Invasive Pneumococcal Infection in Baltimore, Md

Implications for Immunization Policy

Lee H. Harrison, MD; Diane M. Dwyer, MD; Lillian Billmann, RN, MPH; Margarette S. Kolczak, PhD; Anne Schuchat, MD

Background: *Streptococcus pneumoniae* is a leading cause of infectious morbidity and mortality. Although blacks are known to have a higher incidence of invasive pneumococcal infection than whites, detailed analyses of these differences and their implications for vaccine prevention have not been reported.

Objective: To describe the epidemiological characteristics of invasive pneumococcal infection in Baltimore, Md, and its implications for immunization policy.


Results: Of 1412 cases, 615 patients (43.6%) were classified as white and 766 (54.2%) as black. The annual incidence of invasive pneumococcal infection among white and black residents of the Baltimore metropolitan area was 17.8 and 59.2 per 100 000 population, respectively ($P<.01$). Among patients aged 18 years and older, the median age of blacks with invasive pneumococcal infections was 27 years younger than that of whites ($P<.01$). Among males 40 to 49 years old, blacks had a 12-fold higher average incidence than whites (average incidence, 114.5 and 9.3, respectively; $P<.01$). By the age of 65 years, 83.8% of cases had occurred in black adults, as compared with 43.8% in white adults ($P<.01$). In a regression model, age, black race, male sex, low median family income, and county prevalence of acquired immunodeficiency syndrome were each independently associated with a higher incidence of pneumococcal infection.

Conclusions: Young urban black adults in the Baltimore metropolitan area have a dramatically higher incidence of invasive pneumococcal infection than whites. The vast majority of cases of invasive pneumococcal infection in blacks occur before age 65 years. Current immunization efforts have not addressed the high incidence of pneumococcal infection in this population.

Arch Intern Med. 2000;160:89-94

*Streptococcus pneumoniae* is a leading cause of infectious morbidity and mortality worldwide. In the United States, the pneumococcus is responsible for an estimated 50,000 cases of bacteremia, 3000 cases of meningitis, 7 million cases of otitis media, and several hundred thousand cases of pneumonia each year.1-4 The overall yearly incidence of pneumococcal bacteremia is estimated to be 15 to 35 cases per 100,000 population.5-8

Measures to prevent pneumococcal infection include the immunization of individuals 65 years old and older and those 2 years old and older with certain underlying medical conditions, such as pulmonary and cardiovascular disease, diabetes mellitus, alcoholism, chronic liver disease, asplenia, human immunodeficiency virus (HIV) infection or other illnesses associated with immunodeficiency, certain malignant neoplasms, and immunosuppressive chemotherapy.9 Persons 2 to 64 years old belonging to high-risk populations, such as Alaska Natives and certain American Indian populations10,11 and nursing home residents,12 are also considered to be at high risk and have been targeted for immunization efforts.9

Numerous studies have documented that blacks have a substantially higher incidence of invasive pneumococcal bacteremia than whites.5-7,13-16 Others have documented lower rates of pneumococcal vaccination among African Americans older than 65 years compared with whites.17,18 However, the full implications of racial differences in disease epidemiological characteristics on opportunities for prevention have not been addressed. In this study, we examined the epidemiological characteristics of pneumococcal infection during 1995 and 1996 in the Baltimore (Md) metropolitan area (BMA) and consider racial gaps in the
METHODS

SURVEILLANCE FOR INVASIVE PNEUMOCOCCAL INFECTION

Active surveillance for invasive pneumococcal infection was initiated in the BMA on January 1, 1995, as part of the Maryland Bacterial Invasive Disease Surveillance project. The Bacterial Invasive Disease Surveillance project is a component of the multistate Emerging Infections Program that is coordinated by the Centers for Disease Control and Prevention, Atlanta, Ga. The BMA consists of the jurisdictions of Baltimore city and Baltimore, Anne Arundel, Carroll, Harford, and Howard counties, and accounts for half of Maryland's population of 5 million. The surveillance case definition is the isolation of *S pneumoniae* from a normally sterile body fluid, such as blood or cerebrospinal fluid, from a BMA resident of any age. All acute care hospitals in the BMA participate, as do other microbiology laboratories that process blood cultures. For each eligible case, the hospital infection control professional completes a 1-page case report form, which includes demographic (eg, sex and race) and brief clinical information, and the bacterial isolate is submitted for species confirmation and further testing. The options for the question about race include white, black, American Indian or Alaska Native, Asian or Pacific Islander, not specified, and unknown. Chart reviews to obtain additional medical history were performed for all 233 adults 18 to 64 years old who were listed on the case report form as having no underlying medical conditions. Biweekly telephone calls are made to hospital infection control practitioners to ascertain cases not reported spontaneously. Microbiology laboratory audits to identify unreported cases are performed twice yearly by Bacterial Invasive Disease Surveillance staff by reviewing the laboratory records. Recurrent pneumococcal infection was defined as a second episode of infection during which *S pneumoniae* was isolated from a normally sterile body fluid that occurred at least 7 days after the first episode.

