Changes in Antibiotic-Prescribing Practices and Carriage of Penicillin-Resistant \textit{Streptococcus pneumoniae}: A Controlled Intervention Trial in Rural Alaska

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From 1998 to 2000, 13 rural Alaskan villages (population, 3326) were surveyed annually by nasopharyngeal cultures for \textit{Streptococcus pneumoniae} carriage. Data regarding antibiotic use for the entire population was abstracted from clinic records. In 1999, education of medical providers and the community about appropriate antibiotic use began in 4 villages; this program was expanded to include all villages in 2000. Antibiotic courses per person decreased by 31\% in the initial intervention villages and by 35\% in the remaining villages after education ($P < .01$ for each). Samples were obtained for culture from a mean of 31\% of the population each year; 31\% carried pneumococcus. No sustained decrease in carriage of penicillin-nonsusceptible strains was observed. When linear regression was used, serotype accounted for 81\% of the variance in pneumococcal minimum inhibitory concentrations after the intervention, compared with 7\% for antibiotic use. This suggests that reducing the carriage of serotypes associated with antibiotic resistance by use of pneumococcal conjugate vaccines may have a greater short-term impact than does decreasing antibiotic use.

\textit{Streptococcus pneumoniae} is a leading cause of disease and death worldwide, and, in the United States, it is the most common bacterial cause of meningitis, community-acquired pneumonia, acute otitis media, and sinusitis. The emergence and spread of drug-resistant strains of pneumococcus have complicated treatment of these common infections \cite{1–3}. Higher levels of resistance to penicillin (MIC, $\geq 4 \mu g/mL$) may increase the risk of death among persons with bacteremic pneumococcal pneumonia \cite{4}.

Among Alaska Natives (Eskimos, Indians, and Aleuts), the rate of invasive pneumococcal disease is among the highest in the world, and the age-adjusted rate is 2.5 times higher than that for non–Alaska Natives \cite{5, 6}. The prevalence of drug-resistant \textit{S. pneumoniae} isolates has steadily increased in Alaska during recent years; during the 1990s, $>10\%$ of pneumococcal isolates recovered from normally sterile body sites had reduced susceptibility to penicillin and other antibiotics \cite{3, 6}. Because of the high rates of invasive pneumococcal disease among Alaska Natives and the increasing resistance of this organism in Alaska, the potential threat
of infection with penicillin-nonsusceptible pneumococci is high among Alaska Natives.

The association between antibiotic use and infection due to antibiotic-resistant pneumococci has been well established [7–17]. In response to increasing rates of antibiotic resistance among pneumococci, efforts to encourage the appropriate use of antibiotics have been undertaken to reduce the selective pressure that favors the emergence of antibiotic-resistant strains [18–24]. From 1998 to 2000, we undertook a prospective controlled intervention trial to determine whether we could reduce the carriage of drug-resistant pneumococci among residents of villages in rural Alaska through an education intervention that promoted the appropriate use of antibiotics.

MATERIALS AND METHODS

Setting and subjects. The present study was conducted in 13 remote Alaskan villages located in 3 regions, which are separated by hundreds of miles. The combined population was 3,326 in 1998; >94% were Alaska Natives. After 1999, 1 village that did not undergo the education intervention was excluded from the study because of a substantial decrease in the population. Health care in each community is provided free of charge by regional organizations through a primary care clinic staffed by community-health aides or physician assistants; each region has a referral hospital with a staff of 6–10 physicians. The study was approved by the regional Alaska Native health boards and the Institutional Review Boards of the Alaska Area Native Health Service, the Indian Health Service, and the Centers for Disease Control and Prevention (CDC). No laboratory animals were used in the study. Written informed consent was obtained from adult participants and from a parent or guardian for each child aged <18 years; children aged 7–18 years provided verbal assent for participation.

