Population Immunity to Measles in the United States, 1999

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To estimate population immunity, we examined measles immunity among residents of the United States in 1999 from serological and vaccine coverage surveys. For persons aged ≥20 years, serological data from the third National Health and Nutrition Examination Survey (1988–1994) were used. For persons <20 years of age, immunity was estimated from results of the National Immunization Survey (1994–1998), state surveys of school entrants (1990–2000), and vaccine coverage surveys of adolescents (1997). To estimate immunity from vaccine coverage data, 95% vaccine efficacy was used for recipients of a single dose at ≥12 years of age and 99% vaccine efficacy was used for those with failure of a first dose who were revaccinated. Overall, calculated population immunity was found to be 93%. Although there was not much variation in immunity by region and state, in some large urban centers immunity among preschool-aged children was as low as 86%. Overall, geographic- and age-specific estimates of a high population immunity support the epidemiological evidence that measles disease is no longer endemic in the United States.

The cornerstone of the measles elimination strategy is to achieve a high vaccination level in the population, leading to high immunity [1]. Examination of the status of endemic measles disease in the United States should include a careful assessment of the population’s immunity. In fact, the level of population immunity is an indicator of whether the absence of indigenous disease in the United States is biologically plausible. The goal for the first 26 years after the measles vaccine was licensed in 1963 in the United States was to achieve high population immunity with a single dose of measles vaccine at 12–15 months of age [2, 3]. In December 1989, to improve population immunity by reducing the number of children experiencing vaccine failures, a 2-dose schedule was recommended. Because of the cost of the additional dose of measles vaccine, both the Advisory Committee on Immunization Practices and the American Academy of Pediatrics initially proposed that the second dose be phased in by one birth cohort or grade cohort per year [2, 4]. Administration of the second dose was recommended at school entry (4–6 years of age) or at middle school entry (11–12 years of age).

Currently, 5 sources of data are available to provide the estimate of population immunity [5–11]. The first national serological survey of measles antibody was part of the third National Health and Nutrition Examination Survey (NHANES III), conducted in 1988–1994. This survey estimates humoral immunity among school-aged children and adults. The National Immunization Survey (NIS) (1994–present) estimates vaccine coverage of preschool-aged children, and statewide school surveys estimate first-dose vaccine coverage among school-aged children. The National Health Interview Survey (NHIS) (1997) and the Health Plan Employer Data Information Set (HEDIS) (1997) estimate second-dose vaccine coverage of children and adolescents. Vaccine coverage estimated from data on state-specific school-entry requirements is considered elsewhere in this supplement issue.

To assess population immunity in the United States, we review available data on measles immunity to answer the specific question: Does population immunity support the conclusion that measles is no longer endemic? The methods and results from the 5 data sources are...
presented by major age groups, and we compute an overall estimate of population immunity in the United States in 1999 from age-specific estimates.

**PREVALENCE OF MEASLES ANTIBODY AMONG PERSONS ≥6 YEARS OLD**

NHANES III’s design and results have been described elsewhere [6]. In brief, NHANES III was a household survey of personal interviews conducted across the United States. A random sample of households in 89 counties was selected by use of a multistage probability sample design. Interviews were conducted of 40,000 civilian, noninstitutionalized persons ≥2 months of age. Children <6 years of age were excluded from the study because of their very low participation rate (<10%). Demographic, socioeconomic, health, and nutritional data were examined. Serum collected during a physical examination was tested for measles-specific IgG antibody by means of an EIA developed at the Centers for Disease Control and Prevention (CDC). This EIA is the most practical assay for analyzing tens of thousands of specimens.

Overall, the participation rate for the survey was about two-thirds, and 85% of participants were eligible for the study because they had a physical examination and blood drawn. For persons >70 years of age, the overall participation rate was lower. However, these elderly persons represented only 9% of the United States population in 1990; thus, a potential bias is probably minimal.

The prevalence of measles antibody among persons ≥6 years of age was 93% (95% confidence interval [CI], 92%–94%). Prevalence was similar for all geographic regions: Northeast, 92% (95% CI, 90%–94%); South, 94% (95% CI, 92%–95%); West, 94% (95% CI, 92%–95%), and Midwest, 93% (95% CI, 92%–94%). Because of the survey design, the prevalence of measles antibody by smaller geographic units (i.e., states and cities) was not available.