A person was considered to have an Advisory Committee for Immunization Practices (ACIP) indication for pneumococcal immunization if one of the following conditions was present: age of 65 years or older; chronic cardiовascular disease, including congestive heart failure and cardiomyopathy; chronic pulmonary disease, including chronic obstructive pulmonary disease and emphysema; diabetes mellitus; alcoholism; chronic liver disease; cerebrospinal fluid leaks; functional or anatomic asplenia; and conditions associated with immunodeficiency, including HIV infection, leukemia, lymphoma, Hodgkin disease, multiple myeloma, generalized malignant neoplasms, chronic renal failure, nephrotic syndrome, immunosuppressive therapy, and bone marrow or organ transplantation.  

STATISTICAL ANALYSIS

Age, race, and county-specific intercensus population estimates for Maryland for 1995 were obtained from the Centers for Disease Control and Prevention and the Maryland Department of Planning. County- and race-specific median annual family income data were derived from the 1990 census and were dichotomized into strata of less than $40,000 and greater than or equal to $40,000. Information on the number of cases of acquired immunodeficiency syndrome (AIDS) was obtained from the Maryland AIDS Administration. The number of persons living with AIDS was estimated by including all of the patients with AIDS diagnosed during or before 1995 who had not yet been reported as deceased. County-specific AIDS prevalence was based on the county of residence on the initial AIDS report. The prevalence of persons living with AIDS was determined for each demographic group (ie, white males, white females, black males, and black females) and age group in each of the 6 counties in the BMA. Cutoffs for AIDS prevalence strata were derived by using the tercile values of the prevalence values greater than 0. This resulted in the following strata: low AIDS prevalence, 0 to 44 AIDS cases per 100,000 population; intermediate, 45 to 200; and high, more than 200.

Data were analyzed with Epi Info version 6.04 (Centers for Disease Control and Prevention), SPSS for Windows 7.0 (SPSS Inc, Chicago, Ill), and SAS 6.12 (SAS Institute Inc, Cary, NC). The *χ*² and Kruskal-Wallis tests were used for the analysis of dichotomous and continuous variables, respectively. We performed a multivariate analysis to identify factors associated with increased rates of pneumococcal disease. We used Poisson regression analysis and the SAS GENMOD procedure. In our model, incidence of pneumococcal disease in specific population subgroups at the county level was the outcome (or dependent) variable. After assessment of the interaction among covariates, we assessed the independent effect of age (0-4, 5-19, 20-29, 30-44, 45-64, 65-year age categories), race (black, white), sex, AIDS prevalence (by tercile), and race-specific median household income on the rate of pneumococcal disease. Interaction terms for race and age, race and AIDS prevalence, and age and income were included in the model.

RESULTS

A total of 1412 cases were reported from January 1, 1995, through December 31, 1996. There were 615 patients (43.6%) classified as white, 766 (54.2%) as black, 4 (0.3%) as American Indian or Alaska Native, and 6 (0.4%) Asian, and race was not indicated for 21 (1.5%). Because there were too few individuals of other races to allow for a meaningful analysis, only whites and blacks were included in subsequent analyses. Seventy-nine percent of black patients resided in Baltimore city (Table 1). Among whites, a third of patients resided in Baltimore city and Baltimore County each, with the remaining patients residing in the 4 other BMA counties.

Among patients aged 18 years and older, the median age of blacks with invasive pneumococcal infections was 27 years younger than that of whites (*P*<.01) (Table 1). In addition, 57.1% of black adult patients were male vs 46.8% of white patients (*P*<.01). There were no differences in the clinical syndromes or the sterile body fluid from which *S pneumoniae* was isolated. Black patients 18 to 64 years old were more likely (72.4%) than whites (61.7%) to have an ACIP indication for pneumo-

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Recurrent pneumococcal infection was more common in black adults (3.0%) than in whites (0.8%) (P = .02) (Table 1). Of the 3 recurrent infections in children, all but 1 occurred in children with HIV infection. None of the 4 white adults with recurrent infection had identified HIV infection. Of the 17 black adults with recurrent infection, 11 (65%) were patients with identified HIV infection. In no instance was the interval between the first and subsequent episodes less than 14 days.