Study design. The study was a prospective controlled intervention trial to determine the penicillin susceptibility of nasopharyngeal S. pneumoniae isolates in relation to the community-wide use of antibiotics. The study included 3 phases: baseline assessment, initial intervention, and expanded intervention. For the baseline assessment and after each intervention phase, we collected nasopharyngeal swab specimens for culture annually from village residents of any age who were willing to submit a specimen, and we reviewed village clinic records to document antibiotic-use patterns and clinic visits for all village residents in each village. The baseline assessment took place during April and May 1998. An education campaign promoting the appropriate use of antibiotics was conducted from October 1998 through March 1999 in 1 region (region A; population, 1,296). The 2 remaining regions (regions B and C; population, 2,030) received no intervention at this time. We conducted a follow-up assessment in April and May 1999, 6 months after we started the initial intervention. After the initial intervention, we determined that the education intervention appeared to have reduced the prevalence of penicillin-nonsusceptible S. pneumoniae (PNSP), and we then expanded the intervention to all 3 regions from October 1999 through March 2000. Another follow-up assessment of nasopharyngeal pneumococcal carriage and antibiotic use was conducted in April and May 2000.

Data collection. In each year of the study, all available individual medical records in the village clinics were reviewed to assess the reason for all clinic visits and hospitalizations and to count the number of courses of antibiotics prescribed during the previous October–March period. Clinic visits and hospitalizations for respiratory infections included visits or hospitalizations for health care provider–diagnosed viral upper respiratory tract infection, the common cold, acute otitis media, pharyngitis, tonsillitis, sinusitis, croup, bronchitis, bronchiolitis, pneumonia, or influenza. In the largest village, we reviewed every other record for 1998 and every record for each year thereafter. Continuously administered antibiotics were counted as 1 course of antibiotics per month.

Laboratory assays. Sterile calcium alginate–tipped swabs (Calgiswab type 1; Harwood Products) were inserted through the nares into the nasopharynx. The swabs were streaked immediately onto gentamicin-blood agar plates (Remel Microbiology Products), placed into plastic bags with CO2 gas generators (Remel), and incubated on site at 37°C until they were transported to the CDC’s Arctic Investigations Program Laboratory in Anchorage, where they were processed for isolation of S. pneumoniae according to standard methods [25]. Three to 5 colonies that were morphologically typical of S. pneumoniae were selected for identification by Gram stain, bile solubility, and optochin susceptibility. MICs of penicillin were determined using Etest (AB Biodisk). We defined isolate susceptibility as follows: susceptible, MIC of ≤0.064 μg/mL; nonsusceptible, MIC of >0.064 μg/mL; resistant, MIC of >1.0 μg/mL; and intermediate, MIC of >0.064 μg/mL and ≤1.0 μg/mL. Serotyping was performed by use of the quellung reaction with reagents purchased from Statens Serum Institut.

Education intervention. We developed education programs that targeted the community-health aides (the primary health care providers in rural Alaska villages), physicians at the regional hospitals, and community residents [26]. The goal was to promote understanding of upper respiratory tract infections and the appropriate indications for antibiotic therapy. This goal was based on the principles of appropriate antibiotic use promoted by the CDC, the American Academy of Pediatrics, and the Alliance for Prudent Use of Antibiotics and an assessment of the knowledge of Alaska Native mothers about antibiotics [17, 27–30]. The intervention included workshops for community-health aides and physicians and follow-up visits to the
community-health aides to review the principals of appropriate use. Community residents also received information on appropriate antibiotic use in village-wide meetings, at community fairs, and in high school classrooms. We sent 4 health newsletters to each household from the carriage study to provide further information about upper respiratory infections and antibiotic resistance. The materials used in the interventions are available at http://www2.cdc.gov/ncidod/aip/Village_news/Village_news.asp.

**Statistical analysis.** The number of courses of antibiotics per clinic visit was calculated by dividing the total number of courses of antibiotics prescribed during the 6-month period by the number of clinic visits for each chart reviewed. Similarly, the number of courses of antibiotics per respiratory infection visit was calculated by dividing the total number of courses of antibiotics for respiratory illnesses by the number of clinic visits for respiratory illnesses. For the purpose of comparing data from year to year, “village residents” were defined as persons with a clinic chart in both years or infants born before the 2-year comparison period. For comparisons of PNSP carriage between 1999 and 2000, data were not included from the village that was removed from the study after 1999. Generalized linear models were used to compare outcome measures between the baseline and follow-up years within the treatment areas. The test of significance for an interaction term between treatment area and year was used to compare the differences among the treatment areas. Univariate comparisons of proportions were made using the χ² test. All statistical analyses were performed by use of SAS software, version 6.12 (SAS Institute).

