Epidemiology of Invasive Group B Streptococcal Disease in the United States, 1999-2005

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IN THE 1970s, GROUP B STREPTOCOCCUS emerged as the leading cause of sepsis and meningitis in the first week of life.1 By 1996, a perinatal disease prevention strategy based on intrapartum chemoprophylaxis was issued by the Centers for Disease Control and Prevention (CDC), the American College of Obstetricians and Gynecologists, and the American Academy of Pediatrics.2-4 Two recommended approaches for identifying chemoprophylaxis candidates were widely adopted in the United States and resulted in substantial declines in disease in infants younger than 7 days (also known as early onset disease).5,6

In 2002, revised guidelines recommended antenatal culture-based screening as the optimal method for identifying chemoprophylaxis candidates.7 Disease trends following the release of these guidelines have not yet been well studied. In addition to illness in the first week of life, group B streptococcus also causes invasive disease in older infants, pregnant women, children and young adults with underlying medical conditions, and older adults. Cases outside the perinatal risk period account for nearly 90% of the national burden of disease,8 and the proportion of patients who die in these age groups, particularly the elderly, are higher than for

Context  Group B streptococcus is a leading infectious cause of morbidity in newborns and causes substantial disease in elderly individuals. Guidelines for prevention of perinatal disease through intrapartum chemoprophylaxis were revised in 2002. Candidate vaccines are under development.

Objective  To describe disease trends among populations that might benefit from vaccination and among newborns during a period of evolving prevention strategies.

Design and Setting  Analysis of active, population-based surveillance in 10 states participating in the Active Bacterial Core surveillance/Emerging Infections Program Network.

Main Outcome Measures  Age- and race-specific incidence of invasive group B streptococcal disease.

Results  There were 14,573 cases of invasive group B streptococcal disease during 1999-2005, including 1348 deaths. The incidence of invasive group B streptococcal disease among infants from birth through 6 days decreased from 0.47 per 1000 live births in 1999-2001 to 0.34 per 1000 live births in 2003-2005 (P < .001), a relative reduction of 27% (95% confidence interval [CI], 16%-37%). Incidence remained stable among infants aged 7 through 89 days (mean, 0.34 per 1000 live births) and pregnant women (mean, 0.12 per 1000 live births). Among persons aged 15 through 64 years, disease incidence increased from 3.4 per 100,000 population in 1999 to 5.0 per 100,000 in 2005 (χ² for trend, 57; P < .001), a relative increase of 48% (95% CI, 32%-65%). Among adults 65 years or older, incidence increased from 21.5 per 100,000 to 26.0 per 100,000 (χ² for trend, 15; P < .001), a relative increase of 20% (95% CI, 8%-35%). All 4882 isolates tested were susceptible to penicillin, ampicillin, and vancomycin, but 32% and 15% were resistant to erythromycin and clindamycin, respectively. Serotypes Ia, Ib, II, III, and V accounted for 96% of neonatal cases and 88% of adult cases.

Conclusions  Among infants from birth through 6 days, the incidence of group B streptococcal disease was lower in 2003-2005 relative to 1999-2001. This reduction coincided with the release of revised disease prevention guidelines in 2002. However, the disease burden in adults is substantial and increased significantly during the study period.

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newborns. Moreover, black race is associated with an increased incidence of invasive group B streptococcal disease across the age spectrum.

Current prevention strategies may be inadequate to address racial disparities in incidence of early onset disease. Furthermore, strategies to prevent disease after the first week of life have yet to emerge. New prevention strategies are therefore critical, and polysaccharide-protein conjugate vaccines have been developed for each of the major disease-causing group B streptococcus capsular types (Ia, Ib, II, III, and V), and their safety and immunogenicity have been evaluated in healthy nonpregnant adults and pregnant women.

The epidemiology of group B streptococcal disease is dynamic, and continued surveillance to monitor trends across age groups is necessary. For example, an increase in disease incidence among nonpregnant adults has been documented in past decades, but whether that trend has continued is unknown. In addition, the long-term impact of widespread intrapartum chemoprophylaxis against perinatal disease on incidence trends and antimicrobial susceptibilities is still unfolding. Finally, current information on disease-causing serotypes is critical to optimize conjugate vaccine formulations for group B streptococcus. To address these issues, we evaluated trends and characteristics among nearly 15,000 cases of laboratory-confirmed invasive group B streptococcal disease identified by population-based, multistate surveillance over a recent 7-year period (1999-2005).

