Meningococcal Disease Trends in Los Angeles County, 1995-2008

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Neisseria meningitidis is an important cause of morbidity and mortality worldwide and a leading cause of bacterial meningitis and septicemia in the United States (U.S.).[1] Infection with *N. meningitidis* in a normally sterile site, invasive meningococcal disease (IMD), is characterized by a sudden onset of fever, headache, stiff neck, petechial rash and lethargy which can progress to overwhelming sepsis, shock and death within hours. Despite antibiotic treatment, 10-14% of cases are fatal. Among those who survive, 10-20% have permanent hearing loss, cognitive deficiencies, or loss of limbs.[1,2]

Of the 13 serogroups of *N. meningitidis*, almost all invasive meningococcal disease is caused by serogroups A, B, C, Y, and W-135. Two vaccines are available in the U.S. that protect against serogroups A, C, Y, and W-135, but not B.[3] Quadrivalent meningococcal polysaccharide vaccine (MPSV4), Menomune®, was licensed in 1981for use among those ≥2 years old. In 2005, a new quadrivalent meningococcal conjugate vaccine (MCV4), Menactra®, was approved for use in the US. MCV4 is recommended for use in persons aged 2 to 55 years, although the use of MPSV4 is acceptable when MCV4 is not available. As of 2007, MCV4 is recommended for all adolescents between ages 11-18 years. Routine vaccination is also recommended for college freshman living in dormitories as they are at higher risk for meningococcal disease.[4]

Suspected cases of IMD are reportable at the local, state, and national level. Laboratory results indicating the detection of *N. meningitidis* from a sterile site are also reportable to the California Department of Public Health (CDPH) and Los Angeles County (LAC) Department of Public Health (DPH). The LAC DPH conducts surveillance of meningococcal disease to monitor disease trends and to identify close contacts of cases to ensure prophylaxis is offered and counseling on the symptoms of disease is provided. Antimicrobial chemoprophylaxis of close contacts of sporadic cases remains the primary means for prevention of MD.

This study describes trends of IMD cases reported to LAC DPH in Los Angeles County from 1995 through 2008, with focus on changes in age, serogroup, and race/ethnicity distribution.

Methods

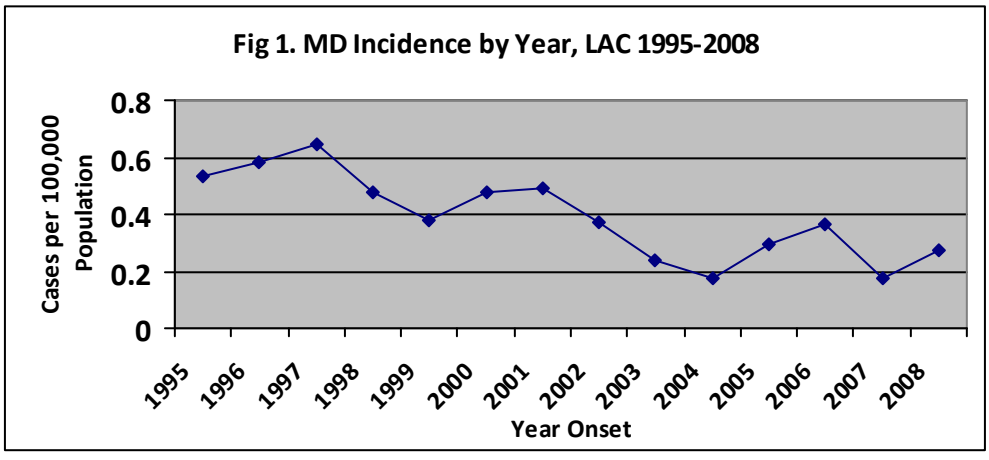
Cases included in this study had culture-confirmed *N. meningitidis* from a normally sterile site, consistent with the CDC case definition of a confirmed IMD case, were residents of LAC, and had onset of illness between January 1, 1995 through December 31, 2008. Patients who were diagnosed with meningococcal disease by other laboratory evidence, such as by Gram stain or positive polymerase chain reaction (PCR) testing of sterile material, were excluded as cases of IMD. Suspected cases of IMD were interviewed with a standardized reporting form that includes variables for age, gender, residence, race/ethnicity, outcome, culture site, and date. Information was obtained via case interview and medical record review. LAC Public Health Laboratory performed serogrouping on all available culture isolates. Cases were defined as sporadic if no close contacts were reported with IMD within a 10 day period. Non-sporadic cases were then classified as either co-primary or secondary to another case. An organization-based outbreak is one that involves the occurrence of 3 or more confirmed or probable cases of meningococcal

disease of the same serogroup in ≤3 months among persons who have a common affiliation but no close contact with each other.[5]

