Measles Herd Immunity

The Association of Attack Rates With Immunization Rates in Preschool Children

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Objective.—To examine the association between incidence of measles and immunization coverage among preschool-age children.

Design.—An ecological study in which measles incidence was compared with immunization coverage among census tracts. The independent effects of race and population density were controlled for.

Setting.—A recent measles outbreak in Milwaukee, Wis. Immunization coverage data were estimated from a retrospective, school-based survey of Milwaukee grade school students.

Patients.—One thousand eleven persons (≤17 years) who had confirmed measles from September 1989 through June 1990.

Main Outcome Measures.—Confirmed measles cases grouped by census tract, corresponding census tract preoutbreak immunization coverage, racial breakdown, and population density.

Results.—Census tracts stratified into four levels, with mean immunization rates of 50.4%, 60.2%, 69.9%, and 81.0%, had respective median attack rates of 11.6, 5.0, 1.7, and 0.0 cases per 1000 persons ($P<.01$). The association between immunization coverage and measles attack rate remained significant even after controlling for race and population density.

Conclusions.—Modest improvements in low levels of immunization coverage among 2-year-olds confer substantial protection against measles outbreaks. Coverage of 80% or less may be sufficient to prevent sustained measles outbreaks in an urban community.

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OUTBREAKS of measles involving predominantly unvaccinated, preschool-age children have contributed almost half (44.9%) of all cases recorded during the nationwide upsurge of measles noted in 1989 and 1990.[1] This type of outbreak, recently reviewed by Markowitz and coworkers,[2] is likely to contribute an ever-increasing share of cases as the incidence of measles is progressively reduced among grade school, high school, and college students through implementation of the new recommendation that all students receive two doses of measles vaccine.[3] A recent study comparing immunization coverage in eight US cities suggests that large outbreaks are most likely to occur in cities with low immunization rates among preschool-age children.[4] In an outbreak in one large city, neighborhoods with the highest measles attack rates were shown to have the lowest immunization coverage among 2-year-olds.[5] To better understand the relationship between measles transmission and immunization coverage among preschool children, the following epidemiological study was completed following a measles outbreak in Milwaukee, Wis.

From September 1989 through June 1990, Milwaukee experienced an extensive measles outbreak, reported more fully elsewhere.[6] The outbreak was notable for its size, 1095 recorded cases (attack rate of 181 per 100 000 population), and its severity, 233 cases (21%) hospitalized and three deaths. Also notable was the disproportionate number of cases in blacks (82% of cases but only 30% of the total population) and the very young (61% of individuals contracting measles were <5 years old and 96% were ≤17 years old). Children under 5 years old with measles (64.5% of whom were unvaccinated) were at highest risk for severe disease, accounting for 75% of all those hospitalized and 100% of those who died.

The magnitude of the outbreak suggested that the local population was not as well protected against measles as previously thought. Because of the known high efficacy (>90%) of the measles vaccine,[7] our attention focused on vaccine coverage. Although the Wisconsin Division of Health reported that 93% of all schoolchildren in Milwaukee were immunized against measles, no vaccine coverage estimates were available for the subpopulation of most concern: preschool-age children. In other cities experiencing measles outbreaks, measles immunization rates in preschool-age children in selected areas have been reported as low as 49%.[5,8]

To reliably estimate preoutbreak immunization coverage, we undertook a retrospective, school-based survey of student records in Milwaukee's public and private schools. By comparing immunization rates with measles attack rates among census tracts, we were able to measure the strength of association between them and to quantify the protection provided by different levels of immunization during an epidemic.

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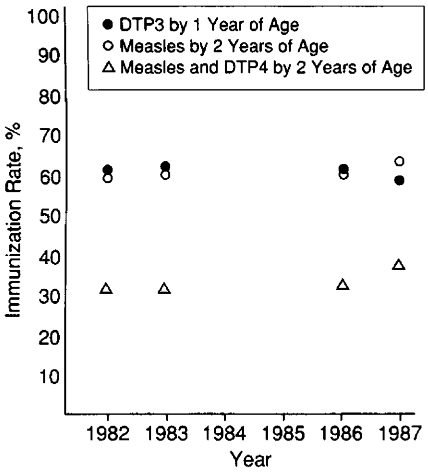

Fig 1.—Estimated immunization rates for four Milwaukee Public School cohorts identified by the year each group was age 2 years. DTP3 and DTP4 indicate diphtheria, tetanus, and pertussis vaccine doses 3 and 4.

