Evaluation of Innovative Surveillance for Drug-resistant *Streptococcus pneumoniae*

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To monitor disease incidence and antibiotic resistance, effective, practical surveillance strategies are needed at the local level for drug-resistant *Streptococcus pneumoniae* (DRSP). Knox County, Tennessee, participates in three forms of DRSP surveillance: an active system sponsored by the Centers for Disease Control and Prevention (CDC; Atlanta, Georgia); a novel county-sponsored system; and conventional state-mandated reporting. Ascertainment of invasive *S. pneumoniae* infection cases by each system in 1998 was evaluated, and completeness of reporting, antibiotic resistance patterns, costs, and other attributes were compared. The county-sponsored system collects patient identifiers and drug susceptibility data directly from hospital laboratories, whereas the CDC-sponsored system performs medical chart abstractions and reference laboratory susceptibility testing. Similar numbers of invasive *S. pneumoniae* cases were detected by the county-sponsored (n = 127) and CDC-sponsored (n = 123) systems; these systems held >75% of all cases in common, and each system achieved >85% sensitivity. Conventional reporting contained 88% and 76% of the DRSP cases identified by the county- and CDC-sponsored systems, respectively, but did not capture infections produced by susceptible isolates. Both the county- and CDC-sponsored systems indicated that large proportions of isolates were resistant to penicillin and extended-spectrum cephalosporins. The county-sponsored DRSP surveillance system was inexpensive, simple to execute, and relevant to local needs. *Am J Epidemiol* 2001;154:1000–5.

Community-acquired *Streptococcus pneumoniae* infection remains a major cause of morbidity and mortality (1). During 1998, *S. pneumoniae* infection was associated with approximately 63,000 cases of invasive disease and 6,100 deaths in the United States (2). The difficulties inherent in managing patients with this infection have been magnified by the rising incidence of drug-resistant *S. pneumoniae* (DRSP) (3–5), which complicates medical care, increases costs, and impacts patient outcomes (6–10).

Effective, affordable strategies for DRSP surveillance are needed at the local level to monitor disease incidence and antibiotic resistance rates and to guide empiric therapy (1). Active, population-based surveillance for invasive pneumococcal disease is sponsored by the Centers for Disease Control and Prevention (CDC; Atlanta, Georgia) at a selected number of sites across the United States as part of the Emerging Infections Program’s Active Bacterial Core surveillance (ABCs) (2, 3, 11). This system effectively characterizes antibiotic resistance patterns by testing pneumococcal isolates at reference laboratories and is also used to conduct special studies. However, because of its costs and complexity, this type of program is beyond the means of most local and state health agencies (12).

Knox County, Tennessee (1998 population: 367,000), is unusual because it is involved in ABCs and also has implemented a simpler, alternative DRSP surveillance system designed and conducted by the local Knox County Health Department. In addition, the Tennessee Department of Health conducts routine passive surveillance for DRSP. This situation afforded the opportunity to measure the alternative county-sponsored surveillance strategy against recognized standards.
MATERIALS AND METHODS

DRSP surveillance systems

ABCs. Since 1995, all five Knox County acute care hospitals have participated in the CDC-sponsored ABCs program (2). In 1998, ABCs personnel performed a monthly review of printed data from the computerized records of each hospital’s microbiology laboratory to prospectively identify all cases of invasive S. pneumoniae infection in Knox County residents (table 1). In cases, S. pneumoniae was isolated from a normally sterile site. For each case, surveillance personnel also reviewed the medical chart to abstract clinical and demographic information, and they requested that clinical isolates from invasive S. pneumoniae cases be subcultured and forwarded to a reference laboratory (University of Texas Health Sciences Center at San Antonio) for antibiotic susceptibility testing. Antibiotic susceptibilities were determined by using broth microdilution (2, 13). Feedback to local medical providers and hospitals was limited in this system; primarily, system- or state-level results have been communicated principally through peer-reviewed publications and the CDC’s Morbidity and Mortality Weekly Report.

Knox County Health Department. In 1997, the Knox County Health Department, in partnership with the surrounding regional health department, initiated a surveillance program for invasive S. pneumoniae infections with the aim of generating timely data to monitor resistance trends and inform medical providers. This surveillance program was motivated by awareness of high resistance rates among S. pneumoniae isolates in the region and by a recent outbreak of drug-resistant pneumococcal meningitis (14). As with ABCs, all five Knox County hospitals participated in the Knox County Health Department program in 1998; in addition, three large hospitals serving the region surrounding Knox County were also included (table 1). Each month, hospital laboratories forwarded a report of all invasive S. pneumoniae isolates to the Knox County Health Department. In addition to the normally sterile sites used in the ABCs case definition, the Knox County Health Department system also included isolates from middle ear, tracheal, and sinus aspirates (not reported here).

