INVASIVE PNEUMOCOCCAL DISEASE AND ANTIMICROBIAL SUSCEPTIBILITY PATTERNS FOR *STREPTOCOCCUS PNEUMONIAE* IN LOS ANGELES COUNTY, 1997-1999

BACKGROUND

Streptococcus pneumoniae, or pneumococcal, infection is a major cause of morbidity and mortality worldwide and is the leading cause of pneumonia, bacteremia, and meningitis in the United States. An effective polysaccharide vaccine is available which protects individuals from 23 pneumococcal types that cause over 90% of the infections in the US. A major drawback to this vaccine is that it does not protect children less than two years of age who are high risk for severe disease. According to the Centers for Disease Control and Prevention, a conjugate vaccine for use in this age group was approved in 2000 and results indicate that the vaccine is safe and induces primary and booster antibody responses in children less than two years of age.[1]

With the widespread use of antibiotics, the problem of drug-resistance has emerged. In a report by the Centers for Disease Control and Prevention Working Group on *S. pneumoniae*, their nationwide population-based surveillance system observed a 14% to 25% increase of penicillin-nonsusceptible *S. pneumoniae* isolates from 1993-1994 to 1997.[2] Other classes of antimicrobials such as the macrolides, cephalosporins, and fluoroquinolones have also developed resistance.

In September 1995, the Los Angeles County (LAC) Department of Health Services (DHS) initiated a laboratory- and hospital infection control-based surveillance system for ten diseases and conditions including invasive pneumococcal disease (IPD). IPD was selected to measure the incidence in LAC, track antibiotic resistance patterns, potentially monitor immunization efficacy, and target vaccine coverage.

The following is a description of the trends of reported IPD and *S. pneumoniae* antimicrobial susceptibility patterns from 1997 to 1999 in individuals residing in LAC (excluding the cities of Long Beach and Pasadena).

METHODS

Demographic and laboratory information including antimicrobial susceptibility results were obtained from the surveillance system established by LAC-DHS. Cases were defined as LAC residents with a positive isolate for *S. pneumoniae* from a normally sterile site collected

in 1997, 1998, or 1999. To calculate incidence rates, 1997-1999 population data were derived from the 1990 census using sophisticated estimation techniques developed by the LAC Urban Research Section. Antimicrobial susceptibility was determined by disk diffusion or dilution diffusion. It was assumed that minimum inhibitory concentration (MIC) breakpoints utilized by participating laboratories were based on the National Committee for Clinical Laboratory Standards. The breakpoints for selected antimicrobial agents are illustrated in Table 1. An isolate of *S. pneumoniae* was considered nonsusceptible to an antimicrobial agent if the results indicated intermediate or high-level resistance. Data were entered in Microsoft Access 97 and analyzed using Epi-Info 6.04 and SAS Version 6.12.

Table 1. MIC Breakpoints for Selected Agents Used to Treat *Streptococcus pneumoniae* Infection

Antimicrobial	**MIC (μg/mL)** Susceptible	Intermediate	Resistant
Penicillin	≤0.06	0.12-1.0	≥2.0
3rd generation Cephalosporin (cefotaxime,ceftriaxone,cefuroxime)	≤0.5	1.0	≥2.0
Erythromycin	≤0.25	0.5	≥1.0
Trimethoprim-sulfamethoxazole (TMP-S)	≤0.5/9.5	1/19-2/38	≥4/76

DATA ANALYSIS

The annual incidence of reported IPD increased 13% from 8.7 cases per 100,000 (n=818) in 1997 to 9.8 cases in 1999 (n=894). As indicated by Table 2, the male-to-female rate ratios indicated that there were slightly more males who acquired IPD for all three years. In 1999, the mean age for IPD cases was 47 years (median 53 years, range 1 day to 100 years) which was comparable to that observed in 1997 and 1998.