Table 1.—Immunization Coverage by 1 and 2 Years of Age Estimated From Kindergarten Records in Milwaukee, Wis (1989)*

Type of School	No. of Students	DTP3 by Age 1 Year, No. (%)	MMR by Age 2 Years, No. (%)	MMR + DTP4 by Age 2 Years, No. (%)
Public	7899	4757 (60.2)	4670 (59.1)	2501 (31.7)
Private	1654	1431 (86.5)	1393 (84.2)	913 (55.2)
Total	**9553**	**6188** (64.8)	6063 (63.5)	3414 (35.7)

*DTP3 and DTP4 indicate diphtheria, tetanus, and pertussis vaccine doses 3 and 4; MMR, measles, mumps, and rubella vaccine.

METHODS

To estimate preoutbreak immunization rates we used computer-stored immunization records of all Milwaukee Public School (MPS) students enrolled in 5-year-old kindergarten and in third and fourth grades in 1989 and in 5-year-old kindergarten in 1990 (31 678 total records). The four grades selected represent four age cohorts of children who were 2 years old in 1982, 1983, 1986, and 1987, respectively. The MPS record contains the dates of all school-required immunizations received: diphtheria, tetanus, and pertussis (DTP) vaccine, doses 1 through 5; oral polio vaccine (OPV), doses 1 through 5; and measles, mumps, and rubella (MMR) vaccine. The record also contains the student's date of birth, census tract of home address, race/ethnicity, and sex. We calculated each child's age at receipt of MMR vaccine.

The MPS student records were grouped by residence into one of Milwaukee's 218 census tracts. The proportion of children who had received measles vaccine by their second birthday was used to represent measles vaccine coverage within each census tract. The census tract immunization rates used in our analysis are the averages of the four MPS age-and-grade cohorts (1982, 1983, 1986, and 1987) combined. Because there was little change in overall immunization rates from year to year (Fig 1), the average rates for each census tract used in our analysis should closely approximate the actual rates at the onset of the measles outbreak in September 1989.

We also assessed, using sampling methods recommended by the Centers for Disease Control (CDC) (unpublished recommendations, July 1990), vaccine coverage among Milwaukee's private kindergarten classes, which included 1654 students in 1989. A two-stage cluster sample of 35 classes including 607 students (37% of all children in private kindergartens) was selected. The data were collected manually at each school. Because private schools' records were not computerized and because private schools represented a relatively small group of children and were an incomplete sample of this group, we excluded them from the comparisons of measles attack rates and immunization levels among census tracts. These data are, however, presented in the aggregate in Table 1.

Of the 1095 measles cases that occurred in Milwaukee between September 1, 1989, and June 30, 1990, 1011 (92.3%) were included in this study. We excluded 71 cases (6.5%) because they occurred in adults (≥18 years of age) and 13 cases (1.2%) because home addresses were not available. A case was considered confirmed when a positive indirect fluorescent antibody test for rubeola was obtained from the affected individual or when the standard CDC clinical case definition was met: fever, with a temperature of 38°C or higher if measured; a generalized maculopapular rash lasting 3 or more days; and at least one of the following: cough, coryza, or conjunctivitis.

Measles cases were grouped by census tracts. Measles attack rates (MARs) were calculated for individuals 17 years of age and younger using population data obtained from the US Special Census of 1985.[9] We excluded from the analysis 10 census tracts with five or fewer MPS vaccination records because of the unreliability of rates calculated from small numbers.

Our primary analysis examined the association between MARs and immunization rates among census tracts. To characterize this association, we made box-and-whisker plots[10] that summarize the distribution of attack rates for four immunization ranges defined by dividing the ranked immunization rates into four equal groups.

Because the MARs are not distributed normally and do not have constant variance across immunization levels, we used Spearman's rank correlation coefficients[11] to quantify the association between MARs and immunization rates.