METHODS
Surveillance

Data were collected through the Active Bacterial Core surveillance (ABCs)/Emerging Infections Program Network, a collaboration between the CDC, state health departments, and universities. The ABCs methods have been described elsewhere. Briefly, participating states conduct active, population-based, laboratory surveillance for invasive disease due to group B streptococcus and other pathogens. A group B streptococcus case is defined as isolation of the organism from a normally sterile site (for example, blood or cerebrospinal fluid [CSF]) in a surveillance area resident. Cases with group B streptococcus isolated from a sterile site in a stillborn infant—or from the placenta, amniotic fluid, or conceptus in the context of a fetal death—were classified as maternal, since the infant was not live born. For the case of liveborn infants, placental and amniotic isolates were not considered sterile sites. Cases were actively ascertained by routine contact with all laboratories processing sterile-site specimens for surveillance area residents. Periodic laboratory audits were performed to ensure completeness of reporting. Epidemiologic and clinical data, including patient deaths, were captured by medical record review using a standardized form. However, cause of death (as determined, for example, at autopsy) was not captured.

For case individuals younger than 1 year, areas under continuous surveillance for group B streptococcus from 1999-2005 included all of Connecticut, Maryland, and Minnesota, and parts of California (3 Bay Area counties), Georgia (20-county Atlanta area), New York (15-county Rochester and Albany areas), Oregon (Clackamas, Multnomah, and Washington counties), and Tennessee (5 urban counties). After the start of the study period, surveillance was expanded to cover 6 additional urban counties in Tennessee (since August 1, 1999), the 5-county Denver area in Colorado (since July 1, 2000), and all of Georgia and New Mexico (since January 1, 2004). For individuals 1 year or older, the same surveillance areas applied with the following exceptions: in Connecticut and Colorado (5-county Denver area), data were collected for only 1999-2003; in Georgia, surveillance was limited to the 20-county Atlanta area throughout 1999-2005. Overall, in 2005, surveillance covered a population of 27,350,255 persons and 454,476 live births.

Definitions

Neonatal cases were categorized as early onset if group B streptococcus was isolated from infants younger than 1 week or as late-onset if infants were 7 through 89 days old. Neonatal cases were classified as fatal when a liveborn infant with invasive disease died; stillbirths and spontaneous abortions were not counted as neonatal fatalities. Preterm birth was defined as birth at less than 37 weeks’ gestation and was captured for cases younger than 90 days. After early infancy, cases were classified as pediatric (90 days-14 years and not pregnant), pregnancy-associated, or adult (≥15 years and not pregnant).

Clinical syndromes were assigned based on physician diagnoses recorded in the medical record; for meningitis, all cases of group B streptococcus isolated from CSF were also included. Cases could be categorized into multiple syndromes with the exception of bacteremia without focus, which was defined as a positive blood culture result in the absence of another clinical syndrome. Race was determined by medical record review (and thus may represent self-identification or clinician identification) and categorized by ABCs personnel.

Group B Streptococcus Isolates

Two reference laboratories (CDC and Minnesota Department of Health) performed group B streptococcus serotyping and susceptibility testing on a subset of isolates. Isolates were serotyped with rabbit antisera to group B streptococcus capsular polysaccharide types Ia, Ib, and II through VIII by latex agglutination. When latex tests were indeterminate, the Lancefield method was used. When both tests were indeterminate, the isolate was classified as nontypeable. Isolate susceptibility to penicillin, ampicillin, erythromycin, clindamycin, and vancomycin was determined by broth dilution using interpretive standards established by the Clinical and Laboratory Standards Institute. Inducible clindamycin resistance was not evaluated.

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Statistical Analysis

Incidence calculations for case individuals 90 days or older used National Center for Health Statistics bridged-race postcensal population estimates as denominators for the years 2000-2005 and US Bureau of Census estimates for 1999. Incidence data for those younger than 90 days and for pregnancy-associated cases used the number of live births to surveillance area residents as determined by State Vital Records or National Vital Statistics Reports from 1999-2004; 2004 data were used for the 2005 denominator.

