C59

Streptococcus pneumoniae Susceptibility to Cefotaxime and Ceftriaxone, 1994-2001: Results of the Antimicrobial Resistance Management (ARM) Program

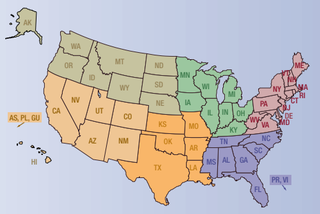
John G. Gums, PharmD, University of Florida, Gainesville, FL

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 251 institutions have enrolled as of April 22, 2003
  - 199 (79.3%) nonteaching
  - 52 (20.7%) teaching
- For the purposes of comparison, US hospitals are grouped in 6 geographic regions (see map, below); one non-US state is also included (Puerto Rico), which is grouped with the Southeast



- The number of hospitals included from each region is as follows:
  - North Central: 46 (18.3%)
  - Northeast: 68 (27.1%)
  - Northwest: 5 (2.0%)
  - South Central: 46 (18.3%)
  - Southeast: 74 (29.5%)
  - Southwest: 12 (4.8%)

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

RATIONALE: *S pneumoniae* is the most common pathogen in respiratory tract infections and causes the greatest morbidity and mortality. This pathogen also has a significant resistance profile, including to penicillin and specific agents within antibiotic classes. The ongoing ARM program was developed to document susceptibility patterns, including for *S pneumoniae*, in both US inpatient and outpatient isolates nationally and within geographic regions.

METHODS: Antibiograms and sensitivity reports of pneumococcal isolates collected between 1994 and 2001 were reviewed for resistance to penicillin and two third-generation cephalosporins, cefotaxime and ceftriaxone, and compared using a Web-based analysis tool.

RESULTS: Nationally, penicillin-resistant *S pneumoniae* rates were 38.4% (n=28,544). *S pneumoniae* nonsusceptibility to cefotaxime was 28.1% (n=6439) and to ceftriaxone, 18.8% (n=19,514). *S pneumoniae* isolates in North Central and Northeast showed less resistance to penicillin than in South Central and Southeast (Table). Across all regions, S pneumoniae nonsusceptibility was greater to cefotaxime than to ceftriaxone, with the difference greatest in the Southeast and least in South Central.

	***S pneumoniae* resistance, 1994-2001**		
	Penicillin	Cefotaxime	Ceftriaxone
North Central	29.4% (n=4185)	21.5% (n=647)	14.1% (n=2458)
Northeast	30.1% (n=3708)	20.6% (n=1082)	12.5% (n=2549)
South Central	36.6% (n=1734)	15.8% (n=709)	9.0% (n=689)
Southeast	42.6% (n=18,383)	33.4% (n=4001)	21.6% (n=13,445)

CONCLUSIONS: Susceptibility data from the ARM program suggest ceftriaxone is more susceptible than cefotaxime against *S pneumoniae*. These results are based on data through 2001 and therefore do not reflect the new NCCLS breakpoint changes. Use of the most active agent within an antibiotic class may delay the emergence of *S pneumoniae* resistance.

Rationale

- Approximately 1.7 million hospitalizations for community-acquired pneumonia (CAP) are estimated to cost $23 billion annually,[1,2] with the elderly comprising the majority of patients
- Treatment of CAP requires a careful balance between providing optimum care for patients and protecting against drug resistance
- Respiratory isolates of *S pneumoniae*, the most common pathogen in respiratory tract infections, have shown increasing resistance to a number of antimicrobial agents, including levofloxacin
- Cefotaxime and ceftriaxone are generally regarded as therapeutically equivalent for the empiric treatment of adults with CAP; however, given the reduced susceptibility of *S pneumoniae* to cefotaxime previously reported,[3] we continued to investigate resistance rates between these two third-generation cephalosporins among isolates in the ongoing ARM database

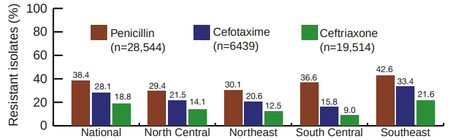
Methods

- Antibiograms and sensitivity reports for *S pneumoniae* isolates in the ARM database were examined for susceptibility to penicillin, cefotaxime, and ceftriaxone
- Using a Web-based analysis tool, isolates were compared nationally and regionally (North Central, Northeast, South Central, Southeast) for the years 1994-2001, both collectively (ie, 1994-2001 inclusive) and for each individual year

