

## National and regional susceptibility of *Streptococcus pneumoniae* and gram-negative isolates to third-generation cephalosporin antibiotics, 1994-2001: results of the Antimicrobial Resistance Management (ARM) Program

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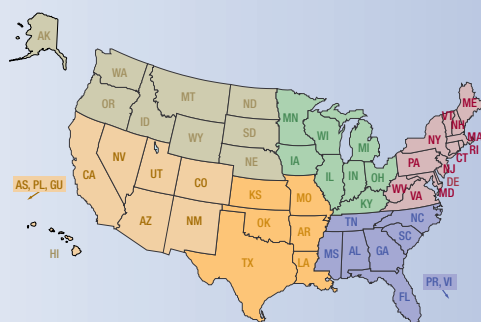


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### What is the Antimicrobial Resistance Management (ARM) Program?

#### 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

**PURPOSE:** This study determined national and regional susceptibility rates of *Streptococcus pneumoniae* and the gram-negative organisms *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis* to third-generation cephalosporin antibiotics.

**METHODS:** The ongoing ARM program has collected more than 18 million isolates from 261 US institutions. Antibiograms and sensitivity reports of pneumococcal isolates for 1994-2001 were reviewed for susceptibility to cefotaxime and ceftriaxone; *E coli*, *K pneumoniae*, and *P mirabilis* were reviewed for susceptibility to cefotaxime, ceftazidime, and ceftriaxone.

**RESULTS:** Nationally, from 1994-2001, *S pneumoniae* isolate susceptibility was 75.6% to cefotaxime (n=9190) and 81.7% to ceftriaxone (n=25,481). Regionally, susceptibility was higher in the Northeast (85.1% cefotaxime; 90.6% ceftriaxone), South Central (80.7% cefotaxime; 86.0% ceftriaxone); and North Central (82.8% cefotaxime, 86.2% ceftriaxone) and lower in the Southeast (71.1% cefotaxime; 79.7% ceftriaxone). Nationally, *E coli* susceptibility was 99.2% to cefotaxime (n=101,176), 97.8% to ceftazidime (n=160,493) and 99.3% to ceftriaxone (n=469,328).

*K pneumoniae* susceptibility was 98.0% to cefotaxime (n=31,304), 93.7% to ceftazidime (n=45,254), and 98.1% to ceftriaxone (n=143,214). *P mirabilis* susceptibility was 99% to cefotaxime (n=17,384), 98.0% to ceftazidime (n=28,180) and 99.4% to ceftriaxone (n=81,795). Regionally, rates were similar for *E coli*, *K pneumoniae*, and *P mirabilis*.

**CONCLUSIONS:** Nationally and regionally, *S pneumoniae* isolates were more susceptible to ceftriaxone than cefotaxime, with sensitivity artificially suppressed, given that all isolates reflect breakpoints prior to January 2002, when NCCLS adopted a MIC  $\geq 4$  mg/L for ceftriaxone and cefotaxime. Overall, gram-negative organisms had a high susceptibility rate to the third-generation cephalosporin antibiotics.

#### Purpose

- Over the past decade, *S pneumoniae* antimicrobial resistance has emerged as a significant problem, with resistance rates among clinical isolates of *S pneumoniae* to commonly administered antimicrobials steadily increasing<sup>1</sup>
- With increased resistance, especially to the penicillins and macrolides, many physicians are now prescribing third-generation cephalosporins as empiric therapy for *S pneumoniae*<sup>2</sup>
- Use of more active third-generation cephalosporins, ceftriaxone and cefotaxime, are unlikely to lead to clinical failure; however, use of poorly active cephalosporins (cefazolin, cefuroxime, and ceftazidime) may result in clinical failures due to inadequate serum levels<sup>3</sup>
- This study sought to determine national and regional susceptibility rates of *S pneumoniae* isolates to cefotaxime and ceftriaxone; recently, clonal PFGE type or subtype and serotype have been associated with different ceftriaxone and cefotaxime MIC interpretations as well as increased resistance to both agents<sup>4</sup>
- Also investigated were susceptibility rates of *E coli*, *K pneumoniae*, and *P mirabilis* isolates to cefotaxime, ceftazidime, and ceftriaxone, given increased empiric use of the fluoroquinolones for gram-negative infections and the subsequent observed rapid development of resistance and cross-resistance within this antibiotic class
- All *S pneumoniae* susceptibility rates reflect breakpoints prior to January 2002, when NCCLS adopted a MIC of  $\geq 4$  mg/L for ceftriaxone and cefotaxime for nonmeningeal isolates

