MAJOR ARTICLE

Increasing Burden of Invasive Group B Streptococcal Disease in Nonpregnant Adults, 1990–2007

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Background. Group B *Streptococcus* (GBS), traditionally considered to be a neonatal pathogen, is an important cause of morbidity and mortality among older adults and among those with underlying medical conditions. We used population-based surveillance to examine trends in adult GBS disease during the period 1990–2007 and to describe the epidemiology of adult GBS disease to guide prevention efforts.

Methods. Active Bacterial Core surveillance was conducted in selected counties in 10 US states. A case was defined as isolation of GBS from a normally sterile site in a nonpregnant resident of a surveillance area who was ⩾18 years of age. Rates were calculated using US Census data. Demographic and clinical information was abstracted from medical records. Serotyping and susceptibility testing were performed on isolates collected from a subset of case patients.

Results. A total of 19,512 GBS cases were identified in nonpregnant adults during 1990–2007 (median patient age, 63 years); the incidence of adult GBS disease doubled from 3.6 cases per 100,000 persons during 1990 to 7.3 cases per 100,000 persons during 2007 ($P < .001$). The mean difference in incidence between black and white persons was 4.6 cases per 100,000 persons (range, 3.1 cases per 100,000 persons during 1991 to 5.8 cases per 100,000 persons during 1999). Common clinical syndromes in 2007 included bacteremia without focus (39.3%), skin and/or soft-tissue infection (25.6%), and pneumonia (12.6%). Most (88.0%) GBS cases in adults had ⩾1 underlying condition; diabetes was present in 44.4% of cases. Serotypes V, Ia, II, and III accounted for 80.8% of infections during 1998–1999 and 78.5% of infections during 2005–2006.

Conclusions. Invasive GBS disease in nonpregnant adults represents a substantial and increasing burden, particularly among older persons, black persons, and adults with diabetes. Prevention strategies are needed.

Invasive group B *Streptococcus* (GBS), a leading cause of illness and death among infants in the first week of life and of infection in pregnant women, also causes significant morbidity and mortality among nonpregnant adults [1]. Among adults, older age, black race, and underlying medical conditions are frequently associated with higher rates of invasive GBS disease [2–11]. Common presentations of GBS disease in adults include skin and/or soft-tissue infection, bacteremia without focus, pneumonia, and osteomyelitis; serious clinical syndromes, such as meningitis, streptococcal toxic shock syndrome, and endocarditis, are rare but are often associated with considerable morbidity and mortality [1, 3–6, 8, 10–12]. The case fatality rate is markedly higher among adults than among neonates [1, 4–8, 10, 12, 13].

GBS emerged rapidly in the United States during the 1970s to become the leading cause of neonatal sepsis. Several reports in recent years suggest that the incidence of GBS disease is also increasing among adults [4, 5, 7–10, 13–15]. The driving force behind this change has not been fully explained, and recent trends in disease

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incidence have not been characterized. To date, there are no guidelines for the prevention of adult GBS disease; vaccines in development may hold promise [16, 17].

We reviewed data from 18 years of active, population-based surveillance for invasive GBS infection in a large, multistate catchment area to characterize trends over time in the incidence of GBS disease among nonpregnant adults. We also describe the burden and epidemiology of disease in adults from 2007 to guide the development of prevention efforts.

METHODS

Population-based surveillance. Active, population- and laboratory-based surveillance for invasive GBS disease was conducted from 1 January 1990 through 31 December 2007 as part of Active Bacterial Core surveillance (ABCs), Emerging Infection Program Network, as described elsewhere [18]. The surveillance area included California (3 counties since 1990), Colorado (5 counties during 2001–2003), Connecticut (statewide during 1996–2003), Georgia (8 counties since 1990; 12 additional counties since 1997), Maryland (statewide since 1992), Minnesota (7 counties since 1996; statewide since 1999), New Mexico (statewide since 2004), New York (7 counties since 1998; 8 additional counties since 1999), Oregon (3 counties since 1996), and Tennessee (4 counties since 1990; 1 additional county since 1995; 6 additional counties since 2000). The population under surveillance ranged from 5,397,861 adults in 1990 to 21,147,657 adults in 2007 (representing 2.2% of the US adult population in 1990 and 7.0% in 2007). Epidemiologic and clinical information was abstracted from medical records. Outcome of illness was based on patient status at the time of hospital discharge; no information was collected on whether death was attributed to GBS infection. Underlying conditions were collected at all surveillance areas during 1998–2007, with the exception of Georgia and Maryland. Georgia only collected underlying conditions during 2000–2007, and Maryland only collected them during 2001–2007. Regular laboratory audits were conducted to identify cases missed during routine surveillance.