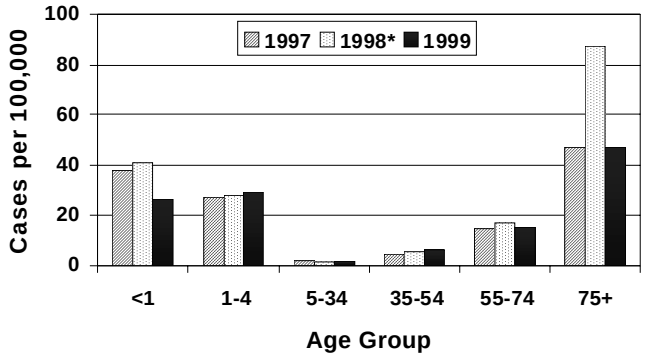
Table 2. Characteristics of IPD Cases Los Angeles County, 1997-1999

Characteristics*	**1997** (N=818)	**1998** (N=814)	**1999** (N=894)
Male:Female Ratio	1.10:1.00	1.06:1.00	1.03:1.00
Age (years)			
Mean	44	44	47
Median	49	50	53
Range	1 mo.-106	<1 day–102	1 day–100
Case fatality rate	15% (59/383)	15% (53/346)	17% (55/328)
Culture site			
Blood	771 (95%)	776 (96%)	836 (94%)
CSF/CSF&Blood	30 (4%)	28 (3%)	44 (5%)
Other	13 (2%)	10 (1%)	14 (2%)

*Data not available on race/ethnicity and characteristic information not available for all cases.

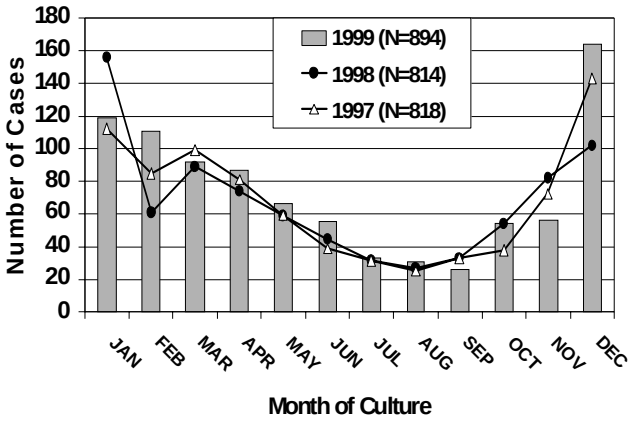
From 1997 to 1999, the case fatality rate increased from 15% to 17% (Table 2). The validity of this data is questionable since the outcome status of approximately 58% of the cases for 1997, 1998, and 1999 were reported as "unknown". The case fatality rates may be underestimated since reporting of positive isolates is required within 24 hours. Unless the patient is severely ill, many times the final outcome of current infection has not yet been determined. The distribution of cases by culture site varied little from 1997 to 1999. Mortality was not significantly associated with having meningitis in 1998 (odds ratio [OR]: 2.53; 95% confidence interval [CI]: .61 to 7.77, p=.10) and 1999 (OR: 1.57; 95%CI: .39 to 4.61, p=.34).

Figure 1. Incidence Rates of IPD by Age
Los Angeles County, 1997-1999



*1998 population data estimated using a different technique than previous years.

Figure 2. IPD Cases By Month of Culture
Los Angeles County, 1997-1999

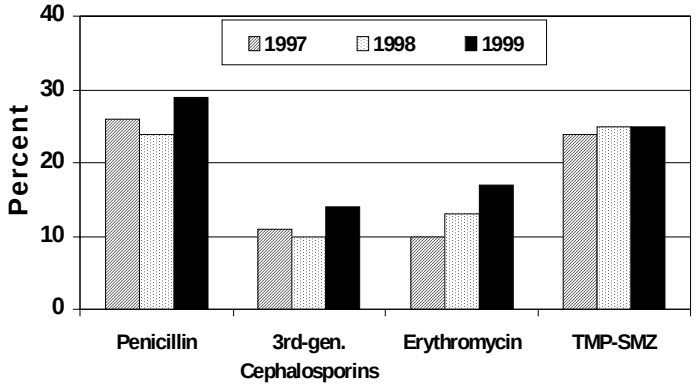


For 1999, the highest age-specific incidence rates occurred in children under five years and adults 75 years and over, which is common with IPD (Figure 1). Comparing 1999 to 1998, the age-specific incidence rates decreased appreciably in the less-than-one-year (-36%) and 75-years-and-over (-46%) age groups. However, in the 75 and older age group, the 1998 rate was skewed because different methodology was utilized to estimate the 1998 population data than in 1997 and 1999.

The IPD cases for 1997-1999 followed the typical seasonal pattern, peaking in late winter then gradually declining through spring. In February and December 1999, the frequency of cases was substantially higher than the previous year (Figure 2). In January 1998 and

December 1999, the observed increases mirrored severe respiratory illness seasons in the winter of 1997-1998 and 1999-2000.