Orenstein and coworkers[12] have cautioned investigators to be careful to evaluate whether vaccinees and nonvaccinees have equal risk of exposure to disease. In our study black children had markedly higher MARs. However, because of Milwaukee's highly segregated living conditions,[13] they also likely had greater risk of exposure to disease. Of the 1011 measles cases, 767 (75.9%) occurred in the 67 census tracts with populations greater than 49% black. Because racial segregation reduces mixing of populations and may produce unequal risks of exposure and because other factors, such as increased population density, may increase transmission within races, we examined whether race (<10%, 10% to 49%, and ≥50% black) or population density (<965 and ≥965 persons ≤17 years of age per square kilometer) confounded the association between MARs and immunization coverage. We also performed a stepwise regression analysis of the ranked data,[14,15] in which race, population density, and immunization coverage were included as candidate independent variables.

RESULTS

To estimate citywide immunization rates for one cohort of children who were 2 years old in 1986, ie, those who entered 5-year-old kindergarten in 1989, we combined records for 7899 MPS students with records for 1654 students in private kindergartens (Table 1). The total (9553) is 92% of the total number of 2-year-olds living in the city of Milwaukee in mid-decade (10 363), based on the 1985 US Special Census.[9]

A significantly lower immunization coverage rate was seen in children who attended public schools compared with private schools—59.1% vs 84.2% for one MMR vaccination by the second birthday ($P<.01$). The citywide average estimated immunization rate for one MMR vaccination by 2 years of age (63.5%)

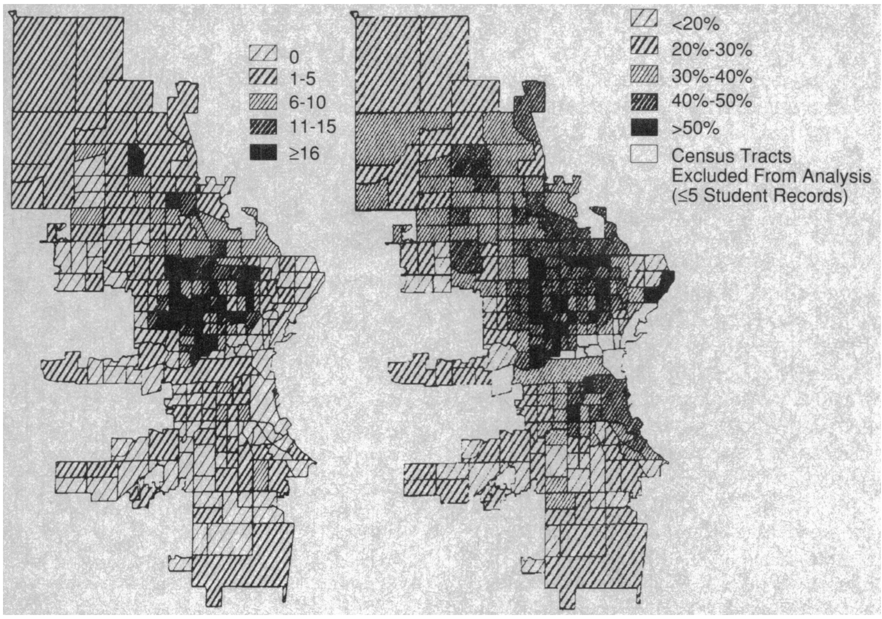

Fig 2.—Map of Milwaukee, Wis, by census tract. Left, Measles attack rates, cases per 1000 persons 17 years old or younger. Right, Immunization gap rates, percentage of 2-year-olds not immunized with one measles, mumps, and rubella vaccine.

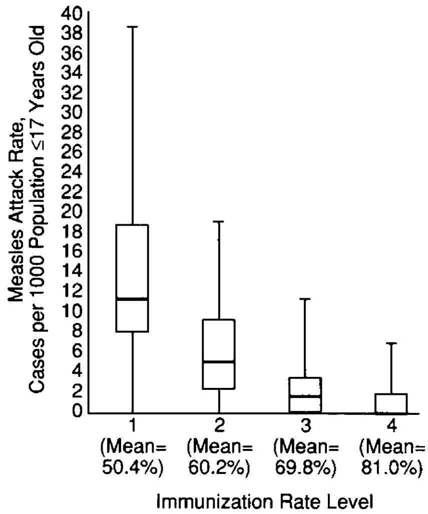

Fig 3.—Box and whisker plots of measles attack rates by immunization rate level group.