Results

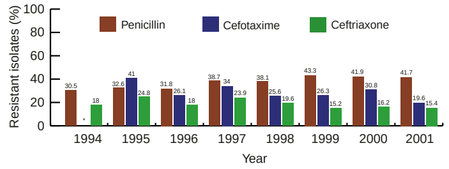
- Nationally and regionally, pneumococcal isolates were more susceptible to ceftriaxone than to cefotaxime or to penicillin (Figure 1)

Figure 1. National and regional* S pneumoniae *resistance to penicillin, cefotaxime, and ceftriaxone, 1994-2001



- When compared by year, penicillin resistance increased in 1999 and has remained high (above 40%) (Figure 2)
- Compared with cefotaxime, ceftriaxone resistance rates were consistantly lower (Figure 2)

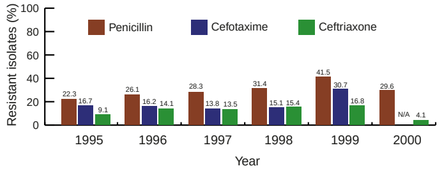
Figure 2. National* S pneumoniae *resistance to penicillin, cefotaxime, and ceftriaxone, by year, 1994-2001



*For 1994, 7 isolates were 100% susceptible to cefotaxime

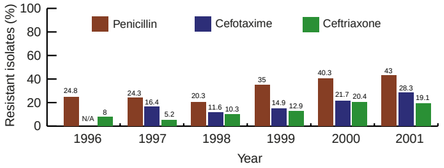
- When compared regionally by year, penicillin resistance was highest in 1999 in North Central (Figure 3); in 2001 in Northeast (Figure 4); in 1997 and 1998 in South Central (Figure 5); and between 1997-2001 in Southeast (Figure 6)

Figure 3. S pneumoniae resistance to penicillin, cefotaxime, and ceftriaxone in the North Central region, by year, 1995-2000*



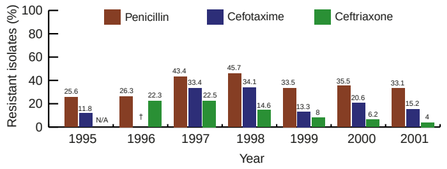
*Data not available for 1994 or 2001
N/A = not available

Figure 4. S pneumoniae resistance to penicillin, cefotaxime, and ceftriaxone in the Northeast region, by year, 1996-2001*



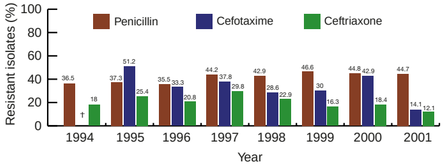
*Data not available for 1994 or 1995
N/A = not available

Figure 5. S pneumoniae resistance to penicillin, cefotaxime, and ceftriaxone in the South Central region, by year, 1995-2001*



*Data not available for 1994
†For 1994, 94 isolates were 100% susceptible to cefotaxime

Figure 6. S pneumoniae resistance to penicillin, cefotaxime, and ceftriaxone in the Southeast region, by year, 1994-2001



†For 1994, 7 isolates were 100% susceptible to cefotaxime

- For all years in all regions (with 2 exceptions; see footnotes), pneumococcal isolates were more resistant to cefotaxime than to ceftriaxone; this difference was most apparent in the Southeast (Figure 6).

Conclusions

- Susceptibility data from the ongoing ARM Program show that nationally and regionally, *S pneumoniae* isolates are more susceptible to ceftriaxone than to cefotaxime
- Use of ceftriaxone for CAP may delay emergence of *S pneumoniae* resistance
- Sensitivity numbers for both cefotaxime and ceftriaxone are artificially suppressed, given that all isolates in the database reflect breakpoints prior to January 2002, when NCCLS adopted an MIC ≥ 4 mg/mL for cefotaxime and ceftriaxone
- The clinical significance of the differences in resistance rates observed between cefotaxime and ceftriaxone is currently under investigation; the disparity is believed to be due to clonal variations

REFERENCES

1. Sue DY. Community-acquired pneumonia in adults. *West J Med.* 1994;161:383-389.
2. Bartlett JG, Mundy M. Community-acquired pneumonia. *N Engl J Med.* 1995;333:1618-1624.
3. Gums JG. *Streptococcus pneumoniae* susceptibility from 1995-2000: Results of the Antimicrobial Resistance Management (ARM) program [abstract]. *Am J Respir Crit Care Med.* 2002;165(8). Abstract J70.

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.
Presented at the 2003 American Thoracic Society 99th International Conference, Seattle, WA, USA, May 19, 2003.