To ensure comparability over time, annual incidence calculations excluded New Mexico, since data from this state were only available during 2004-2005; for cases 1 year or older, Connecticut, Colorado, and areas of Georgia outside the 20-county Atlanta area were excluded, since data for these areas were not collected in 2004-2005. Other analyses comparing case characteristics over time were similarly restricted. Analyses of isolate characteristics over time were similarly restricted. Analyses of isolate characteristics were limited to areas for which at least 50% of case isolates were serotyped annually, which included Georgia, New York, and Oregon (1999-2005); Colorado and Minnesota (2001-2005); Maryland (2003-2005); and New Mexico (2005). All other analyses used all available data.

Risk ratios (RRs) and confidence intervals (CIs) are presented for categorical data. To evaluate annual trends over time, \( \chi^2 \) for trend was calculated after confirming no departures from linearity. Percentage change was used to compare incidence from a baseline period to a later period (eg, before vs after the release of early onset disease guidelines or first vs last year of study period). Percentage change was calculated as \( \frac{[(\text{later rate} - \text{baseline rate})/\text{baseline rate}] \times 100}{\text{to assess seasonal variability, a 3-month moving average was used to calculate monthly incidence over time. For all incidence calculations, cases with unknown race were distributed according to those with known race for each surveillance site within 8 age categories (<1 year, 1 year, 2-4 years, 5-17 years, 18-34 years, 35-49 years, 50-64 years, and ≥65 years). For all other statistics (for example, the proportion of individuals who died, by race), race as recorded was used. For national estimates of cases, age- and race-specific incidence of disease were applied from the aggregate surveillance area to the age and racial distribution of the US population or live births as appropriate. Data were analyzed using SAS version 9 (SAS Institute Inc, Cary, North Carolina); \( P < .05 \) was considered statistically significant.

TABLE 1. Number of Cases of Invasive Group B Streptococcal Disease, Number of Deaths, and Incidence by Age in Surveillance Areas (1999-2005) and the United States as a Whole (2005)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Birth-6 d</th>
<th>7-89 d</th>
<th>1-14 y</th>
<th>≥15-64 y</th>
<th>≥65 y</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observed counts for surveillance areas, 1999-2005</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of cases</td>
<td>1232</td>
<td>1036</td>
<td>90</td>
<td>6496</td>
<td>5576</td>
<td>14,573b</td>
</tr>
<tr>
<td>No. of deathsc</td>
<td>83</td>
<td>48</td>
<td>11</td>
<td>472</td>
<td>730</td>
<td>1,348d</td>
</tr>
<tr>
<td>Estimated incidence and projected counts for United States, 2005e</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence</td>
<td>0.35/1000 live births</td>
<td>0.33/1000 live births</td>
<td>0.22/100,000 population</td>
<td>4.6/100,000 population</td>
<td>25.3/100,000 population</td>
<td>7.2/100,000 population</td>
</tr>
<tr>
<td>No. of cases</td>
<td>1425</td>
<td>1375</td>
<td>124</td>
<td>9207</td>
<td>9308</td>
<td>21,439</td>
</tr>
<tr>
<td>No. of deathsc</td>
<td>63</td>
<td>46</td>
<td>8</td>
<td>557</td>
<td>1067</td>
<td>1741</td>
</tr>
</tbody>
</table>

aIncludes 409 pregnant women.
bTotal number of cases includes 143 individuals aged 90 days to 12 months.
cOutcome was known for 99% of surveillance individuals younger than 1 year and 95% of those 1 year or older; thus, the observed and projected number of deaths is a minimum and should not be used to generate direct estimates of case-fatality rates.
dTotal number of deaths includes 4 deaths among individuals aged 90 days to 12 months.
eAge- and race-specific incidence of disease was applied from the aggregate surveillance area to the age and racial distribution of the US population or US live births as appropriate.

RESULTS

From 1999 through 2005, surveillance identified 14,573 cases of invasive group B streptococcal disease. TABLE 1 shows the standardized incidence and estimated national burden of disease and death associated with group B streptococcus by age group for the United States in 2005, when an estimated 21,500 cases occurred, including 1700 fatalities. The observed incidence among surveillance area residents in 2005 was 7.5 per 100,000 population; among individuals with known outcome (2027/2056 [98.6%]), 160 (7.9%) died.