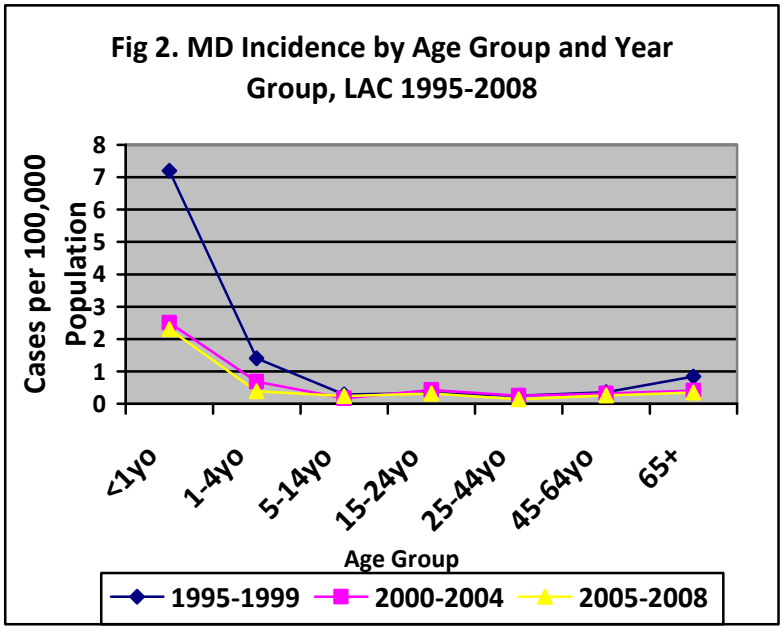
Cases with missing outcome information were cross-referenced with death certificate records. If no death certificate was found indicating death, the case was presumed to have survived. Incidence rates were calculated based on LAC population estimates created by the Population Estimates and Projections System (PEPS) provided to the LAC DPH by Los Angeles County Urban Research. To analyze incidence trends through time, cases were grouped into three groups comprised of cases with onsets from 1995-1999, 2000-2004, and 2005-2008. Differences in proportions were evaluated by chi square analysis. Pearson's coefficients were calculated from simple linear regression models.

Results

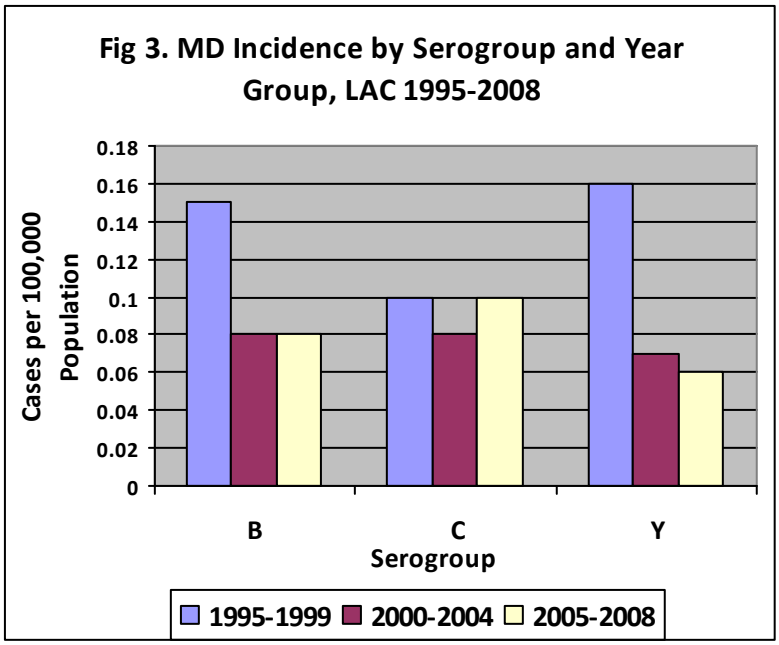
A total of 523 confirmed cases of IMD were reported to LAC DPH between 1995 and 2008. The number of cases confirmed annually ranged from 17-60 per year, with an annual mean of 37.4 cases. The overall incidence across the study period was 0.39 cases per 100,000, however, there was a steady decline in incidence from 0.53 cases per 100,000 in 1995 to 0.28 cases per 100,000 in 2008, a 47% decline (Fig 1). All cases were sporadic except for 14 (2.6%). There were four secondary cases, including two that were a part of serogoup B clusters, one serogroup C, and one unknown serogroup (the primary case was serogroup C). Two pairs of cases were co-primaries (serogroup B clusters). The remaining case was involved in the only outbreak recorded during the 1995-2008 study period. An organizational outbreak occurred in 2001 involving three unacquainted men aged 19-22 years old who attended the same bar on the same night. The three MD cases included two culture- confirmed serogroup C cases and an additional third probable case that was associated with the outbreak.