The prevalence of measles antibody varied by age (figure 1). Prevalence of antibody was examined by 5-year birth cohorts (e.g., born before 1942, 1942–1946, 1947–1951). Birth during the vaccine era was defined as births in 1957 and later. Although measles vaccine was licensed in 1963, many persons born during 1957–1962 were vaccinated in school or in early childhood and had a reduced risk of measles; therefore, we consider them to be a part of the vaccine era [12–14]. Persons born during the prevaccine era had a higher prevalence of antibody than those born during the vaccine era (average, 99% vs. 87%) [6]. Among persons born in the vaccine era, prevalence of antibody at 81% was lowest among those born during 1967–1976. That is, a substantial number of persons aged 24–33 years in 1999 likely escaped disease and vaccination.

**VACCINE COVERAGE OF PRESCHOOL-AGED CHILDREN, 1994–1998**

The NIS provides the best estimate of current immunity among 19- to 35-month-old children in the United States. NIS is a national probability sample of young children identified by a random-digit-dialing survey in all 50 states and 28 urban centers that were considered at high risk for undervaccination and measles disease [15]. The survey has been conducted since 1994. Information collected during the interview includes vaccination history (from records or parental recall) and demographic and socioeconomic data. Participants’ health care providers are contacted to validate vaccination history.

The NIS is a large, complex survey. Each year nearly 3 million telephone numbers are sampled and 2 million numbers are dialed [15]. Nearly 1 million households are identified, and most are screened for eligible children. About 33,000 interviews of eligible children are completed each year, an average of 442 interviews per survey area. The overall participation rate of children has been 68% (range, 54%–88%). Vaccine coverage estimates are based on data from children with adequate immunization provider information (65% in 1999).

Across the United States, measles vaccine coverage among children 19–35 months of age increased from 89% (95% CI, 88%–90%) in 1994 to 92% (95% CI, 91%–92%) in 1999 [16]. There was not much variation by region and state, although in some urban centers, immunity among preschool-aged children was as low as 86%. In 1999, among the 50 states, 41 reached point estimates of coverage with a measles-containing vaccine of ≥90%; 9 states achieved coverage levels under 90% but at least 86% [17]. Among the 28 urban areas targeted by the NIS, 18 reached point estimates of coverage of ≥90%; the remaining reached coverage levels under 90% but at least 86% [17]. Many of these urban centers had continuous transmission.
of measles during the 1980s or a large outbreak during the 1989–1991 measles resurgence [18].

During the 1989–1991 resurgence, populations at highest risk for measles were racial/ethnic minority and low-income children [18]. After the resurgence, average vaccine coverage among preschool-aged children with an initial dose of measles vaccine has been very high for racial and ethnic minority populations (86%–90%) [19]. In fact, the immunization gap between white and black preschool-aged children has narrowed from 20 percentage points during the 1970s and 1980s to 2 percentage points in the late 1990s, although the survey methods varied during the 30 years (figure 2). In 1999, national vaccine coverage levels with a measles-containing vaccine among 19- to 35-month-old children living at or above the poverty level were very close to those for children living below the poverty level (92% and 90%, respectively) [17]. Although coverage among children living below the poverty level was, in general, slightly lower than that among those living at or above the poverty level, vaccination coverage was close to 90% for children in all racial and ethnic minority populations regardless of poverty status [17]. The lowest coverage among children in poverty in any urban area was 81%, compared with 82% coverage among children living at or above the poverty line.

VACCINE COVERAGE OF SCHOOL-AGED CHILDREN

First-dose coverage with measles vaccine, 1990–2000. The only source of national estimates of first-dose vaccine coverage of school-aged children was statewide school surveys. All states require that children be appropriately immunized against measles on or before entry into kindergarten and grade 1. State immunization programs conduct annual school-based surveys to assess vaccination levels. Yearly, summary reports of vaccination levels from each of the 50 states and 5 large cities are submitted to the National Immunization Program at the CDC [7]. National coverage is estimated by weighting the vaccination level reported by state and city immunization programs.

From the 1990–1991 school year through the 1999–2000 school year, the national coverage levels with the first dose of measles vaccine among children entering school (kindergarten and grade 1) were ≧96% [20]. For most years, vaccination coverage was 98%. Over the 10-year reporting period, 47 states reported an average coverage of ≧95%. During this period, nearly all states reported each year to the CDC.

Second-dose coverage with measles vaccine, 1997. To assess current immunity among school-aged children, vaccine coverage for the second dose of measles is needed. Two surveys provide estimates of second-dose coverage: the NHIS and the HEDIS of commercial, managed care organizations.

