Sentinel Surveillance as an Alternative Approach for Monitoring Antibiotic-Resistant Invasive Pneumococcal Disease in Washington State

Daniel B. Jernigan, MD, MPH, Leonard Kargacin, MA, Angela Poole, and John Kobayashi, MD

ABSTRACT

Objectives. As an alternative to statewide, mandated surveillance for antibiotic-resistant *Streptococcus pneumoniae*, a sentinel surveillance network of 27 hospitals was developed in Washington State.

Methods. The utility of targeted surveillance in population centers was assessed, current laboratory susceptibility testing practices were evaluated, and a baseline of pneumococcal resistance in Washington State was obtained for use in a statewide campaign promoting the judicious use of antibiotics.

Results. Between July 1997 and June 1998, 300 cases were reported; 67 (22%) had diminished susceptibility to penicillin. Only 191 (64%) were fully tested with penicillin and an extended-spectrum cephalosporin (ESC) as nationally recommended; 10.5% were resistant to penicillin and 6.8% were resistant to an ESC. The number of isolates inadequately tested declined through the year. The findings were similar to those from more comprehensive active surveillance in Oregon for the same time period.

Conclusions. Targeted surveillance may be an adequate alternative for limited monitoring of antibiotic resistance for states that choose not to mandate reporting. (*Am J Public Health.* 2001;91:142–145)

The dramatic rise in the prevalence of antibiotic-resistant *Streptococcus pneumoniae* has prompted national recommendations for routine surveillance of invasive pneumococcal infections.[1] Ideally, surveillance data would be shared with clinicians and used to promote judicious use of antibiotics.[2] Laboratory-based, mandated reporting of pneumococcal cases has been endorsed; however, implementation has been slow.[3] Possible reasons for the delay are staffing constraints and lengthy requirements for adding a reportable condition to state regulations.[4–6] As an alternative to statewide mandatory reporting, we developed an Antimicrobial Resistance Sentinel Network (ARSN) and assessed the utility of targeted surveillance in population centers, evaluated current laboratory susceptibility testing practices, and obtained a baseline of pneumococcal resistance in Washington State for use in a statewide campaign promoting the judicious use of antibiotics.

Methods

Using hospital utilization data collected by the Washington State Department of Health, we identified 3 distinct patient catchment regions of the state. These regions represented 70% of the population of Washington State and included all tertiary pediatric centers and all facilities with more than 375 beds. Letters requesting participation in ARSN were sent to infection-control staff at all hospitals in the selected regions. The network was initiated by the department of health to monitor antimicrobial resistance and to help formulate control measures.

Infection control practitioners at participating hospitals identified *S. pneumoniae* isolated from either blood or cerebrospinal fluid that was submitted to their laboratories between July 1, 1997 and June 30, 1998. For each isolate, microbiologic and patient demographic information was collected and submitted once each quarter to the department of health on a paper form. Information included age, sex, date of specimen collection, site of collection, antibiotics tested, methods used (i.e., disk diffusion, agar dilution, antimicrobial gradient strips, or broth dilution), numeric results, and interpretations of minimum inhibitory concentration (MIC) testing. Duplicate reports were not included in the analysis.

A case of invasive pneumococcal disease was defined as illness in a patient in whom *S. pneumoniae* was isolated from blood or cerebrospinal fluid. Antimicrobial susceptibility interpretive standards defined by the National Committee for Clinical Laboratory Standards (NCCLS) were used as breakpoints to classify isolates as susceptible (S), intermediate (I), or resistant (R).[7,8] For penicillin, the MIC breakpoints were S≤0.06 μg/mL, I=0.12–1.0 μg/mL, and R≥2.0 μg/mL. For extended-spectrum cephalosporins such as cefotaxime or ceftriaxone, the MIC breakpoints were S≤0.5 μg/mL, I=1 μg/mL, and R≥2.0 μg/mL. For oxacillin disk diffusion, interpretation of zone diameters was S≥20 mm and nonsusceptible (NS)<20 mm. Isolates that were oxacillin nonsusceptible were also considered penicillin nonsusceptible (i.e., penicillin intermediate and penicillin resistant combined) as described by the NCCLS.