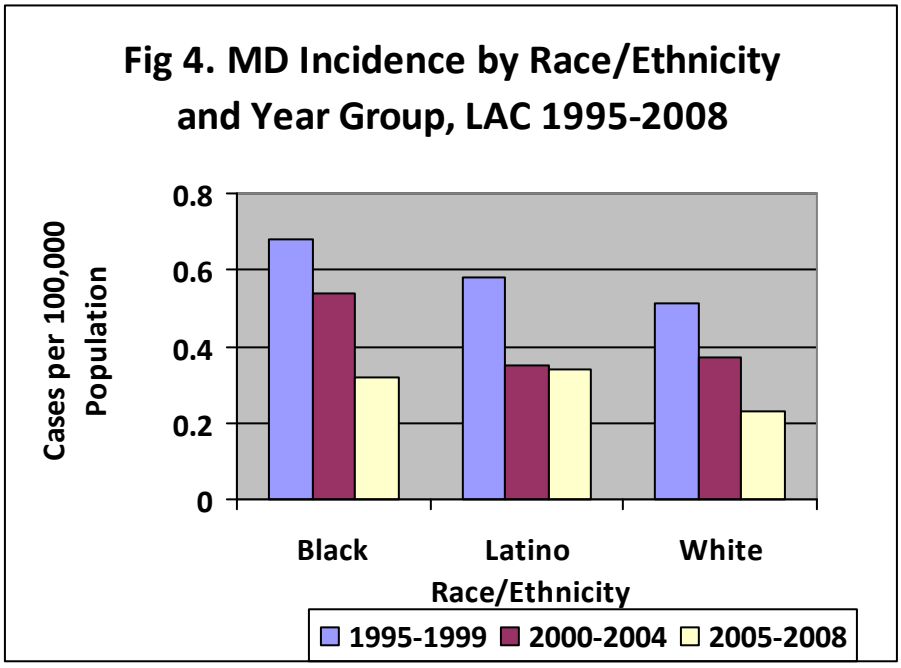
Infants <1 year old had the highest age group incidence for each of the three study periods, ranging from 7.2 per 100,000 during 1995-1999 and declining to 2.3 per 100,000 during 2005-2008 (R^2=0.78) (Fig 2). The most significant linear declines in incidence from 1995-1999 through the 2005-2008 year groups were seen in the <1, 1-4 (from 1.4 to 0.39 per 100,000, R^2=0.943), and ≥65 (from 0.84 to 0.35 per 100,000, R^2=0.840) year old age groups. All other age groups also experienced declines but with much less significant linear trend.



Serogroup was determined for 410 cases (78%). Over the 14-year study period, 35% of cases were serogroup B (n=144), 32% were Y (n=132), 30% were C (n=125), and 2% were W-135 (n=8). One case was determined to be Z and there was no case of type A; 113 (22%) were not determined. Young children less than 1 year old and those 1-4 years old accounted for the largest proportion of serogroup B cases (22%, n=32 and 19%, n=28, respectively). The largest proportion of serogroup C cases occurred among 25-44 year olds (22%, n=27), and in serogroup Y cases among those 65 years and older (28%, n=37). During the years 1995-1999, serogroup B constituted 37% (n=72) of cases among those with serogroup B or the vaccine-preventable serogroups C, Y, and W-135 (n=197). The proportion of serogroup B cases remained stable compared to the vaccine-preventable serogroups in 2000-2004 (35%, n=40) and in 2005-2008 (33%, n=32) (chi square p=0.8297). The proportion of serogroup C cases increased from 24% (n=48) to 41% (n=40) while serogroup Y cases decreased from 38% (n=75) to 25% (n=24). The incidence of serogroup B cases, however, declined from 0.15 per 100,000 in 1995-1999 to 0.08 per 100,000 in 2005-2008 (R^2=0.75), a 47% decline. The incidence of serogroup Y cases also declined from 0.16 per 100,000 in 1995-1999 to 0.06 per 100,000 in 2005-2008 (R^2=0.824), a 63% decline. Serogroup C incidence remained stable ranging from 0.08 per 100,000 to 0.1 per 100,000 through the three year groups (Fig 3).