The NHIS is a continuous household survey that uses a multistage probability sampling design to assess the civilian, noninstitutionalized population residing in the United States [11]. Estimates for second-dose vaccine coverage with measles vaccine among school-aged children 7–17 years of age were available in 1997. In this study, vaccination history was obtained from parental recall and vaccination records. Vaccination histories were not verified by health care providers.

The response rate for the ongoing core part of the survey has been 94%–98%, and for special health supplements such as immunization, the response has been 80% [11]. Vaccination coverage with the second dose of measles vaccine ranged from 66% to 90% depending on the source of information. Only one-fourth of the children 7–17 years of age had written vaccination records at home, and coverage estimated from these records was 66%. Coverage reported by parental recall of the child’s vaccination status was 88%. When both record and recall were combined, coverage with second-dose measles vaccine was 90%.

The other survey, HEDIS, is a set of performance measures used by managed care organizations to assess quality of health care services [8]. Sponsored, supported, and maintained by the National Committee for Quality Assurance, HEDIS measures are in use by >90% of all United States health plans and collectively cover >60 million Americans [9]. HEDIS collects information on adolescent immunization by use of the overall number of doses administered plus vaccination history from chart review.

In 1997, among 212 managed care organizations that collected immunization data on 13-year-old children, nearly two-thirds of the children had received 2 doses of a measles-mumps-rubella vaccine [10]. The mean coverage estimate for a managed care organization was 61%, the median was 62%, and the range was 21%–96% (figure 3).

OVERALL POPULATION IMMUNITY IN THE UNITED STATES, 1999

To estimate overall population immunity in the United States in 1999, all vaccine coverage estimates and serological data across age groups available by 1999 were combined. The prevalence of measles antibody was the primary estimate of immunity for persons ≥20 years of age. For persons <20 years of age, population immunity was derived from vaccine coverage by multiplying the coverage estimate of the population with age-specific vaccine efficacy. For example, if a single dose of vaccine was administered at ≥12 months of age, we estimated vaccine efficacy as 95%. Among those who received 2 doses of measles vaccine, the estimate of immunity for first-dose coverage was added to the estimate of immunity for second-dose coverage. Population immunity for the second dose was computed by multiplying second-dose coverage by a 5% vaccine failure rate and a 99% vaccine efficacy [21] (CDC, unpublished data).
Measles immunity among preschool-aged children 0–4 years of age in 1999 was estimated to be 82%. To compute this immunity, we assumed that 60% of infants had maternal antibody and all were immune (infants <6 months and 20% of infants 6–11 months of age) [22], that 92% of the remaining preschool-aged population 1–4 years of age had a single dose of measles vaccine (findings from annual NIS of preschool-aged children 19–35 months of age in 1997–1999), and that vaccine efficacy was 95% for the single dose administered at 12 months of age to 1- to 4-year-old children.

Population immunity among school-aged children 5–9 years of age in 1999 was computed considering first-dose estimates of vaccination coverage from school surveys of entrants in school years between 1990–1991 and 1999–2000. Multiplying 97% of this age group (the average vaccine coverage with the first dose of measles vaccine from school surveys) by 95% vaccine efficacy, we estimated a 92% immunity among children 5–9 years of age. Because 46 states require 2 doses of measles vaccine for children entering kindergarten and grade 1, this is a conservative estimate of immunity for this age group. Estimates of second-dose coverage from school surveys for this age group were not available for 1999.

Population immunity among school-aged children 10–19 years of age in 1999 was computed with data from first- and second-dose coverage. Vaccine coverage estimates of the second dose of measles vaccine from NHIS and HEDIS results (10- to 19-year-olds in 1999) were used to estimate second-dose coverage. Estimated immunity for this age group was 95%. This estimate of 95% immunity was computed by adding 90% immunity from first-dose coverage (derived from first-dose coverage from school surveys between 1990 and 1994) plus 5% immunity from second-dose coverage (derived from second-dose coverage of children 10–19 years of age). Immunity to second-dose measles vaccination was a conservative estimate. We used an average vaccine coverage estimate derived from the median estimate for HEDIS of 62% among 13-year-old children and the estimate from NHIS among children aged 7–17 years from written records of 66%. This average coverage estimate of 64% was multiplied by a 5% vaccine failure rate and 99% vaccine efficacy.

For persons ≥20 years of age, prevalence of measles antibody from NHANES III was used to estimate population immunity. Immunity for this age group was 93%.

Average immunity of the US population in 1999 was computed by multiplying age-specific immunity by the fraction that each age group represented in the population (weight of each age group) (table 1). For example, preschool children aged 0–4 years represented 7% of the population. This fraction was multiplied by the age-specific immunity of 82% to obtain an overall immunity estimate of 6% for ages 0–4 years. Overall, estimated population immunity in the United States was 93%.