**RESULTS**

During the 3 years of the study, a total of 3144 nasopharyngeal swab samples were cultured (from 3144 patients), and 10,809 individual medical records were reviewed (table 1). A mean of 1048 persons provided samples for culture per year (29% of those with medical charts). In 1998, compared with village residents who did not provide a nasopharyngeal swab sample for culture, study participants were younger (mean age, 23 vs. 28 years; P<.01), had more clinic visits during the winter months (mean, 3.6 vs. 2.4 visits per person; P<.01, controlling for age), and received more courses of antibiotics during the winter months (mean, 1.2 vs. 0.7 courses per person for 6 months; P<.01, controlling for age). However, these differences were similar in each study year, which allowed us to compare the main study outcome between study years without a biased result.

The percentage of persons who were pneumococcal carriers (mean, 31%) did not differ substantially during the 3 years of the study (table 1). Carriage was higher for children aged <7 years than it was for persons aged ≥7 years (P<.01). The mean age of participants did not differ between the baseline and follow-up years within each region; thus, analyses that compared rates between years were done without controlling for age. The proportion of PNSP isolates (MIC, >0.064 μg/mL) in the baseline survey was 35% (128 of 366 isolates), and the proportion of penicillin-resistant S. pneumoniae (PRSP; MIC, >1.0 μg/mL) was 22% (79 of 366 isolates). An MIC of ≥4.0 μg/mL was found for 24 (7%) of 366 isolates. Before any interventions were performed, the proportions of isolates that were PNSP or PRSP were significantly higher in region A (41% and 25%, respectively), compared with isolates recovered from regions B and C (24% [P<.01] and 16% [P = .05], respectively; figure 1). During the baseline year, 144 (39%) of 366 isolates were serotypes found in the conjugate vaccine licensed in the United States (i.e., serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F). Isolates of conjugate-vaccine serotypes were more likely to be PNSP (83 [58%] of 144 isolates) and PRSP (54 [38%] of 144 isolates) than were isolates of serotypes not in the vaccine (45 [20%] of 222 isolates [P<.01] and 25 [11%] of 222 isolates [P<.01], respectively).

After the initial education intervention, antibiotic prescribing by health care providers decreased from baseline levels, as measured by the number of courses per person (−31%; P<.01), the number of courses per clinic visit (−33%; P<.01), and the number of courses per respiratory infection visit (−27%; P< .01). Pharmacy records confirmed a 33% reduction in the amount of antibiotics sent to the education-intervention villages (region A) during the winter months, compared with the baseline year. By comparison, these measures did not change

<table>
<thead>
<tr>
<th>Year</th>
<th>No. of medical records reviewed</th>
<th>No. of nasopharyngeal swab specimens cultured</th>
<th>No. of positive cultures (% of participants)</th>
<th>Characteristics of participants who provided nasopharyngeal swab specimens for culture, % of participants</th>
<th>Age distribution, years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Female Alaska Natives</td>
<td>0–6</td>
</tr>
<tr>
<td>1998</td>
<td>3513</td>
<td>1103</td>
<td>366 (33)</td>
<td>54.7 94.5</td>
<td>20.8</td>
</tr>
<tr>
<td>1999</td>
<td>3824</td>
<td>1015</td>
<td>294 (29)</td>
<td>54.4 95.1</td>
<td>18.5</td>
</tr>
<tr>
<td>2000</td>
<td>3472</td>
<td>1026</td>
<td>317 (31)</td>
<td>53.7 94.3</td>
<td>17.8</td>
</tr>
</tbody>
</table>
The proportion of clinic visits that were for respiratory infections decreased 11% ($P = .05$) after the initial education intervention, whereas, in the control regions, there was an overall increase of 19% ($P < .01$). After the initial education intervention, the overall proportion of PNSP isolates decreased from 41% (96 of 234 isolates) to 29% (47 of 162; $P < .01$); the proportion of PRSP isolates decreased from 25% (58 of 234) to 11% (18 of 162; $P < .01$; figure 1). In the control regions, the overall proportion of pneumococci that were PNSP did not change significantly ($P = .24$% of 132 isolates to 29 [22%] of 132 isolates), nor did the proportion that were PRSP (21 [16%] of 132 isolates to 14 [11%] of 132 isolates).