Among all 2056 case individuals identified in 2005, 1119 (54%) were white, 566 (28%) were black, 51 (2%) were Asian or Pacific Islander, 33 (<2%) were American Indian or Alaska Native, and 287 (14%) were of unknown race. Incidence of invasive...
group B streptococcal disease was 12.8 per 100,000 among blacks, 6.5 per 100,000 among whites, and 5.1 per 100,000 among all other races combined. Overall incidence among blacks was 2 times higher than among whites (RR, 2.0; 95% CI, 1.8-2.2) and at least 1.5 times higher in every age category (Figure 1A). The magnitude of the association was greatest for neonates (RR for early onset disease, 4.0; 95% CI, 2.9-5.5; RR for late-onset disease, 5.1; 95% CI, 3.7-7.0) and pregnant women (RR, 5.0; 95% CI, 2.9-8.7) and least for adults 15 years or older (RR, 2.0; 95% CI, 1.5-2.6). Finally, the proportion who died was significantly higher for blacks than whites among individuals younger than 7 days and those 45 years or older (Figure 1B).

**Early Onset Disease**

Surveillance identified 1232 cases of early onset disease. Disease incidence decreased 27% (95% CI, 16%-37%) after the 2002 release of revised early onset disease prevention guidelines, from 0.47 per 1000 live births in 1999-2001 to 0.34 per 1000 live births in 2003-2005 (Figure 2). However, successive small increases in incidence occurred in 2004 and 2005 (Figure 2). These increases were driven primarily by black infants, in whom there was a significant increase in incidence from 0.52 per 1000 in 2003 to 0.89 per 1000 in 2005 ($\chi^2$ for trend, 7.9; $P = .005$). From 2003-2005, white infants born at term were the only group in whom...
incidence trended toward a decline, from 0.23 per 1000 to 0.16 per 1000 ($\chi^2$ for trend, 3.1; $P = .08$).

Among infants with early onset disease, 72% had positive sterile-site culture results within the first 24 hours of life, and 95% had positive results within the first 48 hours. Most isolates were from blood (96%) or CSF (4%). The most commonly identified syndromes were bacteremia without focus (83%), pneumonia (9%), and meningitis (7%). Overall, among 1224 infants for whom outcome was known, 83 (6.8%) died. The proportion who died varied by year (range, 5%-9%), although no trend over time was observed. It also varied by syndrome, from 9% (10/114) for pneumonia to 4% (3/81) for meningitis. Among infants with early onset disease, 23% were born preterm. From 1999-2005, the percentage of infants with early onset disease who were born preterm increased from 18% to 33% ($\chi^2$ for trend, 16; $P < .001$); however, the incidence of early onset disease among preterm infants did not increase significantly. The median gestational age of infants born preterm was 31 weeks (first and third quartiles, 26 and 35 weeks), and the risk of death among preterm cases was nearly 8 times that of term cases (preterm: 19.9% died; term: 2.6% died [RR, 7.7; 95% CI, 4.9-12.3]).

Late-Onset Disease

Surveillance identified 1036 cases of late-onset disease. Incidence remained generally stable, averaging 0.34 per 1000 live births. Similar to early onset disease, incidence of late-onset disease increased slightly during 2003-2005 (Figure 2).

The median age at first positive culture result for infants with late-onset disease was 37 days (first and third quartiles, 23 and 53 days). Isolates were predominantly obtained from blood (79%) or CSF (19%). When compared with early onset cases, a higher proportion of late-onset cases manifested as meningitis (27% vs 7%; $\chi^2$ test, $P < .001$). Other disease manifestations included bacteremia without focus (65%), bacteremic cellulitis (3%), and pneumonia (3%). Overall, the proportion of infants with known outcome who died was 4.7% (48/1027). By syndrome, the proportion who died was 3% (23/669) for bacteremia without focus, 18% (5/28) for pneumonia, and 7% (19/279) for meningitis. Among the 69% (718/1036) of late-onset cases for whom gestational age was known, 52% (373/718) were born preterm, and that proportion was stable over time. Among infants with late-onset disease that occurred in 2003-2005 (for whom information on gestational age was >90% complete), the median gestational age of infants born preterm was 30 weeks (first and third quartiles, 27 and 34 weeks), and the risk of death for preterm infants was more than 3 times that of term infants (preterm: 5.3% died; term: 1.4% died [RR, 3.7; 95% CI, 1.1-13.0]).