Definitions. A case of invasive disease was defined as isolation of GBS from a normally sterile site (e.g., blood or cerebrospinal fluid) in a surveillance area resident aged $\geqslant$18 years who was not pregnant or $\leqslant$30 days postpartum on the date that a culture-positive specimen was obtained. Disease was recurrent if the case patient had $\geqslant$2 cultures positive for GBS that were performed $\geqslant$30 days apart. Nosocomial disease was defined as the isolation of GBS from a specimen from a hospitalized case patient >2 days after hospital admission. Case patients were considered to be nursing home residents if they had a long-term care facility address at the time when a culture sample was obtained.

Specimen collection and testing. Sterile site specimens were collected for 464 (76.2%) of 609 cases from 3 ABCs areas during 1998–1999 (Georgia, New York, and Oregon) and for 1933 (78.7%) of 2457 cases from 6 ABCs areas during 2005–2006 (Georgia, Maryland, Minnesota, New Mexico, New York, and Oregon). Serotyping was performed at the Centers for Disease Control and Prevention (CDC; Atlanta, GA) by latex agglutination with use of CDC-prepared rabbit antisera to 9 GBS capsular polysaccharide types (Ia, Ib, and II–VIII). The Lancefield method was used for isolates that could not be typed by latex agglutination. Isolates were characterized as nontypeable when both latex and Lancefield methods yielded indeterminate results [19, 20]. Susceptibility to ampicillin, cefotaxime, clindamycin, erythromycin, levofloxacin, penicillin, tetracycline, and vancomycin was determined for isolates from the period 2005–2006 by reference broth microdilution at the CDC or at the Minnesota Department of Health Laboratory (St. Paul, MN) with use of interpretive standards established by the Clinical and Laboratory Standards Institute [21].

Analytic methods. Disease incidence was calculated using observed case counts as numerators and using surveillance population estimates from the US Census Bureau (1990–1999) or race-bridged, postcensal population estimates from the National Center for Health Statistics (2000–2007) as denominators. Because the population under surveillance expanded over time and because age and race are strongly associated with GBS incidence [3, 5, 6, 9–12, 15, 22], we compared observed incidence for each year of analysis with (1) age- and race-adjusted incidence standardized to the US population for the corresponding year and (2) age- and race-adjusted incidence standardized to the 1990 US population. Because the 3 methods for calculating incidence yielded similar results, observed incidence is reported throughout the study. Observed incidence for consistent surveillance areas over time did not differ significantly from incidence calculated for the total area under surveillance for each year; therefore, annual observed incidence was calculated using all available data for each year. Trends over time were assessed using the χ^2 linearity test and test for trend; when data were not linear, we reported the percent change in incidence or proportion. The case-fatality rate was calculated using the proportion of cases with known outcome as the denominator. Race was classified as white, black, or other; cases in patients with unknown race (226 of 1546 cases in 2007) were distributed on the basis of known racial distribution within each ABCs site and age group. Pearson's χ^2, 2-tailed Fisher's exact test, and risk ratios were used for the comparison of proportions; $P < .05$ and 95% confidence intervals (CIs) that excluded 1.0 were considered to be statistically significant.

RESULTS

Trends over time. A total of 19,512 cases of GBS disease in nonpregnant adults were identified from 1990 through 2007.