The Knox County Health Department system was a “stimulated” passive system in which health department personnel solicited reports by telephone if hospitals seemed to lag in submitting their monthly reports. Reports included basic demographic data along with the specimen collection site and date. The results from hospital laboratory antibiotic susceptibility testing were performed by using antimicrobial gradient strip tests. No additional patient follow-up or susceptibility testing was conducted. The program used discretionary resources, absent specific funding. After a Knox County Health Department medical epidemiologist established the system, health department personnel requirements were limited generally to the part-time efforts (1 or 2 days per month) of a communicable disease control nurse and an administrative assistant. Feedback to medical providers took place primarily via local publication of data and related articles in the Knox County Health Department’s quarterly newsletter.

Conventional reporting. States typically maintain surveillance for a list of notifiable diseases and conditions (15, 16). Laboratories, hospitals, and health-care providers are required by law to report the occurrence of these conditions to their local health department. The Tennessee Department of Health then collects and monitors weekly case reports by using the National Electronic Telecommunication System for Surveillance (17); this passive system is referred to here as “conventional reporting” (table 1). In 1996, Tennessee adopted the national case reporting criteria for DRSP (clinical cases for whom S. pneumoniae has been isolated from a normally sterile site that exhibits intermediate- or high-level resistance to at least one antibiotic approved for treating pneumococcal infections) (15). DRSP case reports typically

| TABLE 1. Attributes of the three surveillance systems used to identify cases of invasive Streptococcus pneumoniae infections in Knox County, Tennessee, 1998 |
|---------------------------------|-----------------|-----------------|-----------------|
| Attribute                       | CDC*-sponsored Active Bacterial Core surveillance | Knox County Health Department | Conventional, state-mandated reporting |
| System type                     |                 |                 |                 |
| Participating hospitals          |                 |                 |                 |
| Knox County                     | Active          | Passive, stimulated | Passive         |
| Regional                        | Yes             | Yes             | Yes             |
| Reporting frequency             | Monthly         | Monthly         | Weekly          |
| Chart review                    | Yes             | No              | No              |
| Invasive S. pneumoniae infections captured | Yes | Yes | No |
| Susceptible isolates            | Yes             | Yes             | Yes             |
| Nonsusceptible isolates         | Yes             | Yes             | Yes             |
| Susceptibility testing source   | Reference laboratory | Hospital laboratory | Hospital laboratory |
| Range of drugs                  | Extensive       | Limited         | Does not capture testing data |

* CDC, Centers for Disease Control and Prevention.

Am J Epidemiol Vol. 154, No. 11, 2001
originate with hospital infection control practitioners and include demographic information and the specimen collection date. Antibiotic susceptibility results were not collected, and no additional patient follow-up or susceptibility testing was performed. State-level data, summarizing the numbers of DRSP cases, have been published and distributed to medical providers by the Tennessee Department of Health in its bimonthly newsletter.

Comparison of the systems’ quantitative attributes

For the present analysis, invasive \textit{S. pneumoniae} infection cases were defined as Knox County residents for whom \textit{S. pneumoniae} had been isolated from a normally sterile site (e.g., blood, cerebrospinal fluid, pleural fluid) during 1998. Residence in Knox County was determined from a review of patient addresses. Cases meeting this definition were ascertained by reviewing the total set of cases collected by each system.

Completeness of reporting. Cases with invasive \textit{S. pneumoniae} were cross-checked between systems by using available identifiers such as patient name and address, date of birth or age, and specimen date. To estimate the number of additional cases not detected by either ABCs or the Knox County Health Department, capture-recapture analysis was applied by using standard methods (18, 19). Completeness of reporting (i.e., sensitivity) was calculated for the ABCs and Knox County Health Department systems by dividing the number of cases in each system by the total number of cases derived from the capture-recapture analysis. Because conventional reporting included only invasive cases of \textit{S. pneumoniae} deemed drug resistant, comparison with ABCs and the Knox County Health Department was limited to DRSP cases.