Pregnancy-Associated Disease

A total of 409 invasive group B streptococcal infections occurred in pregnant teenagers and women (0.12 per 1000 live births; yearly range: 0.11-0.14 per 1000 live births) (Figure 2). The median age at onset was 28 years (first and third quartiles, 22 and 33 years). Half (203/409) of these cases were associated with infection of the upper genital tract, placenta, or amniotic sac, resulting in fetal death. Other manifestations included bacteremia without focus (31%), endometritis without fetal death (8%), chorioamnionitis without fetal death (4%), pneumonia (2%), and puerperal sepsis (2%). Endocarditis was observed in 1 case.

A total of 211 (52%) isolates from pregnancy-associated cases were obtained from blood; 187 (46%) from the placenta, amniotic fluid, or conceptus; 8 (2%) from pelvic tissue; and the remainder from other sterile sites. One individual with pregnancy-associated disease died. Among those for whom pregnancy outcome was known (368/409 [90%]), 61% had a spontaneous abortion or stillborn infant, 30% had infants without apparent illness, 5% had live-born infants who developed clinical infections, and 4% had induced abortions. Most pregnancy-related cases (330/409 [81%]) occurred in the absence of additional underlying conditions; 79 occurred with at least 1 additional underlying condition or risk factor including, in order of decreasing frequency, smoking, asthma, diabetes, obesity, and alcohol or drug abuse.

Childhood Disease

Surveillance identified 233 cases of invasive group B streptococcal disease in children aged 90 days through 14 years. Incidence of pediatric disease was 0.56 per 100 000 (yearly range, 0.37-0.73 per 100 000), and no sustained change over time was observed. Sixty-one percent (143/233) of these cases occurred in children aged 90 days through 12 months, and the remaining third (90/233) were evenly distributed among children aged 1 through 14 years. Among all 233 children, bacteremia without focus was the most common syndrome, accounting for 58% of the cases, followed by meningitis (19%), pneumonia (7%), septic arthritis (5%), and peritonitis (4%). The proportion with known outcome who died was lower among children aged 90 days through 12 months (4/132 [3%]) than among those aged 1 through 14 years (11/85 [13%]). Only 11% (16/143) of children aged 90 days through 12 months had an underlying condition (excluding preterm birth), but 44% (40/90) of children aged 1 through 14 years had at least 1 condition. Among these 40 older children, the most common underlying factors were neurologic disorders (25%), immunosuppressive conditions (23%), asthma (23%), malignancy (15%), and renal disease (13%).

Adult Disease

Surveillance identified 6087 cases among persons aged 15 through 64 years (and not pregnant) and 5576 among those 65 years or older (me-
dian age overall, 63 years; first and third quartiles, 50 and 77 years). Disease incidence increased significantly during the study period (FIGURE 3). Among persons aged 15 through 64 years, incidence increased from 3.4 per 100 000 population in 1999 to 5.0 per 100 000 in 2005 ($\chi^2$ for trend, 57; $P < .001$), a relative increase of 48% (95% CI, 32%-65%); among those 65 years or older, incidence increased from 21.5 per 100 000 to 26.0 per 100 000 ($\chi^2$ for trend, 63; $P < .001$), a relative increase of 20% (95% CI, 8%-35%). These values translate to a 32% (95% CI, 22%-43%) increase in the overall incidence of adult disease, which increased from 6.0 per 100 000 in 1999 to 7.9 per 100 000 in 2005 ($\chi^2$ for trend, 63; $P < .001$). The proportion with known outcome who died was highest in the oldest age groups (Figure 1B). Seasonal variability was evident, with distinct peaks occurring each year during the later summer months (FIGURE 4). The same seasonal periodicity was observed for both age groups (data not shown).