We did not collect information on isolates other than blood and cerebrospinal fluid, because (1) collection of noninvasive isolates (e.g., sputum, ear swabs, tympanocenteses) varies by provider more than collection of blood and cerebrospinal fluid isolates; (2) respiratory isolates are often collected because of treatment failure and thus are more likely to be resistant; and (3) collection of blood and cerebrospinal fluid isolates allowed us to more easily compare our results with other surveillance data collected by the Centers for Disease Control and Prevention (CDC) (98.5% of invasive isolates collected through the CDC Emerging Infections Program, Active Bacter-

Daniel B. Jernigan is with the Office of Surveillance, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Ga. Leonard Kargacin, Angela Poole, and John Kobayashi are with the Office of Communicable Diseases, Washington State Department of Health, Seattle.

Requests for reprints should be sent to Daniel B. Jernigan, MD, MPH, Office of Surveillance, National Center for Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd, MS D59, Atlanta, GA 30333 (e-mail: dbj0@cdc.gov).

This brief was accepted May 1, 2000.

TABLE 1—Characteristics of Case Patients With *Streptococcus pneumoniae* Isolated From Blood or Cerebrospinal Fluid Identified Through the Antimicrobial Resistance Sentinel Network: Washington State, 1997–1998

	Total (% of Total)	No. Nonsusceptible to Penicillin (%)[a,b]
All cases	300 (100)	67 (22)
Source		
Cerebrospinal fluid	15 (5)	2 (13)
Blood	285 (95)	65 (23)
Age, y		
<2	71 (24)	25 (35)[c]
2–17	25 (8)	4 (16)
18–64	114 (38)	20 (17)
≥65	90 (30)	18 (20)
Male	158 (53)	40 (25)
Region		
Puget Sound	169 (56)	37 (22)
Southern/Valley	110 (37)	22 (20)
Spokane	21 (7)	8 (38)

[a]Nonsusceptible refers either to isolates nonsusceptible to oxacillin (zone diameter <20 mm) or to isolates intermediate or resistant by penicillin minimum inhibitory concentration (MIC) testing (MIC ≥ 0.12 µg/mL).
[b]We calculated percentages for isolates nonsusceptible to penicillin by using the number in the adjacent column for each characteristic.
[c]$P = .003$ when compared with all other ages.

ial Core Surveillance (EIP ABCs) are from blood and cerebrospinal fluid).[9,10]

We sent letters to network participants each quarter to encourage the submission of case reports. Informational materials were sent quarterly and included interim summaries of the data submitted to the Department of Health, newsletters, pamphlets for distribution to patients, and recent journal articles on antibiotic resistance and methods promoting the judicious use of antibiotics. We also sent short descriptions of appropriate methods for pneumococcal susceptibility testing as determined by the NCCLS. After the first year of collection, a set of charts and graphs was sent to participants to summarize the findings. These were made available to participating infection-control staff for presenting the network surveillance data at their hospitals.

Results

Between July 1, 1997 and June 30, 1998, 300 cases of invasive pneumococcal infection were reported from 27 hospitals participating in the surveillance network (Table 1). The patients ranged in age from 1 week to 99 years (mean = 42 years). The majority of patients (54%) were younger than 2 years or older than 65 years; 53% were men. Most isolates were from blood (285; 95%). Ethnicity and race were provided infrequently on case reports. Most cases were from the Puget Sound region (169; 56%).

Isolates from 67 (22%) of the 300 patients were penicillin nonsusceptible. Only 191 (64%) of the isolates had MIC results reported for both penicillin and an extended-spectrum cephalosporin, as determined by the appropriate methods recommended by the NCCLS. Of the 191 isolates, 13.1% were penicillin intermediate and 10.5% were penicillin resistant, for a total of 23.6% nonsusceptible to penicillin (Figure 1); 3.7% were extended-spectrum cephalosporin intermediate and 6.8% were extended-spectrum cephalosporin resistant, for a total of 10.5% nonsusceptible to an extended-spectrum cephalosporin. No isolates were resistant to vancomycin. Isolates that were resistant to an extended-spectrum cephalosporin were also frequently resistant to erythromycin and trimethoprim/sulfamethoxazole; however, most laboratories did not test against all these agents. Decreased susceptibility to penicillin was evident in isolates from both children and adults; however, children younger than 2 years were more likely to have infection with pneumococci nonsusceptible to penicillin ($P = .003$). We found no statistically significant differences in resistance when comparing the 3 ARSN regions (Table 1).