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The median case patient age was 63 years (range, 18–105 years); 19.2% of case patients were aged ⩾80 years. During the study period, the incidence of GBS disease more than doubled, increasing from 3.6 cases per 100,000 persons in 1990 to 7.3 cases per 100,000 persons in 2007 ($P < .001$). Incidence increased in all adult age groups; the largest increases were observed among case patients aged 65–79 years (change of 114.7% from 1990 to 2007) and among case patients aged 40–64 years (change of 92.7% from 1990 to 2007) (figure 1*A*). During 1990–2007, the mean difference in incidence between black and white case patients was 4.6 cases per 100,000 persons; rate differences ranged from a minimum of 3.1 cases per 100,000 persons in 1991 to a maximum of 5.8 cases per 100,000 persons in 1999 (figure 1*B*). The case-fatality rate decreased from 23.7% in 1990 to 8.8% in 1994 ($P < .001$, by test for trend), increased to 13.0% in 1995, and decreased to 7.5% in 2007 ($P < .001$, by test for trend from 1995 to 2007).

The proportion of case patients with underlying diabetes increased significantly from 36.5% in 1998 to 44.4% in 2007 ($P < .001$, by linear test for trend). However, the proportion of case patients with such underlying conditions as cancer, heart failure, and atherosclerotic cardiovascular disease remained relatively stable (figure 2).

The distribution of serotypes also remained stable over time, with serotypes V, Ia, II, and III accounting for 375 (80.8%) of 464 isolates from the period 1998–1999 and 1517 (78.5%) of 1933 isolates from the period 2005–2006. The most notable change was the emergence of serotype IV; overall, the proportion of serotype IV isolates increased from 0.2% during 1998–1999 to 5.7% during 2005–2006 ($P < .001$). Other changes included a decrease in the proportion of serotype III isolates (from 15.9% during 1998–1999 to 11.4% during 2005–2006; $P < .01$) and a decrease in the proportion of nontypeable isolates (from 9.1% during 1998–1999 to 6.3% during 2005–2006; $P = .032$).

Descriptive epidemiology, 2007. The 1546 cases of GBS disease identified in 2007 (table 1) occurred predominantly in white persons. The median age of case patients was 62 years (range, 18–105 years); 16.9% of case patients were aged ⩾80 years. After standardization to the US population and adjust-

