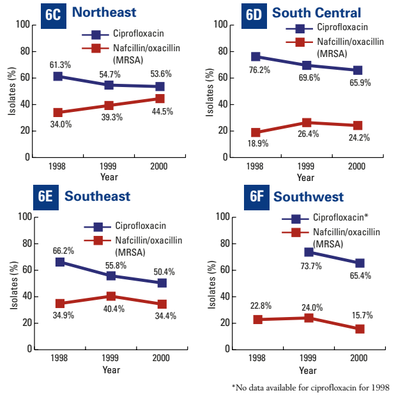
Figure 5. Change in susceptibility to nafcillin/oxacillin and ciprofloxacin, 1990-2000



- *S aureus* isolate susceptibility to ciprofloxacin was most notable in the Southeast, where it declined 15.8% (Figure 6E) from 1998 to 2000; increase in MRSA was greatest (14.1%) in the North Central region (Figure 6B)

Figure 6. MRSA levels have increased as sensitivity to ciprofloxacin has decreased





*No data available for ciprofloxacin for 1998

- Nationally and regionally, percentages of *S aureus* and MRSA isolates susceptible to vancomycin were similar (*S aureus*, range 99.6% to 99.9%; MRSA, range 99.4% to 100%)

Conclusions

- The majority of *S aureus* and MRSA isolates remain sensitive to vancomycin
- For *S aureus*, nafcillin/oxacillin, ciprofloxacin, and levofloxacin show similar rates of susceptibility nationally; however, as sensitivity to ciprofloxacin has decreased, MRSA levels have increased
- These results confirm the importance of judicious use of fluoroquinolones as an interventional strategy to reduce MRSA levels in hospitals and the community

References

1. WHO Global Strategy for Containment of Antimicrobial Resistance. WHO/CDS/CSR/DRS/2001.2a:4.
2. Richards MJ, Edwards JR, Culver DH, Gaynes RP. National Nosocomial Infections Surveillance System. Nosocomial infections in medical intensive care units in the United States. *Crit Care Med*. 1999;27:887-892.
3. Goetz A, Posey K, Fleming, J, et al. Methicillin-resistant *Staphylococcus aureus* in the community: a hospital-based study. *Infect Control Hosp Epidemiol*. 1999;20:689-691.
4. Lowy FD. *Staphylococcus aureus* infections. *N Engl J Med*. 1998;339:520-532.
5. Rubin RJ, Harrington CA, Poon A, Dietrich K, Greene JA, Moiduddin A. The economic impact of *Staphylococcus aureus* infection in New York City hospitals. *Emerg Infect Dis*. 1999;5:9-17.
6. CDC. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*—Minnesota and North Dakota, 1997-1999. *MMWR*. 1999;48:707-710.
7. Archer GL, Climo MW. Staphylococcus bacteremia — consider the source. *N Engl J Med*. 2001;344:55-56.
8. Smith TL, Pearson ML, Wilcox RR, et al. Emergence of vancomycin resistance in *Staphylococcus aureus*. *N Engl J Med*. 1999;340:493-501.

Acknowledgments

The author would like to thank the participating institutions in the R-BUG Database-USA, which make data collection possible, and Roche Laboratories, Inc., which financially supported the study.