After the education intervention was expanded (October 1999–March 2000), the regions that received this education for the first time experienced an overall decrease in antibiotic courses per person ($-26\%$; $P < .01$), the number of courses per clinic visit ($-23\%$; $P < .01$), and the number of courses per respiratory infection visit ($-17\%$; $P = 0.01$; table 2). However, the proportion of pneumococci that were PNSP did not change after the expanded education intervention (for 1999 vs. 2000, 28 [22%] of 126 isolates vs. 35 [26%] of 134 isolates; figure 1), nor was there a change in PRSP carriage (for 1999 vs. 2000, 13 [10%] of 126 isolates vs. 12 [9%] of 134 isolates).

In the region that received the education intervention for the second time (region A), the decreased antibiotic use observed after the initial intervention was sustained for each of the antibiotic-use measures (table 2). However, the proportion of pneumococci that were PNSP increased (for first follow-up visit vs. second follow-up visit, 47 [29%] of 162 isolates vs. 78 [43%] of 183 isolates; $P = .03$). This increase was observed in all 4 villages in this region and also occurred for PRSP (for first follow-up visit vs. second follow-up visit, 18 [11%] of 162 isolates vs. 41 [22%] of 183 isolates; $P = .01$).

By use of chart-review data from each study year, we calculated the change in the number of antibiotic courses prescribed to each person from one year to the next. We then examined the change in the proportion of nasopharyngeal pneumococci that were PNSP carried by each person as it related to antibiotic use, using linear-regression analysis (figure 2). There was a correlation between the change in the number of antibiotic courses and the change in the proportion of nasopharyngeal pneumococci that were PNSP ($P = .01$, controlling for year). Persons whose antibiotic use decreased by 2 or more courses in 6 months during a follow-up year were 14% less likely to carry PNSP than such persons had been in the previous year ($P = .05$). On average, no change in the rates of PNSP carriage was seen among persons who had no decrease in the number of antibiotic courses or for whom the number decreased by only 1 course.

To evaluate the relationship between a person’s antibiotic use and his or her status as a carrier of pneumococci, we chose participants with culture results for 2 consecutive years and stratified these patients according to their initial culture result.
(table 3). Logistic regression was used to adjust for age, study year, and the initial culture result. Antibiotic use, as measured by the number of antibiotic courses, was not associated with whether a person went from being a pneumococcal carrier to a noncarrier or vice versa. However, increased antibiotic use was strongly associated with an increased likelihood that a person would carry PNSP or PRSP, regardless of the culture results from the first year (P = .02). Each additional course of antibiotics was associated with a 20% increase in the odds of carrying an antibiotic-nonsusceptible isolate versus an antibiotic-susceptible isolate (95% CI, 3%–40%).

To evaluate the relationship between pneumococcal penicillin nonsusceptibility (as measured by MIC) and antibiotic use, we used a generalized linear model that adjusted for age group, study region, year, pneumococcal serotype, and an interaction term for year by region. In this model, antibiotic use was significantly associated with pneumococcal MIC (P ≤ .01). However, for the overall model, r² = 0.55, meaning that almost one-half of the variability in pneumococcal MICs remained unaccounted for after the use of the principal variables measured in this intervention. Antibiotic use and serotype accounted for 7% and 81% of the model variance in pneumococcal MICs, respectively.

**DISCUSSION**

We attempted to evaluate whether education about appropriate antibiotic use could reduce carriage of PNSP in villages in rural Alaska. We demonstrated that education can substantially decrease antibiotic use overall and the use of antibiotics to treat respiratory infections. Despite early encouraging results from the initial education intervention, we were unable to demonstrate similar decreases in PNSP carriage in communities after expanding the education intervention to include all villages. Furthermore, in the villages that had the initial education intervention, the decrease in the prevalence of penicillin-nonsusceptible isolates observed in 1999 was reversed only 1 year later. This occurred despite a sustained decrease in the amount of antibiotic prescriptions by the health care providers in this region. Thus, we cannot attribute the decrease in PNSP carriage observed in 1999 to our education intervention. However, individual village residents who had decreased antibiotic use by ≥2 courses per 6 months after the intervention were less likely to carry PNSP.