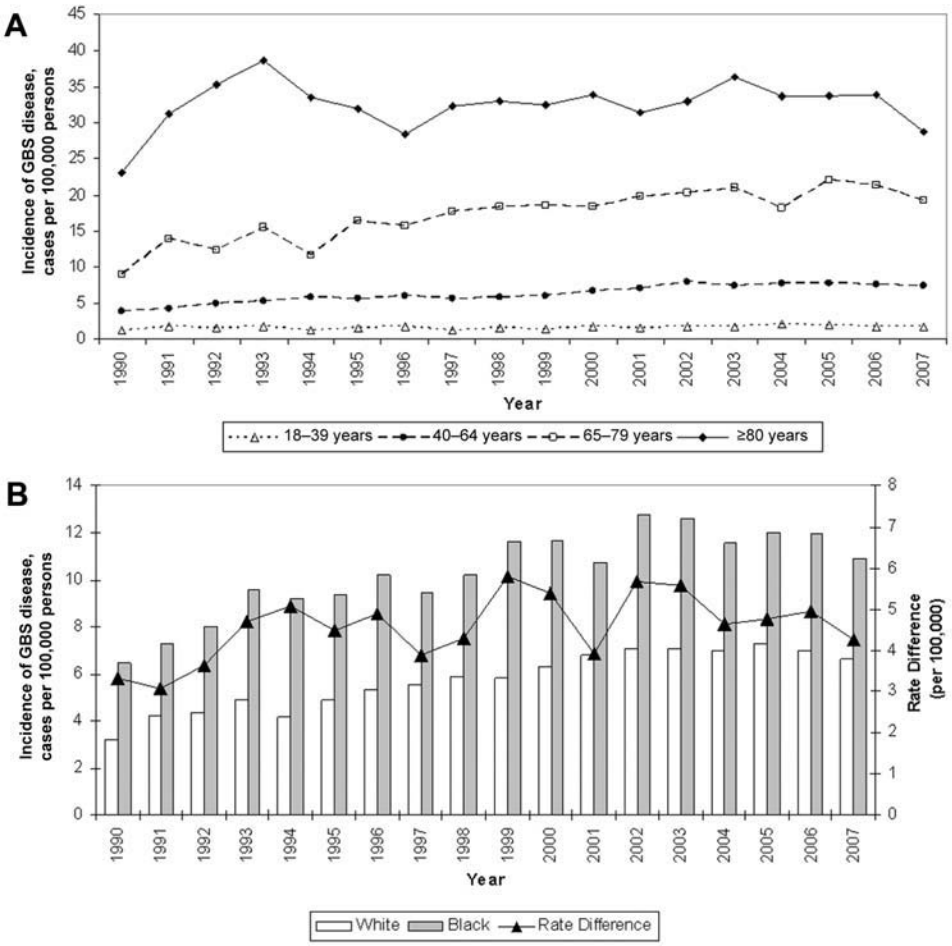

Figure 1. Incidence of invasive group B streptococcal (GBS) disease among nonpregnant adults, by age *(A)* and by race *(B)*, 1990–2007.

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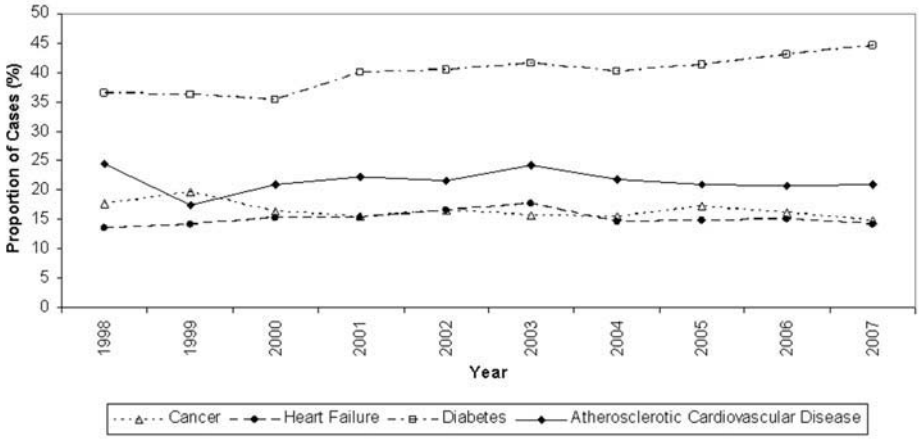

Figure 2. Leading underlying medical conditions among nonpregnant adults with invasive group B streptococcal disease, 1998–2007.

ment for race and age, an estimated 16,700 cases of invasive GBS disease and 1200 deaths occurred in nonpregnant adults in the United States during 2007.

GBS was isolated primarily from blood (82.0%), bone (6.0%), and joint (5.4%) specimens. Polymicrobial sterile-site infections occurred in 117 (7.6%) of 1546 cases; 68.4% of such infections were in the blood, and 18.8% were in bone. The most common additional pathogens included *Staphylococcus aureus* (46.2%), coagulase-negative staphylococcus (12.8%), and *Escherichia coli* (10.3%). Polymicrobial infections occurred in 80 (6.3%) of 1268 cases of GBS bacteremia.

Disease presented primarily as bacteremia without focus, skin and/or soft-tissue infection, pneumonia, osteomyelitis, and joint infection (table 1). Bacteremia without focus and pneumonia were more common among case patients aged ⩾65 years, and osteomyelitis, skin and/or soft-tissue infection, peritonitis, meningitis, and necrotizing fasciitis were more common among young adults. A higher proportion of cases of GBS disease presented as skin and/or soft-tissue infection among case patients aged 40–64 years (29.9%) than among case patients aged 18–39 years (19.1%; $P = .007$) and case patients aged ⩾65 years (22.6%; $P = .002$). Associated osteomyelitis was reported in 44 (11.1%) of 395 case patients with skin and/or soft-tissue infection. Such concurrent infections were 2.5 times more likely to occur in case patients aged 40–64 years than in case patients aged ⩾65 years (14.4% vs. 5.8%; $P = .009$).

Approximately 5% of invasive GBS cases represented recurrent GBS disease; the median time between collection of the first and second culture-positive specimens was 674 days (range, 31–4340 days). Cases of recurrent disease were significantly more likely than cases of nonrecurrent disease to present as skin and/or soft-tissue infection (43.8% vs. 24.6%; $P < .001$).