Antibiotic susceptibility. \textit{S. pneumoniae} isolates from the ABCs and Knox County Health Department systems were categorized (2, 20) as susceptible, having intermediate resistance, or highly resistant to penicillin (susceptible: minimum inhibitory concentration (MIC) ≤ 0.06 \(\mu\)g/ml; intermediate: 0.12 \(\mu\)g/ml ≤ MIC ≤ 1.0 \(\mu\)g/ml; resistant: MIC ≥ 2.0 \(\mu\)g/ml); extended-spectrum cephalosporins (ceftriaxone disodium or cefotaxime sodium) (susceptible: MIC ≤ 0.5 \(\mu\)g/ml; intermediate: MIC = 1.0 \(\mu\)g/ml; resistant: MIC ≥ 2.0 \(\mu\)g/ml); erythromycin (susceptible: MIC ≤ 0.25 \(\mu\)g/ml; intermediate: MIC = 0.5 \(\mu\)g/ml; resistant: MIC ≥ 1.0 \(\mu\)g/ml); chloramphenicol (susceptible: MIC ≤ 4.0 \(\mu\)g/ml; resistant: MIC ≥ 8.0 \(\mu\)g/ml); and clindamycin (susceptible: MIC ≤ 0.25 \(\mu\)g/ml; intermediate: MIC = 0.5 \(\mu\)g/ml; resistant: MIC ≥ 1.0 \(\mu\)g/ml). An isolate was defined as “resistant” to a particular antibiotic if it exhibited either intermediate- or high-level resistance to that agent. The sources of antibiotic susceptibility data were the CDC reference laboratory for ABCs cases and the hospital laboratories for Knox County Health Department cases. MIC values based on gradient strip testing that fell between standard twofold dilutions were rounded upward to the next standard dilution before categorization, per the manufacturer’s instructions (AB Biodisk, Piscataway, New Jersey). Differences between the ABCs and Knox County Health Department systems in the proportions of isolates within particular antibiotic susceptibility categories were evaluated with the Fisher’s exact test by using Stata statistical software, release 6.0 (Stata Corporation, College Station, Texas).

Timeliness and costs. Timeliness was assessed by comparing the median time between specimen collection with the completion of reference laboratory testing (for ABCs) or reporting to the health department (for Knox County Health Department and conventional reporting). Direct and indirect costs were estimated for 1998 on the basis of interviews with relevant personnel from the different surveillance systems. The level of effort associated with conventional reporting was designated as a baseline to which no costs were ascribed. For ABCs, the costs for this surveillance were determined by estimating the additional staff time required by hospital laboratories (e.g., for subculturing), the ABCs program’s personnel and administrative requirements, and the additional costs of testing by the reference laboratory. Interpretation and analysis by CDC personnel were not included. For the Knox County Health Department, costs were based on the estimated staff time required by the hospital laboratories to assemble and transmit monthly reports and by local health department staff to enter and disseminate these data.

RESULTS

Completeness of reporting

During 1998, the ABCs and Knox County Health Department systems detected 123 and 127 cases, respectively, of invasive \textit{S. pneumoniae} infections in Knox County residents (table 2). When the results of both systems were combined, the total number of individual cases was 141; of these, 109 (77 percent) were found to be common to both systems. The remaining cases were found in only one system: 14 cases were unique to ABCs and 18 cases were unique to the Knox County Health Department. Eight (44 percent) of the 18 unique Knox County Health Department cases originated from a hospital geographically outside of Knox County and were not included in the ABCs system. Among the five Knox County hospitals, each surveillance system typically captured at least one case missed by the other, but no consistent hospital-specific pattern was evident. Two additional cases were predicted by the capture-
recapture analysis; the estimated total number of cases was 143. The overall completeness of the ABCs and Knox County Health Department systems was then calculated as 86 and 89 percent, respectively.

**Comparison to conventional reporting**

A total of 52 cases of invasive DRSP infection occurring in Knox County residents in 1998 were reported to the Tennessee Department of Health (figure 1). Cases of invasive *S. pneumoniae* were reportable to the state only if the isolates were drug resistant, so infections produced by susceptible isolates were not captured. All 52 of the DRSP cases captured by conventional reporting were also identified by either the ABCs or Knox County Health Department system; 48 cases were common to all three systems. The conventional reporting system contained 88 percent (50/57) of the reported invasive DRSP infections documented in the Knox County Health Department system. When only the ABCs cases available for testing at the reference laboratory were considered, conventional reporting captured 76 percent (41/54) of the ones determined to be drug resistant.

