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The Changing Face of Empiric Therapy in Skin and Skin Structure Infections: *Staphylococcus aureus.* Results of the Antimicrobial Resistance Management Program

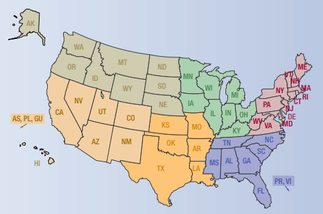
John G. Gums, PharmD, University of Florida, Gainesville, FL

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

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 274 institutions have enrolled as of September 19, 2003
  - 220 (80.3%) nonteaching
  - 54 (19.7%) 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: 50 (18.3%)
  - Northeast: 71 (25.9%)
  - Northwest: 7 (2.5%)
  - South Central: 51 (18.6%)
  - Southeast: 80 (29.2%)
  - Southwest: 15 (5.5%)

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
  - 44 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

Study objectives: *Staphylococcus aureus bacilli frequently are isolated from skin and skin structure specimens. Infection severity determines antimicrobial treatment, with initial empiric therapy guided by reported susceptibility patterns of isolated etiological bacteria. The Centers for Disease Control and Prevention (CDC) recommends targeting definitive therapy to known pathogens to prevent antimicrobial resistance.*

Methods: *The ongoing Antimicrobial Resistance Management (ARM) program was initiated in 1997 with establishment of a surveillance database. To date, 251 US hospital laboratories from 6 regions (Northeast, North Central, Southeast, South Central, Northwest, Southwest) have submitted more than 17 million inpatient and outpatient isolates representing 16 organisms and 44 antibiotics. Data from antibiograms and sensitivity reports of* S aureus*, methicillin-susceptible* S aureus *(MSSA) and methicillin-resistant* S aureus *(MRSA) isolates from 1990-2002 were reviewed using a Web-based analysis tool to determine resistance to commonly prescribed antibiotics, including fluoroquinolone (ciprofloxacin, levofloxacin) and other antibiotics (vancomycin, clindamycin, erythromycin, and nafcillin/oxacillin).*

Results: *Total number of isolates and percentage of isolates resistant to each antibiotic were determined both nationally and regionally. Nationally,* S aureus *isolates were more resistant to levofloxacin (41.4%, n=123,868) than to ciprofloxacin (38.7%, n=256,178), with greater resistance to levofloxacin seen in North Central (47.9% vs 39.4%) and Northeast (52.4% vs 41.9%). These data suggest cross-resistance between ciprofloxacin and levofloxacin. Resistance to ciprofloxacin was greater than to levofloxacin in South Central (34.2% vs 20.0%) and Southwest (32.2% vs 23.0%).* S aureus *isolate susceptibility to erythromycin nationally was 51.1% (n=274,873). Compared with erythromycin,* S aureus *isolates had a much greater susceptibility to clindamycin (73.6%, n=165,683). This difference was seen in every region, with the smallest comparative difference noted in North Central (52.5% vs 54.3%). Susceptibility to nafcillin/oxacillin nationally was 64.9% (n=360,460); this ranged from 62.2% in North Central and Northeast to 72.8% in Southwest. Most of the change in susceptibility to nafcillin/oxacillin and ciprofloxacin over the past decade has occurred in the past 5 years (1998 to 2002), with ciprofloxacin sensitivity declining with increasing levels of MRSA. Percentages of* S aureus *isolates remaining susceptible to vancomycin were similar (range 99.8% to 99.9%).*

Conclusion: *Nationally and regionally, the majority of* S aureus *and MRSA isolates remain sensitive to vancomycin. Nafcillin/oxacillin, ciprofloxacin, and levofloxacin show similar* S aureus *resistance rates, suggesting that even in methicillin-susceptible infections, resistance to fluoroquinolones is increasing. Therefore, fluoroquinolones may not be a reasonable choice for empiric therapy of skin and skin structure infections.*

STUDY OBJECTIVES

- Patients commonly present to the emergency department with skin and soft tissue infections, approximately 10% of which are severe enough to lead to hospital admission to an infectious disease unit
- Skin and soft tissue infections are often caused by *S aureus*
  - Uncomplicated infections include pyodermas impetigo, ecthyma, and folliculitis, furuncles, and carbuncles
  - Complicated infections include cellulitis, erysipelas, and bite wounds from dogs, cats, or humans
  - Diabetic foot infections are polymicrobial (aerobic gram-positive, gram-negative, anaerobic)
- Initial empiric therapy is generally guided by reported susceptibility patterns of isolated etiological bacteria and clinical presentation, rather than results of skin cultures
- This study sought to determine *S aureus* susceptibility to commonly prescribed antibiotics
- ARM program surveillance data are anticipated to complement existing and emerging consensus guidelines for the treatment of a number of disease states, including those for which the fluoroquinolones are most often prescribed