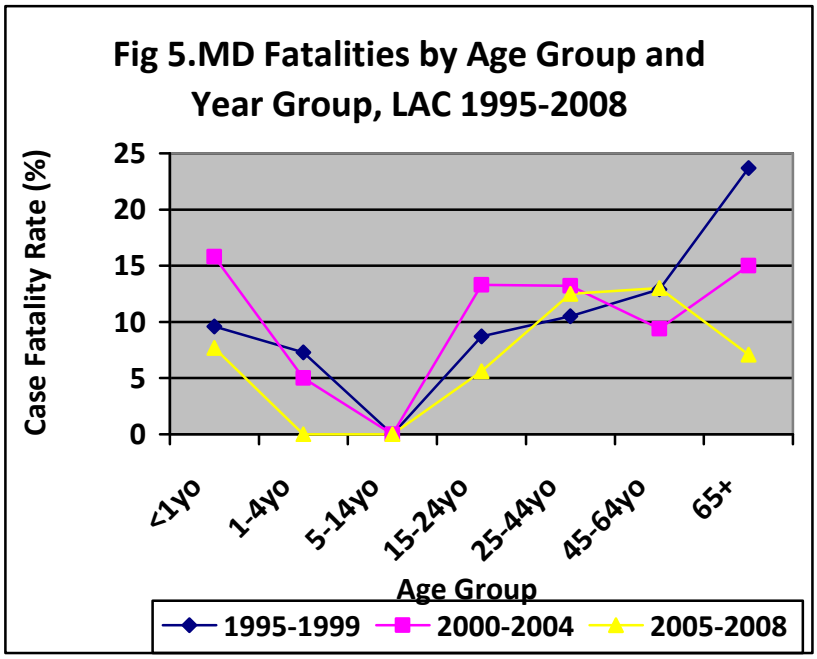


Race/ethnicity data was available for 517 cases (99%). The highest incidence occurred among blacks for two of the three year groups (Fig 4). The incidence of IMD declined among blacks, Latinos, and whites over the three study year groups. Incidence among blacks dropped from 0.68 to 0.32 per 100,000 (R^2=0.983), a 53% decline; Latinos from 0.58 to 0.34 per 100,000 (R^2=0.781), a 41% decline; and whites from 0.51 to 0.23 per 100,000 (R^2=1), a 55% decline.



The overall case fatality rate for the study period was 10.3% (n=54) and ranged from 2.9%-16.7% per year. The number of fatalities ranged from 1-8 cases per year. Fatalities occurred most

frequently among serogroup C cases, 16.8% (n=21). In comparison, fatalities among serogroup B and Y cases occurred at 5.6% (n=8) and 8.3% (n=11), respectively. No deaths occurred for any other serogroups. The highest case fatality rates by age group occurred among those 65 years old and older and those <1 year old (Fig 5). The most dramatic decline in case fatality rates through the year groups occurred among the 65 and older age group, dropping from 23.7% in 1995-1999 to 7.1% during 2005-2008 . No deaths were reported in the 5-14 year age group.



Discussion

The incidence of IMD in LAC has shown a continuous decline over the fourteen year study period with incidence rates declining from 0.53 cases per 100,000 in 1995 to 0.28 cases per 100,000 population in 2008. This follows the declining national trends of IMD incidence, which dropped from 1.23 per 100,000 in 1995[6] to 0.34 per 100,000[7] in 2008[*]. In LAC decreases in incidence were seen in all age groups, particularly among those within the <1 year, 1-4 year old and 65 years and older group. Theoretically, this decline might have resulted from the effect of herd immunity from MD vaccination, as these age groups fall outside of the age range recommended for meningococcal vaccination. However, vaccination cannot completely explain these declines in IMD incidence. Vaccinating children <2 years old is usually not recommended, even those at especially high risk for IMD (e.g. travelers to hyperendemic areas, persons with HIV or other underlying conditions) . MCV4, which can reduce carriage of *N. meningitidis*, was not licensed until 2005 [4] and the most significant incidence declines in both the youngest and oldest age groups occurred before this time. Further, the National Immunization Survey estimated that in 2007, only 32% of adolescents 13-17 years old had received 1 dose of MCV4[8]. Vaccination coverage, however, is rising; estimations

[*] Incidence in 1995 was referenced from the MMWR Summary of Notifiable Diseases which includes both confirmed and probable MD cases. Incidence in 2008 was referenced from Active Bacterial Core Surveillance which includes only confirmed cases.

for 2009 demonstrated that it has risen among that age group to nearly 54% [9]. It is possible that even more substantial decreases in invasive MD will be seen with increased use of vaccines.