**DISCUSSION**

This review of age-specific measles immunity in the United States in 1999 found overall population immunity to be very high (at least 93%). We believe that immunity has been this high for several years before 1999, because vaccine coverage surveys of preschool- and school-aged children have been at or above this level since 1994. Moreover, immunity is likely to be even higher than 93% for several reasons. First, our estimate does not account for more recent administration of 2 doses of measles vaccine since 1990 among children 5–9 years of age and among young adults because of prematriculation requirements for college or requirements of employment for health care workers [3]. In addition, the EIA used to detect measles antibody in NHANES III is 83%–88% as sensitive as the "gold standard" assay (plaque reduction neutralization assay) in detecting measles antibody at titers that correlate with clinical protection [22]. Thus, some persons without antibody detectable by EIA may be immune. Finally, in the serological survey, we measured only humoral immunity and not cellular immunity. Cellular immunity has been reported to protect chil-

Figure 2. Vaccination coverage of children by measles vaccine, selected race, survey, and year, United States, 1970–1998. *Children in this survey were 1–4 years of age; †Children in these surveys were 19–35 months of age. NHIS, National Health Interview Survey; NIS, National Immunization Survey; USIS, United States Immunization Survey.

Figure 3. Percentage of 13-year-old children reported as receiving 2 doses of measles-mumps-rubella vaccine by number of plans, Health Plan Employer Data Information Set 3.0, 1997 (n = 212).
dren from measles in the absence of antibodies [24]. This finding was observed among agammaglobulinemic children who were protected against measles despite having little or no detectable antibody (no ability to make gamma globulins) to induce a humoral response.

A high population immunity among preschool-aged children, a group that was at high risk for measles, before and during the resurgence, is further supported by the lack of sustained transmission of endemic measles. Since the resurgence of measles in 1989–1991, there have been no large outbreaks among preschool-aged children, and endemic measles transmission in urban centers has been interrupted. It is reassuring that high estimated immunity is now found among high-risk populations (e.g., racial/ethnic minority and low-income groups) that had the lowest measles vaccine coverage during the resurgence. This suggests that another resurgence is unlikely and that interruption of endemic measles transmission is likely to be sustained, provided a high level of population immunity is maintained in these high-risk populations.

High population immunity among school-aged children, a group once at highest risk for exposure to measles because of the congregation of children in schools, is also supported by lack of endemic transmission of measles. A 2-dose policy for measles vaccination has improved immunity overall and is probably higher now than estimated in the present study. Second-dose coverage has recently been estimated from the coverage of children by school laws requiring a second dose of measles vaccine [25]. After the resurgence of measles during 1989–1991, the number of states that enacted a school law requiring a second dose of measles vaccination rapidly increased. By 2000, 49 states and the District of Columbia had second-dose requirements. An estimated 80% of students in kindergarten through grade 12 are covered by these requirements, which is a higher estimate of coverage than we assessed in this review of serological and vaccine coverage data. In addition, the 3-fold increase in annual net doses of measles vaccine distributed, from 5 million in 1990 to 14 million in 1999, along with an annual birth cohort of 3–4 million infants, suggests that many persons have been vaccinated with >1 dose of measles vaccine.

Young adults aged 24–33 years in 1999 had the lowest immunity (81%). The most likely reasons for the lowest prevalence of antibody in this cohort born between 1967–1976 are a decrease in vaccine availability during periods of suspended federal funding between 1969 and 1971 and lower vaccine coverage among children before widespread implementation of school vaccination requirements. National estimates of vaccine coverage from the 1978 United States Immunization Survey of 82% among children 1–13 years of age support the low prevalence of antibody for these birth cohorts [5]. In addition, the lower immunity found in 1988–1994 among cohorts born between 1967 and 1976 was associated with higher measles incidence reported in 1988–1994 among the same birth cohorts [6]. Although endemic measles has been interrupted, the incidence of measles in this age group remains one of the highest [26].