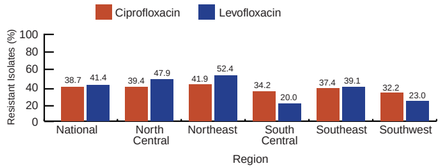
METHODS

- R-BUG Database-USA is one component of the ARM program, established in 1997 to document national and regional antimicrobial susceptibility trends among inpatient and outpatient isolates
- Data from antibiograms and sensitivity reports from 251 hospitals were reviewed to determine *S aureus*, MSSA, and MRSA isolate resistance to ciprofloxacin, levofloxacin, vancomycin, clindamycin, erythromycin, and nafcillin/oxacillin
- National and regional resistance rates were reported as 1990-2002 inclusive for all agents and for each year individually for ciprofloxacin and MRSA

RESULTS

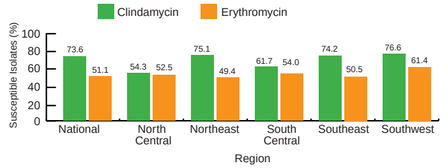
- Nationally, *S aureus* isolates were more resistant to levofloxacin (n=256,178) than to ciprofloxacin (n=123,868) (Figure 1)
- Regionally, isolates were more resistant to levofloxacin than ciprofloxacin in North Central and Northeast, whereas resistance was greater to ciprofloxacin than to levofloxacin in South Central and Southwest; the Southeast most closely reflected the resistance seen nationally (Figure 1)

Figure 1. National and Regional S aureus Resistance to Ciprofloxacin and Levofloxacin, 1990-2002



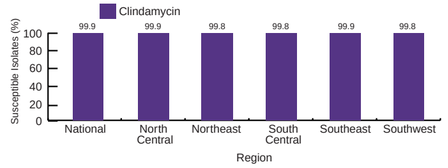
- Nationally, *S aureus* isolates were much more susceptible to clindamycin (n=165,683) than to erythromycin (n=274,873) (Figure 2)
- This difference was observed to a greater extent in the Northeast and Southeast, with the least difference seen in the North Central region (Figure 2)

Figure 2. National and Regional S aureus Susceptibility to Clindamycin and Erythromycin, 1990-2002



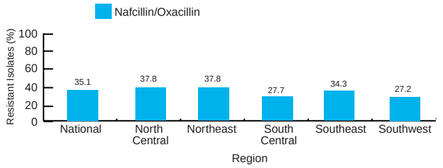
- For 1990-2002 inclusive, susceptibility rates of *S aureus* isolates to vancomycin (n=371,329) were high, both nationally and regionally (Figure 3)
- Similarly, MRSA isolates in the database (n=32,053) were 99.9% susceptible to vancomycin

Figure 3. National and Regional S aureus Susceptibility to Vancomycin, 1990-2002



- *S aureus* isolate resistance to nafcillin/oxacillin nationally was 35.1% (n=360,460); this ranged from 27.2% in the Southwest to 37.8% in North Central and Northeast (Figure 4)

Figure 4. National and Regional S aureus Resistance to Nafcillin/Oxacillin, 1990-2002



- The years 1998 to 2002 have seen the greatest change in susceptibility of *S aureus* isolates to ciprofloxacin and nafcillin/oxacillin, suggesting that sensitivity to ciprofloxacin has declined as levels of MRSA have increased (Figures 5A-5F)

Figures 5A-5F. From 1998 to 2002, MRSA Levels Have Increased as Susceptibility to Ciprofloxacin Has Decreased

Figure 5A. National

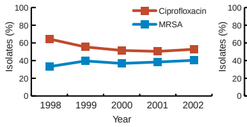


Figure 5B. North Central

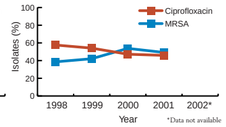


Figure 5C. Northeast

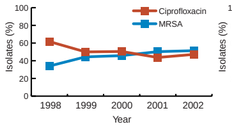


Figure 5D. South Central

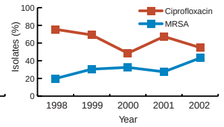


Figure 5E. Southeast

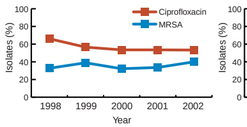
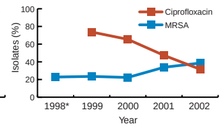


Figure 5F. Southwest



CONCLUSION

- Most *S aureus* and MRSA isolates remain sensitive to vancomycin
- *S aureus* isolates are more resistant to levofloxacin than to ciprofloxacin, suggesting cross-resistance between these two agents
- The fluoroquinolones and nafcillin/oxacillin show similar *S aureus* resistance rates, suggesting that even in methicillin-susceptible infections, resistance to the fluoroquinolones is increasing
- As initial empiric therapy of skin and skin structure infections, many of which have *S aureus* as an etiologic pathogen, the fluoroquinolones as a class may no longer represent a rational choice

Acknowledgment

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