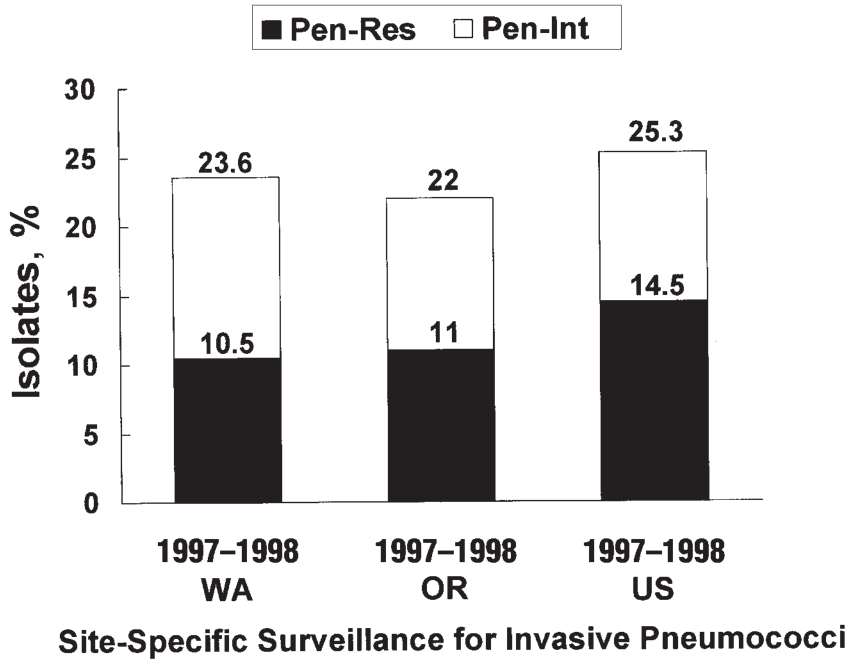
To determine whether ARSN findings were comparable to other recent surveillance data, we compared our findings with those from 8 other sites in North America—including Oregon—participating in the CDC EIP ABCs (total population base = 19.8 million) (Paul Cieslak, MD, MPH, Oregon Health Division, Portland; Cynthia Whitney, MD, MPH, National Center for Infectious Diseases, CDC, Atlanta, Ga; written communications, September 1998). The prevalence of penicillin-resistant pneumococci in Washington was not significantly different from that in Oregon ($P = .85$) or from national estimates ($P = .13$); however, national estimates were higher (Figure 1).

Within the 3 regions selected for surveillance, the 27 hospitals participating in ARSN represented 56% of all hospitals and 74% of all hospital beds. Most hospitals were in western Washington, around the Puget Sound. All major pediatric hospitals participated. Although all isolates were tested with either penicillin or oxacillin, 109 (36%) were not tested for MICs with both penicillin and an extended-spectrum cephalosporin immediately after the initial isolation of pneumococci in the blood and cerebrospinal fluid as recommended by the NCCLS. As the year progressed, the number of isolates that were inadequately tested declined from 75 of 166 (45%) in the first 6 months to 34 of 134 (25%) in the second 6 months ($P < .001$).

Discussion

Mandated, statewide, laboratory-based reporting of invasive pneumococcal infections has been recommended since 1995 as part of a strategy to minimize the impact of resistant pneumococci.[11,12] Although many state health officials believe that more attention should be focused on antibiotic-resistant diseases, staffing constraints and complicated regulatory requirements have hindered implementation of surveillance for resistant infections.[4–6] We used a sentinel network of hospitals in Washington State to estimate the prevalence of antimicrobial-resistant pneumococci and found that 22% of all isolates had diminished susceptibility to penicillin; nearly 11% of those tested by penicillin MIC methods were fully resistant.