Of the 1546 cases, 1360 (88.0%) involved ⩾1 underlying medical condition; this finding was similar by race: 339 (91.6%) of 370 cases in black patients and 792 (89.3%) of 887 cases in white patients involved ⩾1 underlying condition. Compared with cases not involving underlying medical conditions ($n = 84$), cases involving ⩾1 underlying condition tended to occur in older persons (median age, 62 years vs. 55 years; $P < .01$); however, the 2 groups did not differ with regard to case-fatality rate (among those with known outcome; 8.1% [109 of 1344 cases] vs. 3.6% [3 of 84 cases]; $P = .13$) or sex (male: 59.9% vs. 51.2%; $P = .11$). Diabetes was the most common underlying condition among all age groups (44.4%); the prevalence of diabetes was similar among cases in black and white patients (48.9% vs. 43.2%; $P = .06$). Other common underlying conditions are shown in table 1. Cases in patients with underlying diabetes ($n = 687$) were more likely than those in patients without underlying diabetes ($n = 859$) to present with skin and/or soft-tissue infection (222 cases [32.3%] vs. 173 cases [20.1%]), osteomyelitis (103 [15.0%] vs. 43 [5.0%]), and necrotizing fasciitis (15 [2.2%] vs. 2 [0.2%]) but were less likely to present with bacteremia without focus (234 [34.1%] vs. 373 [43.4%]) and meningitis (5 [0.7%] vs. 19 [2.2%]; $P < .05$, for all comparisons).

Among the 1933 invasive GBS isolates evaluated during 2005–2006, type V was the most prevalent serotype (29.2%), followed by types Ia (24.3%), II (13.5%), and III (11.4%) (table 2). When stratified by age, serotype V was the most common serotype, except in the group of case patients aged 18–39 years. All tested isolates were susceptible to ampicillin, cefotaxime, penicillin, and vancomycin. Resistance to tetracycline, erythromycin, and clindamycin was common (83.3%, 40.0%, and 20.2%, respectively). The prevalence of resistance to levofloxicin was low (1.2%). The prevalence of erythromycin resistance was highest among serotype V isolates (56.5%).

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Table 1. Characteristics of nonpregnant adults with invasive group B streptococcal (GBS) disease, 2007.