Serogroup distribution changed over the course of the study period. The proportion of serogroup C cases in each year group increased as serogroup Y cases decreased while the proportion of serogroup B remained unchanged. Nationally, Hershey and Hitchcock report a different scenario documented by Active Bacterial Core Surveillance (ABC) data; serogroups B and C decreased from 46% and 45%, respectively, in 1989-1991 to 35% and 31%, respectively, by 2005-2008.[10] The change in serogroup distribution in LAC was driven by a drop in incidence in serogroups B and Y. As serogroup C incidence remained stable, the number of serogroup C cases increasingly represented more IMD cases overall.

Racial disparities in IMD incidence have also lessened during the study period. In the US, IMD has more commonly occurred among blacks, though this phenomenon is more likely a marker for other risk factors such as crowded living conditions, chronic underlying illness, or exposure to passive or active smoking.[11] In LAC, blacks experienced the highest rates of MD during the 1995-1999 and 2000-2004 year groups compared to whites and Latinos, but declined by 53% by the 2005-2008 year group, by which time the differences in incidence diminished. It is unknown what underlying factors have played a part in this decrease. Results from the LAC Health Survey show a significant decline in the prevalence of adult smoking, from 18.2% in 1997 to 14.6% in 2005. However, smoking prevalence among blacks increased between 2002 and 2005.[12]

The highest proportion of fatalities occurred among cases with serogroup C disease. Nationally, the case fatality rate between 1998 and 2007 was highest among cases with disease caused by serogroup W-135, of which LAC had none.[10] The annual estimated case fatality rates caused by serogroups B, C, and Y nationally were 10.6%, 14.7%, and 12%, respectively. The mortality trends among the serogroups in LAC are much more extreme in comparison; the case fatality rate for serogroup C disease is three times as high as that of serogroup B disease (16.8% v. 5.6%). In LAC, the highest case fatality rates by age group occurred among those 65 years old and older and those <1 year old, while no deaths occurred in those 5-14 years old during14 years of surveillance. This is not the case nationally between 1998 and 2007, where children less than 1 year old had among the lowest fatality rates (6%). The case fatality rate for children ages 5-13 years was 10.6%.[11] Our study data might indicate some relationship between age and serogroup, however, serogroup B and Y affected the youngest and oldest age groups in higher proportions, but resulted in lower fatality rates.

The limitations of this study include underreporting due to our passive surveillance system. Any differences seen when compared with national ABC data, which are obtained by active surveillance, would be understated. The use of only confirmed cases in this analysis may also produce an underestimate of the burden of disease. As many as 10%-37% of cases reported each year to LAC DPH during 1995-2008 were classified as probable and thus excluded from this analysis. The grouping together of multiple years was done to enable a cleaner analysis of multiple variables, however, details of peaks and dips in incidence in specific years may have been missed.

The specific reasons for decline in IMD incidence in LAC from 1995-2008 remain unknown. However, changes in the distribution of cases among different age groups, serogroups, and race/ethnicity groups are clearly seen. These changes may be a result of changes in high risk behaviors and environments in these groups. LAC has seen an overall decrease in smoking prevalence. Emphasis on hand hygiene or respiratory hygiene in disease prevention over the years could also be impacting transmission of bacteria and decreasing colonization among portions of the population. With increased adherence to the childhood vaccine schedule, as evidenced by National Immunization Survey estimates, we would expect to see a greater decline in IMD in the adolescent age group as well as other age groups due to herd immunity. Even with increased vaccination coverage, current available vaccines do not protect against serogroup B disease and have limited use for specific age groups and those with underlying risk factors for invasive MD; they also have no impact on the rate of colonization or carriage. Therefore, clinicians must remain vigilant in suspecting invasive meningococcal meningitis and bacteremia as an important cause of life threatening bacterial meningitis and sepsis.

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