Among all 11,663 adults, 81% were diagnosed by blood cultures alone and the remainder from synovial fluid (7%), bone (6%), peritoneal fluid (3%), pleural fluid (1%), CSF (1%), and other sites (<1%). The most common clinical syndromes were bacteremia without focus (48%), bactereemic cellulitis (22%), pneumonia (11%), osteomyelitis (9%), arthritis (9%), peritonitis (3%), and abscess (3%). Less common manifestations included endocarditis/pericarditis, meningitis, necrotizing fasciitis, and toxic shock–like syndrome. In 2005, underlying conditions and factors included diabetes mellitus (41%), heart disease (36%), and malignancy (17%). Other common factors associated with cases among adults included smoking, obesity, neurologic disorders, renal disease, immunosuppressive conditions, liver disease, and lung disease. Altogether, nearly 88% of adult cases had at least 1 underlying condition.

Serotypes and Antimicrobial Susceptibility

In the 7 surveillance areas that collected isolates during all or part of the study period, 8153 cases occurred; serotyping was performed on 6156 (76%) of these and susceptibility testing on 4882 (60%). Individuals for whom isolates were and were not serotyped did not differ with respect to age, sex, or fatalities. Isolates collected from blood or CSF were more likely to be serotyped than isolates collected from other sterile sites ($\chi^2$ test, $P < .001$).

Among 528 early onset cases with serotype testing, the most frequent...
serotypes were Ia (30%), III (28%), V (18%), and II (13%). The distribution of serotypes for 172 pregnancy-associated cases was similar. In contrast, among 469 late-onset cases with testing, serotype III accounted for half (239/469 [51%]) of all cases; the remainder were predominately serotypes Ia (24%) and V (14%). In 4987 nonpregnant pediatric and adult cases, serotype V predominated, accounting for 31% of cases, followed by serotypes Ia (24%), II (12%), and III (12%). Serotype distribution in 2005 was similar to the overall distribution described above.

Table 2 shows the proportion of cases associated with death or meningitis by serotype and age at onset. In separate regression models that adjusted for age at onset, cases caused by serotype Ia had a significantly higher risk of death than did those caused by any other serotype (RR, 1.3; 95% CI, 1.1-1.6), while those caused by serotype III were associated with an increased risk of meningitis as compared with those caused by other serotypes (RR, 1.6; 95% CI, 1.3-2.1).

All 4882 isolates submitted for susceptibility testing were susceptible to penicillin and ampicillin; 12 isolates, except for vancomycin; 1566 (32%) were resistant to erythromycin; and 757 (15%) were resistant to clindamycin. Virtually all (751/757 [99%]) isolates that were resistant to clindamycin were also resistant to erythromycin. Erythromycin resistance was highest among serotype V isolates as compared with other serotypes (50% vs 26%; \( \chi^2 \) test, \( P<.001 \)).

**COMMENT**

The ABCs system, now covering a catchment of approximately 26 million residents, has provided the United States with a powerful tool for guiding and evaluating group B streptococcus prevention strategies. Following the issuance of the first consensus group B streptococcal disease prevention guidelines, this network documented a 68% decline in incidence of early onset group B streptococcal disease, from 1.7 per 1000 live births in 1993 to 0.6 per 1000 live births in 1998.\(^5\) Guidelines issued in 2002 that recommended universal antenatal screening for group B streptococcus were predicted to further reduce incidence to 0.32 per 1000 live births.\(^24\) Our analysis indicates that incidence of early onset disease in the years following the guidelines decreased to 0.34 per 1000 live births, very close to the predicted impact. Although robust for detecting changes in disease trends over time, our data underestimate the true burden of perinatal disease because the ABCs system focuses on culture-proven disease—thus missing cases of clinical sepsis—and excludes stillbirths and spontaneous abortions, which may be caused by group B streptococcal infection.

Although the overall incidence of early onset disease in 2003-2005 was lower than in preceding years, small successive increases were observed in 2004 and 2005. Whether this trend continues remains to be seen. The significant increase in incidence among black infants in this period is particularly concerning and requires investigation. Additional studies including cases and noncases for comparison are needed to clarify the driving factors.\(^23\)

Analyses of late-onset disease incidence trends in the 1990s suggested that intrapartum chemoprophylaxis does not prevent late-onset disease.\(^5\) Our analysis of late-onset disease trends from 1999-2005 further supports this conclusion. Future years of surveillance will be important to assess whether the upturn in incidence in 2003-2005 is sustained.