These communities were well suited for this intervention because they are small villages with relatively stable populations that use a centralized health care system. This allowed us to reach the residents and health care providers with our educational messages, to test a substantial proportion of village residents for pneumococcal carriage (31% overall), and to evaluate all clinic use and antibiotic prescriptions for the villages. Many of the factors that are likely to contribute to the spread of antibiotic resistance are the same in rural Alaska as they are in other areas. These factors include the presence of penicillin-resistant pneumococci, the crowding of children in schools and care environments, frequent upper respiratory tract infections, immigration from other communities, and frequent antibiotic use.

The theory behind efforts to promote education about appropriate use of antibiotics is based on several assumptions. First, we assumed that the maintenance of antibiotic resistance comes at some metabolic or reproductive cost to the organisms that may render them less fit than antibiotic-susceptible organisms for survival in an environment that lacks antibiotic pressure [31]. Second, we assumed that the evolution of antibiotic resistance can be reversed or that the trend toward increased antibiotic resistance can be slowed by reducing selective pressure. By encouraging medical providers and community members to avoid unneeded courses of antibiotics, overall rates of antibiotic use should decrease. In communities where an-

**Table 2. Comparison of data on antibiotic use and clinic use before and after appropriate antibiotic-use education interventions, Alaska, 1998–2000.**

<table>
<thead>
<tr>
<th>Outcome measure</th>
<th>Initial intervention (region)</th>
<th>Expanded intervention (region)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Education (A)</td>
<td>Control (B, C)</td>
</tr>
<tr>
<td>Antibiotic courses per person</td>
<td>1.24</td>
<td>0.85&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Antibiotic courses per clinic visit</td>
<td>0.39</td>
<td>0.26&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Proportion of clinic visits for respiratory infections</td>
<td>0.47</td>
<td>0.42&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Antibiotic courses per respiratory infection visit</td>
<td>0.64</td>
<td>0.47&lt;sup&gt;b,c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

**NOTE.** Data are mean no. of courses or clinic visits.
<sup>a</sup> From chart review of October–March period prior to the study year.
<sup>b</sup> P<.05, compared with prior year.
<sup>c</sup> Comparisons between years are paired analyses that used persons with medical records in both years of the comparison. There are slight differences in the same year because some persons did not have records in both pairs of years.
tibiotic use has been reduced, antibiotic-susceptible organisms may have a survival advantage and become the dominant carriage and disease-causing types. This should result in improved outcomes in clinical cases in which antibiotics are indicated.

Although we did observe an overall 31% decrease in the rate of antibiotic use after the initial education intervention, as well as a decrease of 26% in the second year, this decrease in antibiotic use may not have been great enough to have an impact on community-level carriage. Furthermore, these data indicate that antibiotic use by individual village residents accounted for only 7% of the variance in MICs of penicillin. Thus, antibiotic use may play a relatively minor role in affecting the overall distribution of pneumococcal MICs, and other factors, such as serotype distributions, may be more important determinants of resistance during a 1–2-year time period. Mathematical models indicate that the decrease in the prevalence of antibiotic-resistant organisms after decreased antibiotic use may be slower than the increase in the prevalence that occurs with increased use [32]. Finally, it is possible that, despite the success in decreasing antibiotic use, we may not be able to measure a decrease in antibiotic resistance because antibiotic-resistant S. pneumoniae may be as fit as antibiotic-susceptible pneumococci. Data from experiments with other bacteria (Mycobacterium tuberculosis, Escherichia coli, and Salmonella typhimurium) have demonstrated that the physiological cost of antibiotic resistance can be overcome by adaptation involving genes other than those conferring resistance [33–37]. To our knowledge, no data have been published to corroborate that such adaptations exist among pneumococci. Taken together, these data indicate that the goal of decreasing the prevalence of community-wide PNSP carriage and disease may not be a simple matter of decreasing the selective pressure exerted by antibiotics. Given that most PNSP are serotypes included in current and planned conjugate pneumococcal vaccine formulations, vaccination appears to be the most promising tool for reducing carriage of PNSP in the short term [6, 38].