Variable	Cases, by age group				P[a]
	All (n = 1546)	18–39 years (n = 157)	40–64 years (n = 699)	⩾65 years (n = 690)	
Male sex	915 (59.2)	91 (58.0)	427 (61.1)	397 (57.5)	.383
Age, median years	62	33	54	77	
Race					
White	887 (57.4)	67 (42.7)	371 (53.1)	449 (65.1)	<.001
Black	370 (23.9)	50 (31.8)	215 (30.8)	105 (15.2)	
Other	63 (4.1)	7 (4.5)	22 (3.1)	34 (4.9)	
Unknown	226 (14.6)	33 (21.0)	91 (13.0)	102 (14.8)	
Case fatality[b]	114 (7.5)	7 (4.6)	39 (5.6)	68 (10.0)	.003
Hospitalized[c]	1393 (90.1)	135 (86.0)	628 (89.8)	630 (91.3)	.125
Nosocomial disease	129 (8.3)	15 (9.6)	67 (9.6)	47 (6.8)	.148
Nursing home resident[d]	160 (10.9)	8 (5.7)	36 (5.4)	116 (17.6)	<.001
Recurrent disease	73 (4.7)	6 (3.8)	50 (7.2)	17 (2.5)	<.001
Clinical syndrome[e]					
Bacteremia without focus	607 (39.3)	58 (36.9)	251 (35.9)	298 (43.2)	.017
Skin and/or soft-tissue infection	395 (25.5)	30 (19.1)	209 (29.9)	156 (22.6)	.001
Pneumonia[f]	194 (12.5)	16 (10.2)	72 (10.3)	106 (15.4)	.011
Osteomyelitis	146 (9.4)	19 (12.1)	86 (12.3)	41 (5.9)	<.001
Joint infection[g]	121 (7.8)	10 (6.4)	53 (7.6)	58 (8.4)	.657
Abscess	61 (3.9)	11 (7.0)	30 (4.3)	20 (2.9)	.047
Endocarditis	46 (3.0)	5 (3.2)	24 (3.4)	17 (2.5)	.561
Peritonitis	42 (2.7)	5 (3.2)	25 (3.6)	12 (1.7)	.101
STSS	24 (1.6)	3 (1.9)	8 (1.1)	13 (1.9)	.499
Meningitis	24 (1.6)	7 (4.5)	13 (1.9)	4 (0.6)	.001
Necrotizing fasciitis	17 (1.1)	4 (2.5)	11 (1.6)	2 (0.3)	.013
Other[h]	48 (3.1)	9 (5.7)	16 (2.3)	23 (3.3)	.072
Unknown	20 (1.3)	2 (1.3)	6 (0.9)	12 (1.7)	.348
Underlying condition[i]					
⩾1 Condition	1360 (88.0)	120 (76.4)	626 (89.6)	614 (89.0)	<.001
Diabetes mellitus	687 (44.4)	42 (26.8)	343 (49.1)	302 (43.8)	<.001
ASCVD	325 (21.0)	4 (2.5)	96 (13.7)	225 (32.6)	<.001
Obesity	259 (16.8)	22 (14.0)	161 (23.0)	76 (11.0)	<.001
Cancer	229 (14.8)	8 (5.1)	87 (12.4)	134 (19.4)	<.001
Heart failure and/or congestive heart failure	220 (14.2)	8 (5.1)	57 (8.2)	155 (22.5)	<.001
Renal disease[j]	204 (13.2)	15 (9.6)	73 (10.4)	116 (16.8)	.001
Current smoker	194 (12.5)	30 (19.1)	124 (17.7)	40 (5.8)	<.001
COPD	151 (9.8)	1 (0.6)	57 (8.2)	93 (13.5)	<.001
Neurologic disease[k]	149 (9.6)	13 (8.3)	54 (7.7)	82 (11.9)	.026
Immunosuppression[l]	142 (9.2)	17 (10.8)	79 (11.3)	46 (6.7)	.009

(continued)

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Table 1. ***(Continued.)***

Variable	Cases, by age group				
	All (n = 1546)	18–39 years (n = 157)	40–64 years (n = 699)	⩾65 years (n = 690)	P[a]
Liver disease[m]	108 (7.0)	6 (3.8)	71 (10.2)	31 (4.5)	<.001
Alcoholism	102 (6.6)	6 (3.8)	72 (10.3)	24 (3.5)	<.001
Asthma	68 (4.4)	4 (2.5)	38 (5.4)	26 (3.8)	.156
Substance abuse	31 (2.0)	11 (7.0)	19 (2.7)	1 (0.1)	<.001

NOTE. Data are no. (%) of cases, unless otherwise indicated. ASCVD, atherosclerotic cardiovascular disease; COPD, Chronic obstructive pulmonary disease (includes emphysema and chronic bronchitis); STSS, streptococcal toxic shock syndrome.

[a] For the comparison of results among the groups of cases in patients aged 18–39 years, 40–64 years, and ⩾65 years.

[b] The numbers of cases with known outcomes (154 for 18–39 years, 691 for 40–64 years, and 681 for ⩾65 years) were used as denominators.

[c] The median length of stay for hospitalized case patients was 7 days.

[d] The numbers of cases in patients with known residence status (140 for 18–39 years, 668 for 40–64 years, and 660 for ⩾65) were used as denominators.

[e] Case patients may have had >1 clinical syndrome (overall, 168 (10.9%) had >1 clinical syndrome); clinical syndromes shown were recorded in case patients' medical records.

[f] Includes empyema.

[g] Includes septic arthritis (n = 119) and bursitis (n = 2).

[h] Includes endometritis, urinary tract infection, pericarditis, otitis media, septic abortion, central line infection, cholangitis, septic shock, sinusitis, panniculitis, thrombophlebitis, enteritis, endophthalmitis, colitis, and perforated diverticulitis.

[i] The most common underlying conditions. Case patients may have had >1 underlying condition; conditions shown were recorded in patients' medical records.