Prior analyses suggested that intrapartum chemoprophylaxis against early onset disease also protected against ma-

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**Table 2.** Proportion of Cases Associated With Death or Meningitis by Serotype and Age at Onset, 1999-2005

<table>
<thead>
<tr>
<th>Serotype, No. (%)</th>
<th>Early Onset Disease (Birth Through 6 d)</th>
<th>Late-Onset Disease (7-89 d)</th>
<th>Pediatric and Adult Disease (&gt;90 d and Not Pregnant)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases, No. (% of total)(^b)</td>
<td>Fatal cases (% of serotype)(^c)</td>
<td>Fatal cases (% of serotype)(^c)</td>
</tr>
<tr>
<td>Ia</td>
<td>157 (29.7)</td>
<td>10 (6.4)</td>
<td>8 (7.2)</td>
</tr>
<tr>
<td>Ib</td>
<td>37 (7.0)</td>
<td>2 (5.4)</td>
<td>1 (3.2)</td>
</tr>
<tr>
<td>II</td>
<td>69 (13.1)</td>
<td>3 (4.3)</td>
<td>0</td>
</tr>
<tr>
<td>III</td>
<td>146 (27.7)</td>
<td>6 (4.2)</td>
<td>5 (7.7)</td>
</tr>
<tr>
<td>V</td>
<td>93 (17.6)</td>
<td>8 (8.6)</td>
<td>5 (7.7)</td>
</tr>
<tr>
<td>Other(^a)</td>
<td>26 (4.9)</td>
<td>1 (3.8)</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>528 (100)</td>
<td>30 (5.7)</td>
<td>19 (4.1)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>121 (25.8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cases, No. (% of total)(^b)</td>
<td>Meningitis cases (% of serotype)(^c)</td>
<td>Meningitis cases (% of serotype)(^c)</td>
</tr>
<tr>
<td>Ia</td>
<td>1203 (24.1)</td>
<td>12 (7.6)</td>
<td>22 (1.8)</td>
</tr>
<tr>
<td>Ib</td>
<td>434 (8.7)</td>
<td>2 (5.4)</td>
<td>16 (3.7)</td>
</tr>
<tr>
<td>II</td>
<td>605 (12.1)</td>
<td>1 (1.4)</td>
<td>6 (1.0)</td>
</tr>
<tr>
<td>III</td>
<td>611 (12.3)</td>
<td>17 (11.6)</td>
<td>11 (1.8)</td>
</tr>
<tr>
<td>V</td>
<td>1563 (31.3)</td>
<td>3 (3.2)</td>
<td>3 (3.2)</td>
</tr>
<tr>
<td>Other(^a)</td>
<td>571 (11.4)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>4987 (100)</td>
<td>35 (6.6)</td>
<td>35 (6.6)</td>
</tr>
</tbody>
</table>

\(^a\)Includes IV, V, VII, VIII, and nontypeable serotypes.

\(^b\)Denominator = number of cases per age stratum.

\(^c\)With known outcome.
ternal pregnancy-associated disease.}\textsuperscript{3,27} Pregnancy-associated disease incidence did not show further declines during the present study period; however, current incidence (0.11-0.14 per 1000 live births) remains well below that of the preprevention era (0.29 per 1000 live births).\textsuperscript{3}

In contrast to neonatal and pregnancy-associated disease trends, the incidence of group B streptococcal disease among nonpregnant adults increased 32\% during 1999-2005, reaching 7.9 per 100 000 in 2005. This value represents an increase over rates reported in a series of population-based studies in metropolitan Atlanta, which documented an incidence of 2.4 per 100 000 in 1982-1983, 4.4 per 100 000 in 1989-1990, and 5.9 per 100 000 in 1992-1993.\textsuperscript{28-30} The high prevalence of underlying medical conditions among infected adults, documented in previous studies,\textsuperscript{31,32} was again seen here. Some investigators have speculated that the increasing incidence of invasive disease in nonpregnant adults may be related to increases in the prevalence of underlying medical conditions such as diabetes or to an aging population. Although we were unable to evaluate the former, we note that the age distribution of nonpregnant adults remained constant throughout. Factors such as the increasing burden of chronic conditions are likely important over the long term but may not fully explain the relatively rapid increase observed during our short 7-year study period. The seasonality in adult disease with peaks in the late summer months has not been established previously and further suggests that factors in addition to age or chronic conditions affect the incidence of disease. Possibilities include seasonal environmental factors affecting the occurrence of skin and soft tissue infections, since those were prominent among adults with diabetes, or a possible enteric source of disease exposure.\textsuperscript{33,34}