**Antibiotic susceptibility**

Isolates of invasive *S. pneumoniae* were classified as susceptible or resistant according to the results of the antibiotic susceptibility testing for the ABCs cases whose isolates were tested by the reference laboratory (n = 98) and for all Knox County Health Department cases (n = 127) (figure 1). (The resistant category was comprised of isolates exhibiting either intermediate- or high-level resistance.) Both the ABCs and Knox County Health Department systems indicated that large proportions of isolates were resistant to penicillin and extended-spectrum cephalosporins (table 3).

The proportion of isolates characterized as penicillin resistant was higher among isolates reported by ABCs than by the Knox County Health Department (55 vs. 45 percent), but this difference was not statistically significant. ABCs testing detected a greater proportion of isolates with high-level penicillin resistance (44 vs. 27 percent, p = 0.01).

For extended-spectrum cephalosporins, ABCs found greater proportions of isolates that were resistant (44 vs. 25 percent, p = 0.004) or had high-level resistance (30 vs. 13 percent, p = 0.002). The proportion of isolates resistant to erythromycin was substantial in both systems, although nominally higher with ABCs (37 vs. 26 percent, p = 0.10). For both clindamycin and chloramphenicol, similarly high

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**TABLE 3. Antibiotic susceptibilities of invasive Streptococcus pneumoniae isolates from the ABCs* and KCHD* systems, Knox County, Tennessee, 1998**

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Susceptibility category†</th>
<th>Proportion of isolates (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ABCs‡</td>
<td>KCHD§</td>
<td>Difference (95% CI*)</td>
</tr>
<tr>
<td>Penicillin</td>
<td>Resistant</td>
<td>55</td>
<td>45</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>11</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>High level</td>
<td>44</td>
<td>27</td>
</tr>
<tr>
<td>Extended-spectrum cephalosporins</td>
<td>Resistant</td>
<td>44</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Intermediate</td>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>High level</td>
<td>30</td>
<td>13</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Resistant</td>
<td>37</td>
<td>26</td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Resistant</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>Resistant</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

* ABCs, Active Bacterial Core surveillance; KCHD, Knox County Health Department; CI, confidence interval.
† Refer to the Materials and Methods section of the text for susceptibility definitions via minimum inhibitory concentration.
‡ Based on 98 isolates tested by the ABCs reference laboratory.
§ Based on isolates tested by hospital laboratories (penicillin and extended-spectrum cephalosporins, n = 127; erythromycin and clindamycin, n = 116; and chloramphenicol, n = 93).
¶ NS, nonsignificant at the α = 0.05 level.
proportions (>96 percent) of isolates were susceptible according to both reporting systems.

**Timeliness and costs**

The average time to complete reporting was approximately 4 months for ABCs compared with 1 month for the Knox County Health Department and 3 weeks for conventional reporting. The annual cost of the ABCs system was an estimated $30,000, including $25,000 for surveillance personnel and administrative costs, $2,000 for hospital personnel requirements, and $3,000 for reference laboratory testing. In contrast, on the basis of hospital and health department personnel requirements, the Knox County Health Department system cost approximately $5,000 annually.

**DISCUSSION**

In Knox County, Tennessee, it was possible to compare the usefulness of three concurrent surveillance systems for invasive infections produced by antibiotic-resistant *S. pneumoniae*: a traditional, passive, state-mandated reporting mechanism; a simple, innovative, county-sponsored system established in response to local needs (Knox County Health Department); and a CDC-sponsored, active, population-based system (ABCs) that served as a relative “gold standard.” The simple local reporting system devised by the Knox County Health Department performed well.

All three surveillance systems successfully recorded a comparable occurrence of penicillin-resistant pneumococcal isolates from usually sterile sites. Somewhat surprisingly, the Knox County Health Department system recorded more total cases of invasive *S. pneumoniae* infection among Knox County residents in 1998 than the ABCs system did. This occurrence was largely explained by the Knox County Health Department system including a hospital in one of the counties bordering Knox County, which was not part of the ABCs network. Geographically delineated surveillance systems will always have the potential to miss patients who seek care outside the catchment area.