[j] Includes, but is not limited to, dialysis, pyelonephritis, chronic renal insufficiency, and chronic kidney disease.

[k] Includes, but is not limited to, cerebral vascular accident, neuropathy, Parkinson disease, multiple sclerosis, paraplegia, encephalopathy, seizure disorder, and dementia.

[l] Includes immunosuppressive therapy, AIDS, human immunodeficiency virus infection, organ transplantation, immunoglobulin deficiency, and splenectomy and/or asplenia.

[m] Includes, but is not limited to, cirrhosis, liver disease, autoimmune or chronic hepatitis, and sclerosing cholangitis.

DISCUSSION

GBS has emerged as an important cause of invasive infection in nonpregnant adults. This multistate, population-based analysis confirms that the incidence of adult GBS disease has continued to increase, more than doubling during the 18-year study period to 7.3 cases per 100,000 persons in 2007. Consistent with previous studies, underlying medical conditions, particularly diabetes, are overrepresented among cases [3–5, 8, 10, 11, 23]. Disease rates are highest among older case patients [3, 5, 24] and black case patients [5, 9, 15]. Race may be a surrogate for other factors, such as socioeconomic status, access to health care, and underlying medical conditions, that increase the risk of disease [5, 9, 22]. Among adults aged ⩾65 years, the incidence of GBS disease (22 cases per 100,000 persons) is 2.2 times higher than the incidence of invasive group A streptococcal disease (9.9 cases per 100,000 persons) and approaches the incidence of *Streptococcus pneumoniae* infection (39.3 cases per 100,000 persons) [25, 26].

Reasons for the increasing incidence of GBS disease among nonpregnant adults are not well understood, and disease surveillance alone is not sufficient to establish the underlying cause. However, our data allowed us to exclude some hypotheses. Because the increase in incidence over time persisted when yearly incidence rates were standardized to the US population during 1990 and when adults were stratified into smaller age groups, the aging of the population is unlikely to have been the primary cause. In addition, it is unlikely that the increasing incidence was associated with the emergence or expansion of new or virulent serotypes. Serotype V, first reported in 1985 [27], may have contributed to an increase in the incidence of disease shortly after its emergence, but it was already established in our surveillance population in 1990. Moreover, although the incidence of GBS disease has continued to increase in recent years, serotype IV was the only serotype for which the proportion increased significantly; however, this serotype accounted for only a small proportion of disease.

The increasing prevalence of adults with chronic medical conditions [4, 8, 9, 11] remains the most plausible explanation for our observed doubling in the incidence of adult GBS disease. The prevalence of diabetes (44.4%) among case patients with GBS disease is markedly higher than that in the US population (10.7% among US adults aged ⩾20 years) [28]. In addition, the prevalences of diagnosed diabetes and obesity have more than doubled among US adults since the early 1980s [29–31]. In contrast, the incidences of cancer and cardiovascular disease, 2 other leading underlying conditions among adult case patients with GBS disease, have not increased in recent years [32, 33]. Because diabetes is a known risk factor for GBS disease among adults [3, 5, 10], trends in the incidence of GBS disease may continue to parallel trends in the prevalence of diabetes in the

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Table 2. Serotype distribution of invasive group B streptococcal disease in nonpregnant adults, by age, erythromycin resistance, and underlying conditions, 2005–2006.