Previous studies identified black race as an independent risk factor for both early onset\textsuperscript{24,35} and late-onset disease.\textsuperscript{35,36} Collectively, these studies suggest that the effects of race cannot be fully explained by prematurity, birth weight, maternal age, adequacy of prenatal care, or socioeconomic status, although the latter has not been well measured. Others have observed that black women are more frequently heavily colonized with group B streptococcus than nonblack women\textsuperscript{37} and that the risk of neonatal group B streptococcal disease is greater in infants born to heavily colonized mothers.\textsuperscript{38} This association may explain the higher disease incidence among black infants,\textsuperscript{3} but direct evidence is lacking. Among adults (\textgeq15 years) in our surveillance system, disease incidence was 2 times higher in black than in white populations—a value that is similar to adult black-to-white rate ratios of 1.5 reported in 1982-1983\textsuperscript{28} and 2.0 reported in 1989-1990\textsuperscript{29} and 1998.\textsuperscript{3} Thus, although the overall incidence of adult disease has increased substantially since the 1980s, relative incidence for black vs white adults has remained constant.

In general, our data confirm that the burden of group B streptococcal disease remains disproportionately high among black populations for all age groups and pregnant women. Similar disparities are observed for other streptococcal pathogens.\textsuperscript{39,40} Reasons for these disparities are not yet understood, and our surveillance system is limited in its ability to evaluate possible explanations in that only case data are captured, and potentially important cofactors such as socioeconomic status and access to health care are missed. Furthermore, race data are collected by medical record review, which includes clinician-identified race determinations of unknown accuracy.

In the United States in 2005, group B streptococcus caused an estimated 21 500 cases of invasive disease and 1700 deaths. Serotype data indicate that a pentavalent conjugate vaccine that included types Ia, Ib, II, III, and V could potentially prevent up to 96\% of neonatal disease and 88\% of pediatric, adult, and pregnancy-associated disease, which translates to approximately 19 000 cases in 2005. These findings are consistent with other recent studies in North America, which report that the same 5 types caused 95\% to 100\% of early onset cases, 91\% to 98\% of late-onset cases, 8\% to 97\% of adult cases, and 91\% to 100\% of pregnancy-associated cases.\textsuperscript{10,41-44} In addition to serotype prevalence, virulence is another important consideration for vaccine formulation. We found modest positive associations between serotype Ia and fatality and between serotype III and meningitis after controlling for age at onset. Otherwise, we found that age, rather than the infecting serotype, was the dominant predictor of outcome.

Despite increasing antibiotic use, all isolates tested were susceptible to penicillin and ampicillin (the first-line agents for intrapartum prophylaxis against early onset disease) and vancomycin. However, 32\% of isolates were resistant to erythromycin, clindamycin, or both. This observation underscores the importance of performing susceptibility testing among pregnant women colonized with group B streptococcus who are at high risk for penicillin anaphylaxis before administering erythromycin or clindamycin for intrapartum prophylaxis to ensure activity against the isolate.

Although further reductions in incidence of early onset disease were seen following the release of revised guidelines for intrapartum chemoprophylaxis, this strategy is unlikely to eliminate the remaining burden of pregnancy-associated and early onset disease—especially in preterm infants, who bear the highest risk of death—and cannot prevent fetal infections and losses occurring before the intrapartum period. Moreover, widespread use of prophylactic antibiotics introduces selection pressure for resistance not only among group B streptococcus but also among other sepsis pathogens. Finally, this strategy does not address late-onset disease or the substantial and growing burden of disease among adults. For these reasons,
maternal group B streptococcus vaccination trials should be a public health priority, followed by expanded vaccine development to target disease among elderly and younger adults with chronic underlying conditions.

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REFERENCES


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Everyone is aware of the vast difference between a number of men as a chance collection of individuals and the same number as an organized group or community. A community has purpose and plan, and there is in us an almost instinctive recognition of the connection between unity and strength.
—J. Glenn Gray (1913-1977)