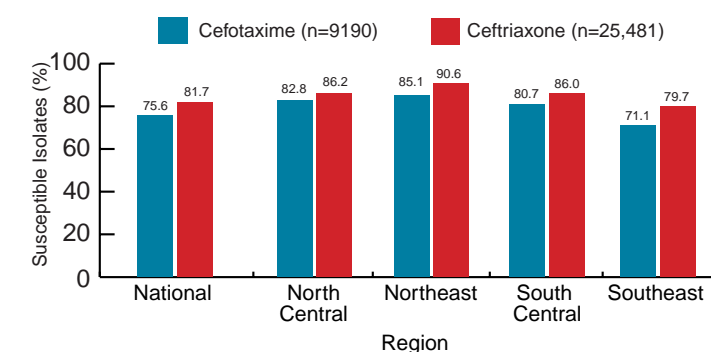
#### Methods

- R-BUG Database-USA is one component of the ongoing ARM program, established in 1997 to document national and regional antimicrobial susceptibility trends among inpatient and outpatient isolates
- To date, the program has collected data on more than 18 million inpatient and outpatient isolates representing 16 organisms and 44 antibiotics from US institutions
- Antibiogram and sensitivity report data for the years 1994-2001 collectively were compared using a Web-based analysis tool
  - Pneumococcal isolates were reviewed for susceptibility to cefotaxime and ceftriaxone
  - E coli*, *K pneumoniae*, and *P mirabilis* isolates were reviewed for susceptibility to cefotaxime, ceftazidime, and ceftriaxone

#### Results

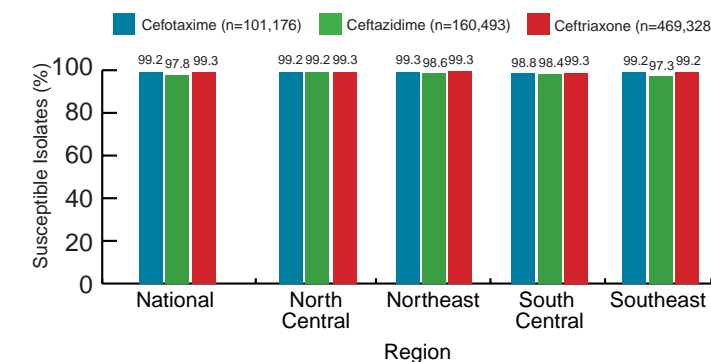
- Nationally, *S pneumoniae* isolate susceptibility was 75.6% to cefotaxime and 81.7% to ceftriaxone (Figure 1)
- Susceptibility to each agent was higher in the Northeast, South Central, and North Central and lower in the Southeast (Figure 1)

Figure 1. National and regional pneumococcal isolate susceptibility to cefotaxime and ceftriaxone, 1994-2001



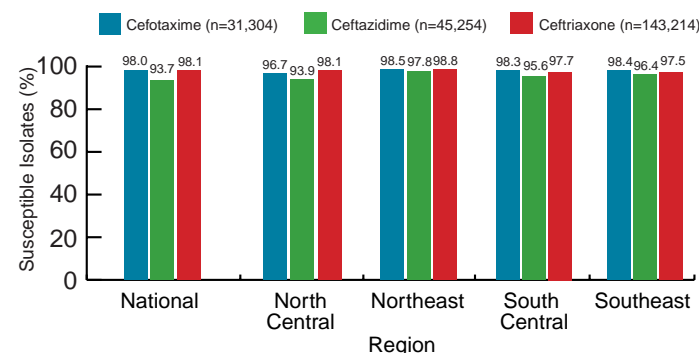
- From 1994-2001, overall rates of *E coli* isolate susceptibility to cefotaxime, ceftazidime, and ceftriaxone were high (Figure 2)

Figure 2. National and regional *E coli* isolate susceptibility to cefotaxime, ceftazidime, and ceftriaxone, 1994-2001



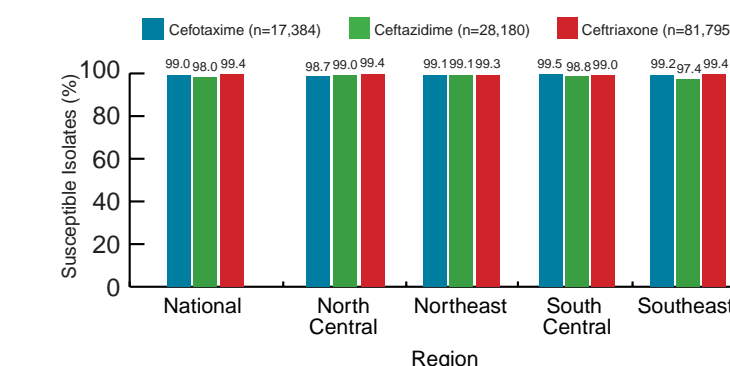
- Overall rates of *K pneumoniae* isolate susceptibility were higher to cefotaxime and ceftriaxone than to ceftazidime (Figure 3)

Figure 3. National and regional *K pneumoniae* isolate susceptibility to cefotaxime, ceftazidime, and ceftriaxone, 1994-2001



- Overall rates of *P mirabilis* isolate susceptibility were high for all 3 cephalosporins (Figure 4)

Figure 4. National and regional *P mirabilis* isolate susceptibility to cefotaxime, ceftazidime, and ceftriaxone, 1994-2001



#### Conclusions

- Overall, *S pneumoniae* isolate susceptibility rates were lower for cefotaxime than ceftriaxone
- S pneumoniae* sensitivity is artificially suppressed, given that all isolates reflect breakpoints prior to January 2002
- E coli*, *K pneumoniae*, and *P mirabilis* had high susceptibility rates to each third-generation cephalosporin antibiotic

#### References

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