We compared ARSN findings with findings from a previous study in Washington that collected 275 pneumococcal isolates from patients with invasive disease.[13] The prevalence of penicillin-resistant pneumococci was significantly higher for the cases in ARSN (10.5%; collected 1997–1998) than for those in the previous study (1.5%; collected 1995–1996) ($P < .001$). Although differences exist between the 2 surveillance systems, the level of resistance in ARSN was significantly higher than that found in the earlier Washington study, suggesting that a possible rapid increase had occurred. Our findings were collected from a limited number of hospitals in selected sentinel regions but were similar to the more resource-intensive, statewide, active surveil-



Note. Data for Washington (WA) were for 300 invasive pneumococcal isolates, submitted by 27 hospitals, that were collected through the Antimicrobial Resistance Sentinel Network from July 1997 to June 1998 (see Methods and Results). Data for Oregon (OR) were collected from 199 invasive pneumococcal isolates through active, population-based surveillance from July 1997 to June 1998 (Paul Cieslak, MD, MPH, Oregon Health Division, Portland, written communication, September 1998). Data for the United States (US) were collected from 3279 invasive pneumococcal isolates through active, population-based surveillance at 8 sites in North America participating in EIP ABCs from July 1997 to June 1998 (Cynthia Whitney, MD, MPH, Emerging Infections Program, National Center for Infectious Diseases, CDC, Atlanta, Ga, written communication, September 1998). Susceptibility to penicillin: resistant (Pen-Res) minimum inhibitory concentration (MIC) ≥ 2.0 µg/mL; intermediate (Pen-Int) MIC = 0.12–1.0 µg/mL.

FIGURE 1—Comparison of penicillin susceptibility testing results for invasive pneumococcal isolates: Washington State, Oregon, and Centers for Disease Control and Prevention (CDC) Emerging Infections Program, Active Bacterial Core Surveillance, 1997–1998.

lance data from Oregon for the same time period (10.5% vs 11%).

We selected sentinel *regions* and encouraged participation among the hospitals within each region rather than selecting 1 or 2 sentinel *hospitals* in many different regions. We found a number of potential benefits to this sentinel approach for monitoring resistance. First, the network allowed for data to be collected while revisions to the state reporting requirements were made. Second, the limited design of the network allowed for a simpler, more rapid collection of information. These data were available and valuable for a statewide campaign promoting the judicious use of antibiotics begun in the fall of 1998. Third, feedback was targeted to infection-control staff, who could then further disseminate the educational materials.

Fourth, feedback on susceptibility testing procedures recommended by the NCCLS probably contributed to improved testing over the first year of data collection. Heightened awareness of resistant pneumococcal isolates in hospital laboratories also led to an investigation of a cluster of multiresistant pneumococcal infections, with subsequent recommendations to improve the pneumococcal vaccination of elderly patients.[14] Fifth, our findings were similar to those collected through comprehensive, active surveillance in Oregon, a state with racial, socioeconomic, and geographic characteristics similar to those of Washington. This suggests that limited, general trends may be measured adequately by a scaled-down approach. Finally, the network is not limited to invasive pneumococcal illness and has the flexibility to be modified for monitoring other emerging resistance problems in the future.

The network approach also has limitations. First, we did not collect or test pneumococcal isolates and therefore relied on testing capabilities in participating laboratories. We identified inappropriate methods and provided information to improve testing; however, we were limited to 191 (64%) isolates for determining the combined prevalence of penicillin and extended-spectrum cephalosporin resistance. Second, because isolates were not collected, we were not able to have serotyping performed. This activity, while costly, may be beneficial as new pneumococcal vaccines are introduced for use in infants and children in the next few years.

Third, in Washington, as in other states, collection of surveillance data is primarily done by the county department of health. Use of the network shifted the duty of data aggregation and the development of valuable materials for provider feedback to the state department of health. Although the overall burden of a mandated approach is lessened with the network, a few dedicated health department staff are required for effective implementation. Finally, we did not perform active surveillance concomitantly in ARSN regions, and therefore we were not able to assess the validity of our findings in comparison with active surveillance findings in Washington. Further evaluation of the sentinel region approach may be needed before broader application of the method.