As anticipated, the traditional, passive, state-sponsored reporting system recorded the smallest number of cases, but the difference was not large. Thus, conventional reporting appeared to provide an effective means of gauging the incidence of invasive DRSP infection. However, conventional reporting had a notable drawback. Because only DRSP was reportable, the proportion of isolates susceptible to penicillin could not be determined. Tennessee now requires that antibiotic-susceptible invasive pneumococcal infections also be reported, which makes the data more useful in determining the proportion of resistant isolates.

Differences were observed between the Knox County Health Department and ABCs systems in the proportions of isolates classified among some antibiotic susceptibility categories. Restricting the analysis to only those isolates tested by both the hospitals and reference laboratory did not affect these results (data not shown). These differences are unlikely to have an impact on the usefulness of either system as a public health tool. However, a potential clinical impact existed in those instances when the hospital laboratory reported an isolate as susceptible to penicillin and the ABCs reference laboratory determined that it was resistant; these types of differences are now under investigation. Similarly, interlaboratory differences in extended-spectrum cephalosporin susceptibility results have been noted previously (21).

The principal motivation for establishing these surveillance systems was the emergence of antibiotic-resistant *S. pneumoniae*. Few areas have successfully implemented DRSP surveillance, despite the fact that practical data exist in most community hospitals (22, 23). Resources available for local surveillance are scarce. For DRSP, formulating the appropriate scope of a local surveillance system presents an additional difficulty. The ABCs system does not provide a suitable model because its considerable scope and resource requirements, which reflect its research-oriented role and national perspective, exceed local needs and capacities. The Knox County Health Department system was innovative in that it established a collaborative mechanism with local hospitals to assemble, monitor, and disseminate community-level DRSP data to providers in an efficient and timely manner.

Many hospitals compile antibiograms from the results of their own susceptibility testing. Typically, they do not distinguish between invasive and noninvasive infections, multiple isolates from individual patients, or intermediate and resistant interpretive categories. A surveillance strategy that provided community-level DRSP data from the aggregation of local hospital antibiograms has been described (12, 24). Similar to the Knox County Health Department system, this alternate strategy also provides a sufficient body of continuous data to enable examination of trends and is useful in both the local public health and clinical arenas. However, the Knox County Health Department system provides a finer level of detail because it accesses the specific microbiologic and demographic data from individual patient isolates. Thus, this system preserves distinctions regarding susceptibility categories, patient demographics, and invasive versus noninvasive infections. In addition, because not all hospitals produce antibiograms, the Knox County Health Department approach might make these data more representative and accessible. Another recent example of alternative DRSP surveillance involved a sample of hospitals from Washington State (2, 25); this system collected periodic reports containing patient-level data on invasive *S. pneumoniae* infections, and it seemed to provide adequate, detailed monitoring of DRSP at the state level.

A heightened level of awareness exists in the Knox County community regarding the public health importance of pneumococcal drug resistance, and this awareness may have enhanced cooperation on the part of the hospital laboratories. It was not possible to evaluate the effect that prior participation in the ABCs program might have had on reporting through the separate Knox County Health Department mechanism. The existence of multiple, overlapping reporting systems in a given locale does raise some concerns, especially for the laboratory, medical, and public health professionals whose responsibility it is to actually perform disease reporting. Integration of disease surveillance systems has become a major focus in recent years, and the proposed CDC National Electronic Disease Surveillance System aims...
to provide an Internet-based communications infrastructure that will streamline disease reporting at the local, state, and national levels (26). Specifically, implementation of electronic data transmission from clinical laboratories should reduce the burden of disease reporting and may also facilitate collection of the detailed susceptibility data needed for enhanced DRSP surveillance.

In summary, the Knox County Health Department surveillance system for DRSP infections was accurate, timely, and simple to execute. This system did not require dedicated funding or the hiring of additional personnel. This surveillance system has been used to supply timely data to medical providers to define the magnitude and nature of the problem of drug resistance, inform empiric therapies, and monitor changes. Resource outlays have been balanced with a scope appropriate and relevant to local needs. The Knox County Health Department system could serve as a model for other communities concerned about the emergence of DRSP.

ACKNOWLEDGMENTS

The authors are grateful to Dr. Laura Fehrs, Dr. Ron Mooienaar, Dr. Cynthia Whitney, Dr. Anne Schuchat, Dr. Paul Erwin, Brenda Barnes, Jan Fowler, Sandra Blakely, and personnel from the participating hospitals and laboratories for their helpful comments and contributions to this project.

REFERENCES