The overall average annual incidence of invasive pneumococcal infection among white and black residents of the BMA was 17.8 and 59.2 per 100,000 population, respectively (P < .01). The average annual incidence was 17.3 for white females, 18.3 for white males, 46.4 for black females, and 73.8 for black males (P < .01 for all comparisons between whites and blacks). Among children 0 to 4 years old, the average incidence was 147.9 for blacks and 42.6 for whites (relative risk, 3.5; P < .01) (Figure 1). The incidence in black men 40 to 49 years old was 115, 12 times the incidence in white men. The incidence in black women 20 to 49 years old ranged from 7 to 11 times higher than in white women of the same age. For both races, the average annual incidence for persons 20 years old or older was higher in Baltimore city than Baltimore County, which was in turn higher than the incidence in the other counties of the BMA.
To further explore geographic and demographic differences in pneumococcal disease burden, we addressed the independent role of several factors on the incidence of pneumococcal disease in population groups at the county level with the use of Poisson regression analysis. Rates of pneumococcal disease were strongly related to age, sex, race, median family income, and community AIDS prevalence (Table 3). With adjustment for the other factors, males had 1.4 times the pneumococcal incidence (95% confidence interval, 1.3-1.6). Although, by multivariate analysis, black race was associated with increased risk of pneumococcal disease among persons younger than 30 years, race was not an independent risk factor for pneumococcal disease in older persons after adjustment for AIDS prevalence and median income. In communities with higher AIDS prevalence, blacks did have significantly higher rates of pneumococcal disease. With adjustment for the other factors, children younger than 5 years and persons 30 years or older living in communities with low median family income had significantly higher pneumococcal rates.

Our exploration of the epidemiological characteristics of invasive pneumococcal disease in metropolitan Baltimore demonstrates major discrepancies between the current disease burden and the targets of active prevention programs. Although previous studies have reported a 3- to 5-fold higher risk of invasive pneumococcal infection among blacks,\textsuperscript{5-7,13-16} and identified the impact of the HIV epidemic and poverty on epidemiological characteristics of pneumococcal disease,\textsuperscript{21-23} the recent emphasis on improving adult immunization programs has primarily targeted elderly populations.\textsuperscript{18} We report dramatic racial differences in the age distribution of pneumococcal cases in adults in Baltimore. These differences appear to be, to a great extent, attributable to higher rates of HIV and poverty; the net effect of these factors is a shift in the burden of pneumococcal disease to a much younger population. The vast majority of black adults who develop pneumococcal disease do so before reaching age 65 years, suggesting that efforts to improve pneumococcal vaccination among the elderly will not be of benefit to most African Americans who develop pneumococcal disease. Although a higher proportion of nonelderly African Americans with pneumococcal disease did have an indication for pneumococcal vaccine compared with

### Table 3. Poisson Regression Model Showing Independent Relative Risks (95% Confidence Intervals [CIs]) for Invasive Pneumococcal Infection\textsuperscript{*}

<table>
<thead>
<tr>
<th>Age, y</th>
<th>Black vs White Race</th>
<th>Low vs High Income</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>1.6 (1.1-2.5)</td>
<td>2.2 (1.4-3.2)</td>
</tr>
<tr>
<td>5-19</td>
<td>3.1 (1.2-7.9)</td>
<td>1.2 (0.5-3.2)</td>
</tr>
<tr>
<td>20-29</td>
<td>3.6 (1.4-8.9)</td>
<td>2.1 (0.8-5.2)</td>
</tr>
<tr>
<td>30-44</td>
<td>1.5 (0.8-2.7)</td>
<td>6.7 (3.9-11.7)</td>
</tr>
<tr>
<td>45-64</td>
<td>1.3 (0.8-2.0)</td>
<td>3.3 (2.2-4.9)</td>
</tr>
<tr>
<td>&gt;65</td>
<td>1.0 (0.7-1.3)</td>
<td>1.6 (1.3-2.1)</td>
</tr>
</tbody>
</table>

\textsuperscript{*} The model included age, sex, race, prevalence of acquired immunodeficiency syndrome (AIDS), and median family income.

\textsuperscript{†} There was no interaction between AIDS prevalence and income.
whites, nearly 50% were patients with HIV infection, in whom pneumococcal infection is often a sentinel illness at which HIV infection is first recognized. Such patients may also be examined after immunological compromise has reduced the efficacy of pneumococcal vaccination.

Our multivariate analysis suggests that racial differences in pneumococcal disease rates are multifactorial. Areas with higher AIDS prevalence and low income had higher rates of disease. Patients with AIDS were reported to have a 100- to 300-fold higher risk of invasive infection than the general population, and low income may be a surrogate for crowding and access to medical care. Race and low income may also be surrogates for medical conditions other than HIV, such as diabetes, which are also risk factors for pneumococcal disease and occur more commonly among African Americans.