A number of different coverage and serological surveys were examined to estimate population immunity. Each survey has its strengths and limitations. Overall, all surveys were national in scope and provided the best and most up-to-date data available on measles vaccine coverage or measles antibody in the United States. For instance, the NIS is an accurate method for estimating recent coverage among preschool children aged 19–35 months. Because of adjustments for nonresponse and for provider-verified records from urban centers and states, the NIS does not seem to either underestimate or overestimate measles vaccination coverage [5, 27]. In addition, estimates of vaccine coverage for children 19–35 months of age also may be a good estimate for a wider age group of preschool children (1–4 years) [5]. Regarding school surveys, despite variation in the design and conduct by state, in the 1999–2000 school year, 62% of the reporting states surveyed at least 90% of the eligible children for first-dose vaccine coverage. In general, this level of assessment has been similar throughout the decade. In addition, most (67%) reporting states assessed the vaccines mandated by law and require the date of receipt of vaccines as documentation of vaccination.

The second dose of measles vaccine is not available in current school surveys, because this dose is a relatively new requirement and second-dose coverage data have not yet been widely collected. However, an average estimate derived from NHIS (parental records only) and HEDIS of second-dose coverage was available for school-aged children 10–19 years of age in 1999. Although generalizability of HEDIS data to the general population is difficult to assess because of the inability to obtain age-specific enrollment in managed care organizations, HEDIS results describe second-dose coverage among adolescents, a population for which very few data are available. Moreover, HEDIS findings of second-dose coverage were similar to the national estimate from NHIS with written records as the source. Estimated coverage from NHIS based on parental recall of vaccination history was higher than that from HEDIS. Parental recall of vaccination history is likely to overestimate coverage with the second dose

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<th>Age group, years</th>
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<th>Percentage of US population</th>
<th>Weighted immunity</th>
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Table 1. Computation of population immunity.
of measles vaccine, whereas vaccination history from a written record with dates of vaccination is more reliable and valid.

Despite the limitations of the data sources for estimating population immunity in 1999 and the conservative pattern of susceptibility by age group computed for the United States, the estimates are very similar to the susceptibility pattern estimated by Gay [28] that should lead to elimination of measles from Europe (figure 4). Gay, by means of a simple mathematical model, has estimated maximum susceptibility targets for achieving measles elimination in Europe. Because Europe and the United States both have diverse populations and cultures, his findings suggest that we may have met maximum susceptibility rates among age groups in the United States for eliminating measles. In the United States, we estimated an overall 19% susceptibility rate among preschool-aged children, including infants who are <1 year of age. This estimate is 4% higher than the target of 15% for Europe, although we have included infants, and 80% of those infants 6–11 months of age are probably susceptible to measles [22]. If we exclude infants as Gay has, susceptibility in the United States is even lower (17%) and closer to the maximum susceptibility target in Europe. Regarding susceptible children 5–9 years of age in the United States, our calculated rate of up to 8% is lower than the maximum susceptibility target of 10% for Europe. The susceptibility rate in this age group in the United States is lower because of high immunity among school-aged children, resulting from school requirements for vaccination. The pattern of susceptibility we observed for older school-aged children 10–19 years of age at 5% is identical to the target for Europe, whereas the susceptibility among adults ≥20 years of age in the United States is slightly higher than the target for Europe (7% vs. 5%).

Population immunity to measles of 93% in the US population supports the epidemiological evidence that measles disease is no longer endemic in this country. In 1999, of the 100 reported measles cases, about two-thirds were internationally associated cases [26]. In addition, 87 of the total cases were in residents of the United States, an extremely low incidence (<0.5 case per 1,000,000 population). Furthermore, the relative proportion of cases in residents by age supports the estimated age-specific immunity found in the present study. For example, 35 cases (40%) in residents were in preschool-aged children <5 years of age, 23 cases (26%) were in school-aged children 5–19 years of age, and 29 cases (33%) were in adults ≥20 years of age.

Although estimates of population immunity were not available during the measles resurgence during 1989–1991, estimated population immunity among preschool-aged children <5 years of age increased from 57% in 1985 to 92% in 1999. Furthermore, high population immunity among high-risk, preschool-aged populations, particularly in urban centers and among racial/ethnic minority and low-income populations, provide evidence that another resurgence is unlikely and that endemic measles transmission has been interrupted in these populations. Although population immunity is now high and the risk of exposure to measles in the United States is very low, health care providers should be aware of the susceptibility pattern in the United States, particularly among persons 24–33 years of age in 1999, and should offer vaccination as recommended. In addition, we must be vigilant to maintain this high level of immunity, particularly among preschool-aged children, to prevent reestablishment of indigenous disease.

Acknowledgments

We thank Janet Heath and staff in the CDC Measles Laboratory for the testing of NHANES III sera; staff in the National Center for Health Statistics responsible for the design, conduct, and analysis of NHANES III, NHIS, and NIS; and Jane Seward, Melinda Wharton, and Mary McCauley for scientific and editorial assistance.

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