Education of the community and health care providers about appropriate antibiotic use is an approach that makes good clinical sense and is consistent with the principle of “first do no harm,” because unnecessary use of antibiotics does carry the risk of a subsequent infection with an antibiotic-resistant organism [17]. Another potential benefit of appropriate antibiotic use may be a reduction of adverse events related to antibiotic use, such as allergic reactions or pseudomembranous colitis. Data from our study support findings from other studies that have shown education regarding appropriate antibiotic use to be effective in increasing knowledge about antibiotics and reducing the number of antibiotic prescriptions [39–41]. However, conclusive data are lacking that demonstrate that reduced antibiotic use leads to a decrease in carriage or infection with antibiotic-resistant pneumococci. Future plans for this project include continuation of yearly follow-up of residents in these study communities to monitor pneumococcal carriage and antibiotic use and to evaluate the impact of the pneumococcal

Figure 2. Relationship between the change in the number of antibiotic courses and the change in the proportion of nasopharyngeal penicillin-nonsusceptible Streptococcus pneumoniae (PNSP) after the education interventions about appropriate antibiotic use, Alaska, 1998–2000. Data shown are for individuals and are grouped according to intervention.
Table 3. The results of nasopharyngeal cultures for *Streptococcus pneumoniae* for individuals enrolled in consecutive years, according to number of antibiotic courses prescribed, Alaska, 1998–2000.

<table>
<thead>
<tr>
<th>Years of consecutive cultures</th>
<th>First culture result</th>
<th>Second culture result</th>
<th>No. of participants</th>
<th>Mean no. of antibiotic courses per persona</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998 and 1999b (n = 571)</td>
<td>Negative</td>
<td>Negative</td>
<td>302</td>
<td>0.76</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>PNSP</td>
<td>24</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>PSSP</td>
<td>33</td>
<td>0.27</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>Negative</td>
<td>36</td>
<td>1.11</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>PNSP</td>
<td>13</td>
<td>2.54</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>PSSP</td>
<td>24</td>
<td>1.17</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>Negative</td>
<td>64</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>PNSP</td>
<td>15</td>
<td>1.73</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>PSSP</td>
<td>60</td>
<td>0.70</td>
</tr>
<tr>
<td>1999 and 2000c (n = 491)</td>
<td>Negative</td>
<td>Negative</td>
<td>254</td>
<td>0.72</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>PNSP</td>
<td>33</td>
<td>1.09</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
<td>PSSP</td>
<td>56</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>Negative</td>
<td>23</td>
<td>1.74</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>PNSP</td>
<td>12</td>
<td>1.75</td>
</tr>
<tr>
<td></td>
<td>PNSP</td>
<td>PSSP</td>
<td>6</td>
<td>0.33</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>Negative</td>
<td>53</td>
<td>0.96</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>PNSP</td>
<td>16</td>
<td>1.50</td>
</tr>
<tr>
<td></td>
<td>PSSP</td>
<td>PSSP</td>
<td>38</td>
<td>1.00</td>
</tr>
</tbody>
</table>

**NOTE.** PNSP, penicillin-nonsusceptible *S. pneumoniae*; PSSP, penicillin-susceptible *S. pneumoniae*.

* a Prescribed during October–March before the culture in the second year of the comparison.

b The initial culture was performed in 1998, and the subsequent culture was performed in 1999.

c The initial culture was performed in 1999, and the subsequent culture was performed in 2000.

conjugate vaccine. The 7-valent vaccine (Prevnar; Wyeth Lederle Vaccines) became part of the routine childhood immunization schedule in Alaska on 1 January 2001. Because the serotypes included in that vaccine are commonly resistant to penicillin, we expect that continued monitoring of pneumococcal carriage will allow us to evaluate the impact of the vaccine on carriage of penicillin-nonsusceptible serotypes and to document changes in patterns of antibiotic resistance.

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