What are the implications of our study for pneumococcal immunization efforts? Our data indicate that increased efforts to provide pneumococcal vaccine to young adults in poor urban areas with a high HIV prevalence are needed. Despite the extraordinarily high pneumococcal incidence in young black adults, the independent association between low income and pneumococcal infection suggests that young white adults in these areas should also be the focus of immunization efforts. Although focusing immunization on adults with chronic medical conditions has been recommended for persons younger than 65 years, this approach alone may fail to have a substantial public health impact for several reasons. It is often difficult to elicit information on diagnosed risk factors at the time of encounters with the health care system. In addition, many patients with indications for pneumococcal vaccine do not access the health care system until they become ill, or do not have underlying medical conditions such as HIV infection diagnosed until they are seen with pneumococcal infection. Although information on the timing of HIV infection was not systematically collected, we incidentally noted in this study that HIV infection was first diagnosed during the admission for pneumococcal infection in 10 patients. With HIV infection and other risk factors, it is advantageous to immunize as early as possible because of the declining immunogenicity of the pneumococcal vaccine as the duration of HIV infection increases. Finally, the risk factor approach to the vaccine prevention of hepatitis B infection failed, which necessitated a shift in policy toward universal immunization.

The pneumococcal vaccine coverage in the United States has been estimated to be only 47% among white adults and 30% among black adults 65 years old and older, indicating substantial underutilization of vaccine, despite evidence that these vaccines are effective in immunocompetent adults older than 65 years and in patients with chronic medical conditions. More disconcerting is that immunization rates for adults younger than 65 years with chronic medical conditions are even lower. Achieving immunization of young adults in underserved communities is also likely to be difficult. Furthermore, the possible need for revaccination to overcome the limited duration of protection of current pneumococcal vaccines would need to be explored. Demonstration studies will be required to determine the optimal approach to delivering pneumococcal vaccine in this setting and the impact on the incidence of pneumococcal infection.

There are several limitations to our study that require mention. Our strict case definition required the isolation of S pneumoniae from a normally sterile body fluid, so we clearly underestimated the burden of clinically significant pneumococcal infection in the BMA. We did not collect information on pneumococcal immunization history; racial differences in disease incidence could have been accentuated by differences in race-specific pneumococcal immunization rates. Although this is likely to have occurred to some extent, it is unlikely to have contributed substantially to the observed race differences because of the poor utilization of pneumococcal vaccine in both groups. It is possible that we underestimated the black population in the BMA, the result of which would have been to overestimate the pneumococcal incidence in blacks. However, it has been estimated that the 1990 census missed at most 10% of black Americans.

In conclusion, our study demonstrates that young black adults in the BMA have extraordinarily high rates of invasive pneumococcal infection, that the vast majority of cases occur before the age of 65 years, and that nearly 25% do not have a recognized ACIP indication for pneumococcal immunization. These data indicate that full immunization of every person with risk factors for pneumococcal infection according to ACIP guidelines is needed. Additionally, these data suggest that other approaches are needed. In the long term, pneumococcal conjugate vaccines currently under investigation may play a role in prevention, either by inducing long-lasting immunity after infant vaccination or by enhancing the clinical efficacy of vaccination among immunocompromised adults. In the short term, pneumococcal disease prevention in inner-city populations not reached by current strategies is a pressing concern. Exploration of community-based approaches to immunizing all younger adults in high-incidence areas may lead to more effective strategies. However, the limited immunogenicity of polysaccharide vaccines in persons with advanced HIV infection and the limited duration of protection of polysaccharide vaccines in general underscore that there are no easy answers to this major public health problem.

Accepted for publication March 25, 1999.

This study was funded by the National Center for Infectious Diseases, Centers for Disease Control and Prevention, and the National Vaccine Program, both in Atlanta, Ga.

We thank the participating hospital infection control practitioners and microbiology laboratory personnel of the Maryland Emerging Infections Program in the Baltimore metropolitan area for identifying the pneumococcal cases and providing the bacterial isolates; Yvonne Dean-Hibbert and Jackie Hunger for assistance in conducting surveillance; Kim Holmes, RN, MS, CIC, for assistance with data collection; Jan Markowitz, PhD, for providing data on AIDS cases in the Baltimore metropolitan area; Althea Glenn for process-
ing the isolates; and Mauro Schechter, MD, PhD, and Lewis Kuller, MD, DrPH, for their thoughtful review of the manuscript.

Reprints: Lee H. Harrison, MD, Department of Epidemiology, University of Pittsburgh Graduate School of Public Health, 521 Parran Hall, 130 DeSoto St, Pittsburgh, PA 15261 (e-mail: lharriso@edc.gsph.pitt.edu).

REFERENCES