	No. (%) of isolates									
	Age group						Underlying condition			
Serotype	All (n = 1933)	18–39 years (n = 169)	40–64 years (n = 808)	65–79 years (n = 585)	⩾80 years (n = 371)	Erythromycin resistance[a]	Diabetes	ASCVD	Obesity	Cancer
Ia	470 (24.3)	47 (27.8)	197 (24.4)	135 (23.1)	91 (24.5)	178 (38.8)	183 (38.9)	99 (21.1)	69 (14.7)	86 (18.3)
Ib	182 (9.4)	15 (8.9)	83 (10.3)	51 (8.7)	33 (8.9)	39 (21.8)	77 (42.3)	35 (19.2)	27 (14.8)	37 (20.3)
II	261 (13.5)	28 (16.6)	99 (12.3)	86 (14.7)	48 (12.9)	91 (35.7)	110 (42.1)	64 (24.5)	43 (16.5)	49 (18.8)
III	221 (11.4)	20 (11.8)	89 (11.0)	77 (13.2)	35 (9.4)	59 (27.4)	77 (34.8)	40 (18.1)	44 (19.9)	37 (16.7)
IV	110 (5.7)	17 (10.1)	56 (6.9)	26 (4.4)	11 (3.0)	31 (28.7)	42 (38.2)	23 (20.9)	20 (18.2)	15 (13.6)
V	565 (29.2)	35 (20.7)	229 (28.3)	173 (29.6)	128 (34.5)	314 (56.5)	240 (42.5)	114 (20.2)	80 (14.2)	102 (18.1)
VI	1 (0.1)	0 (0.0)	1 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (100.0)
VII	2 (0.1)	1 (0.6)	0 (0.0)	1 (0.2)	0 (0.0)	1 (50.0)	2 (100)	0 (0.0)	0 (0.0)	0 (0.0)
NT	121 (6.3)	6 (3.6)	54 (6.7)	36 (6.2)	25 (6.7)	45 (37.5)	60 (49.6)	35 (28.9)	22 (18.2)	24 (19.8)

NOTE. Data are limited to cases with available isolates; isolates were available for 1933 (78.7%) of 2457 cases from 6 Active Bacterial Core surveillance states during 2005–2006. ASCVD, atherosclerotic cardiovascular disease; NT, nontypeable.

[a] Denominators are 459 for Ia, 179 for Ib, 255 for II, 215 for III, 108 for IV, 556 for V, 1 for VI, 2 for VII, and 120 for NT).

US population. Additional studies are needed to further explore the association between GBS disease and key underlying medical conditions. Similarly, efforts targeting improved control and prevention of medical conditions, such as diabetes and its associated complications, might have the added benefit of reducing the risk of invasive GBS disease.

Most studies of GBS disease in nonpregnant adults have reported skin and/or soft-tissue infection as the leading clinical manifestation [4–6, 11]. Because diabetes predisposes individuals to skin and soft-tissue infections, this finding may again reflect the overrepresentation of diabetes among adults with invasive GBS disease. In our study, bacteremia without focus predominated (39.3%), followed by skin and/or soft-tissue infection (25.6%). These findings were likely the result of our focus on sterile-site isolates and of the clinical limitations of chart reviews in documenting the source of GBS bacteremia. When choosing empirical therapy for the treatment of skin and soft-tissue infections, physicians should consider GBS in the differential diagnosis.

Our population-based longitudinal design provided a unique opportunity to characterize the distribution of invasive GBS serotypes in a large population over time. The observation of relative stability of serotype distribution among nonpregnant adults with invasive GBS disease over a 9-year period suggests that a GBS vaccination strategy might be feasible for prevention of GBS disease in adults. We estimated that an effective quadrivalent vaccine (including types Ia, II, III, and V) would have provided protection against 78.5% of cases of invasive GBS disease in nonpregnant adults during 2005–2006. Although serotype coverage is high, impaired immune responses in older adults may make vaccination a prevention strategy that is less effective in adults than it is in neonates.

There were several limitations to our study. First, because there was no control group, risk factors for disease could not be evaluated directly. Denominator data for adults in our population with key underlying conditions and by pregnancy status were not available, and clinical information collected from chart reviews was not comprehensive. The geographic area under surveillance changed during the study period; however, because restricting the analysis to consistent areas over time and standardizing results to the US population in 1990 yielded similar results, the changes in surveillance area were unlikely to have introduced important bias. Finally, GBS isolate collection was optional in the participating surveillance areas, and only a subset of areas (3 during 1998–1999 and 6 during 2005–2006) collected isolates. However, collection at participating sites remained population based, preserving representativeness of serotype distributions among the populations that did participate.

When GBS emerged as a leading cause of infection in newborns in the 1970s, intrapartum chemoprophylaxis was identified as an effective prevention strategy, and implementation led to a >80% reduction in the incidence of perinatal disease [1, 23]. The continued emergence of invasive disease among nonpregnant adults underscores the need for appropriate prevention strategies directed at this large age group.

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