Surveillance for antibiotic-resistant *S. pneumoniae* can provide data valuable for promoting the judicious use of antibiotics. For states that face delays in implementing surveillance or that choose not to mandate reporting cases of invasive pneumococcal disease, a sentinel network approach may be an acceptable option for limited monitoring of antibiotic resistance trends. □

Contributors

D.B. Jernigan planned the study, analyzed the data, and was the primary author of the paper. L. Kargacin and A. Poole contributed to the study design, data collection, data entry, and writing of the paper. J. Kobayashi supervised data analysis and contributed to the writing of the paper.

Acknowledgments

The authors would like to acknowledge the contributions in manuscript review of Cynthia Whitney, MD, MPH, Respiratory Diseases Branch, National Center for Infectious Diseases, CDC, Atlanta, Ga, and Jac Jonas Davies, MS, MPH, Washington State Health Department, Seattle.

References

1. Centers for Disease Control and Prevention. Defining the public health impact of drug-resistant *Streptococcus pneumoniae*: report of a working group. *MMWR Morb Mortal Wkly Rep.* 1996;45(RR-1):1–14.
2. Dowell SF, Butler JC, Giebink GS, et al. Acute otitis media: management and surveillance in an era of pneumococcal resistance—a report from the Drug-Resistant Streptococcus pneumoniae Therapeutic Working Group. *Pediatr Infect Dis J.* 1999;18:1–9.
3. Centers for Disease Control and Prevention. Assessment of national reporting of drug-resistant *Streptococcus pneumoniae*—United States, 1995–1996. *MMWR Morb Mortal Wkly Rep.* 1996;45:947–949.
4. US General Accounting Office. *Emerging Infectious Diseases: Consensus on Needed Laboratory Capacity Could Strengthen Surveillance. Report to the Chairman, Subcommittee on Public Health, Committee on Health, Education, Labor, and Pensions, US Senate.* Washington, DC: US General Accounting Office; February 1999:8–14. Report GAO/HEHS-99-26.
5. Istre GR. Disease surveillance at the state and local levels. In: Halperin W, Baker EL, Monson RR, eds. *Public Health Surveillance.* New York, NY: Van Nostrand Reinhold; 1992:46.
6. Carney JK, Wargo WE, Wilcke BW, Galbraith PD. Models for surveillance: Vermont's 1997 law [abstract, special session 3]. In: *Program and Abstracts of the International Conference on Emerging Infectious Diseases, Atlanta, GA, March 8–11, 1998.* Washington, DC: American Society for Microbiology; 1998:56–57.
7. National Committee for Clinical Laboratory Standards. *Performance Standards for Antimicrobial Susceptibility Testing.* M100-S7/M7-A4. Villanova, Pa: National Committee for Clinical Laboratory Standards; 1997;17(2).
8. Jorgensen JH, Swenson JM, Tenover FC, Ferraro MJ, Hindler JA, Murray PR. Development of interpretive criteria and quality control limits for broth microdilution and disk diffusion antimicrobial susceptibility testing of *Streptococcus pneumoniae*. *J Clin Microbiol.* 1994;32:2448–2459.
9. Schuchat A, Robinson K, Wenger JD, et al. Bacterial meningitis in the United States in 1995. Active Surveillance Team. *N Engl J Med.* 1997;337:970–976.
10. Centers for Disease Control and Prevention. Geographic variation in penicillin resistance in *Streptococcus pneumoniae*—selected sites, United States, 1997. *MMWR Morb Mortal Wkly Rep.* 1999;48:656–661.
11. Jernigan DB, Cetron MS, Breiman RF, DRSP Working Group. Minimizing the impact of drug-resistant *Streptococcus pneumoniae* (DRSP). A strategy from the DRSP Working Group. *JAMA.* 1996;275:206–209.
12. Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. *MMWR Morb Mortal Wkly Rep.* 1997;46(RR-10):32–33.
13. Frick PA, Black DJ, Duchin JS, Deliganis S, McKee WM, Fritsche TR. Prevalence of antimicrobial drug-resistant *Streptococcus pneumoniae* in Washington State. *West J Med.* 1998;169:364–369.
14. Luna VA, Jernigan DB, Tice A, Kellner JD, Roberts MC. A novel multiresistant *Streptococcus pneumoniae* serogroup 19 clone from Washington State identified by pulsed-field gel electrophoresis and restriction fragment length patterns. *J Clin Microbiol.* 2000;38:1575–1580.