Figure 3. Proportion of IPD Cases Nonsusceptible* to Selected Antimicrobial Agents Los Angeles County, 1997-1999



*Nonsusceptible includes intermediate and high-level resistance.

In 1999, South District had the highest rate of IPD at 13.68 per 100,000 population (24 cases) followed by Southwest with a rate of 11.71 (43) and San Fernando with 11.05 (41). The West and West Valley District had the highest number of cases (59 for both). From 1997-1999, San Fernando District was among the top four districts with the highest crude and age-adjusted rates (using the age groups in Figure 1). From 1997 to 1999, the age-adjusted rates were highest in Harbor District (17.12 per 100,000) and San Fernando District (15.12 per 100,000) for 1997 followed by South District (14.27 per 100,000) for 1999.

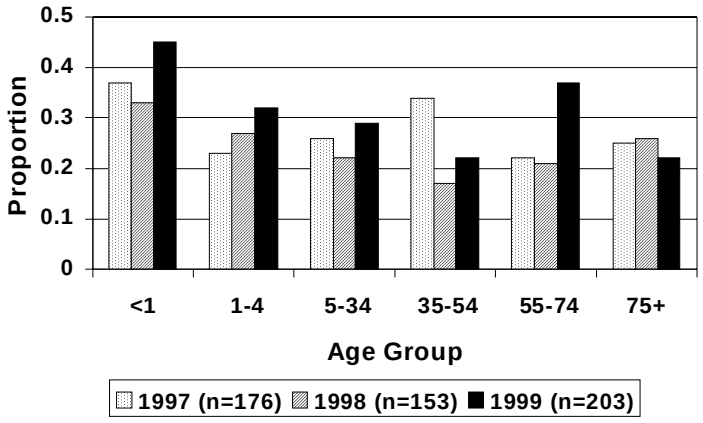
The proportion of penicillin nonsusceptible *Streptococcus pneumoniae* (PNSP) isolates has fluctuated from 26% in 1997, down to 24% in 1998, and up to 29% in 1999 (Figure 3). From 1997 to 1999, the percent of cases nonsusceptible to erythromycin and third generation cephalosporins increased while trimethoprim-sulfamethoxazole (TMP-SMZ) remained about the same.

In 1999, the proportion of PNSP cases was higher than previous years among all age groups except adults 35-54 and 75 years and over. The largest increase (76%) of penicillin resistance in 1999 was in adults 55-74 year old age group (Figure 4). Overall, infants less than one year have the greatest proportion of penicillin nonsusceptibility for the three-year period. In 1999, there was a significant difference between age groups regarding penicillin nonsusceptibility (χ^2=17.64, p-value=.003) but the previous two years were not significant. From the data collected, mortality was not significantly associated with penicillin nonsusceptibility.

DISCUSSION

LAC observed a trend of increasing incidence and antibiotic nonsusceptibility for cases of IPD from 1997 to 1999. Extremes of age were identified as risk factors for acquiring IPD and possibly for penicillin nonsusceptibility. Resistance was not associated with increased mortality.

Figure 4. PNSP Cases by Age
Los Angeles County, 1997-1999



With the current surveillance system, we are limited in describing the epidemiology of IPD because important factors such as race/ethnicity, clinical presentation, medical risk factors, outcome and other possible risk factors (exposure to a nursing home, daycare center, etc.) are not available or are unreliable. To overcome some of the shortcomings of the data, a retrospective case-control study was initiated in 1999 using hospital discharge data to examine possible risk factors associated with acquiring penicillin- nonsusceptible IPD in hospitalized patients in LAC. This study will finish in October 2000. Also, in conjunction with the release of the conjugate vaccine, we plan to use the IPD surveillance system to assess the vaccine efficacy among children aged less than two years.

With the widespread overuse of antibiotics, drug-resistance will continue to increase as a major public health threat. Through educational programs targeting the community and medical establishment about proper antibiotic usage, DHS will be able to reduce the growing numbers of drug-resistant pathogens. In addition, with the newly developed pneumococcal conjugate vaccine for very young children and the pneumococcal polysaccharide vaccine for the elderly and high-risk individuals, vaccination campaigns can help decrease the incidence of penicillin-susceptible and resistant invasive pneumococcal disease.

REFERENCES

1. Centers for Disease Control and Prevention: Prevention of pneumococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1997;46:1-24.
2. enters for Disease Control and Prevention: Geographic variation in penicillin resistance in Streptococcus pneumoniae--selected sites, United States, 1997. *MMWR* 1999;48:656-661.