Table 2.—Association Between Measles Incidence and Characteristics of Census Tracts

Factor	No. of Census Tracts	Attack Rate per 1000 Persons: Median	Attack Rate per 1000 Persons: Mean	Rank Correlation Coefficient*	P
Black, %					
<10	93	0	1.5		
10-49	48	2.8	4.2	.70	<.01
≥50	67	11.3	12.3		
Population density, per square kilometer					
<965	111	1.5	2.9	.52	<.01
≥965	97	6.9	8.7		
Immunization coverage, %					
36.4-55.6	52	11.6	13.4		
55.7-64.6	52	5.0	6.0	−.71	<.01
64.7-74.8	52	1.7	2.0		
74.9-90.0	52	0	1.0		

*Test for rank correlation coefficient greater than 0 for percentage black and population density and for rank correlation coefficient less than 0 for immunization coverage.

was markedly lower than that found by the US Immunization Survey of 1985 (81.7%) (unpublished data, Centers for Disease Control, 1987). Comparing four different years during the 1980s, only slight differences were noted in immunization rates for any of the vaccines (Fig 1).

Immunization rates varied significantly by race/ethnicity. For one MMR vaccination by 2 years of age, 75% of whites had been immunized compared with 62% of Hispanics and 55% of blacks ($P<.01$). The rates for completing the entire recommended immunization series by age 2 years were 44%, 32%, and 28%, respectively.

In the 208 census tracts that had at least six schoolchildren with immunization records, immunization rates (one MMR vaccination by 2 years of age) ranged from 36.4% to 90.0%. Measles attack rates ranged from 0 to 38.7 cases per 1000 persons 17 years of age and under. Sixty-one census tracts had no cases, 105 had between one and nine cases, 33 had between 10 and 19 cases, and nine had 20 or more cases. Census tracts stratified by MARs—0, 1 through 9, 10 through 19, and 20 or more cases per 1000 persons—had respective median immunization rates of 75.0%, 64.4%, 51.8%, and 49.0%.

In comparing geographical maps, a clear correlation can be seen between decreasing immunization coverage and increasing MARs (Fig 2).

Census tracts stratified into four ranges of immunization rates, with means of 50.4%, 60.2%, 69.8%, and 81.0%, had respective median MARs of 11.6, 5.0, 1.7, and 0.0 cases per 1000 persons (Table 2). The rank correlation between MAR and immunization rate was high ($r=-.71$, $P<.01$)

Attack rates also varied significantly according to racial distribution and population density of census tracts (Table 2). Median MARs increased with increasing proportion of black residents, from no cases in census tracts with fewer than 10% blacks to 11.3 cases per 1000 persons in census tracts with a black population greater than 49%. Attack rates were higher in census tracts with a population density greater than 965 people per square kilometer (median, 6.9 cases per 1000 persons) than in those with a lower population density (median, 1.5 cases per 1000 persons).

We repeated the analysis after stratifying census tracts according to racial composition and population density. Increasing immunization coverage levels remained significantly associated with decreasing measles incidence rates among census tracts after controlling for either the proportion of black residents or population density ($P<.01$). The results of a stepwise regression analysis of the ranked data showed that the strongest predictor of MAR was immunization rate. Addition of the proportion of black residents and population density to the regression model improved the rank correlation only slightly.

For example, among the 67 predominantly black census tracts where 75.9% of all measles cases occurred, the MARs decreased as immunization coverage increased ($r = -.44$, $P<.01$). Mean measles immunization levels for the 67 black census tracts ranked and divided into four groups were 46%, 52%, 56%, and 60%. The corresponding mean MARs were 15.8, 11.8, 10.5, and 8.1 cases per 1000 persons.

COMMENT

Although school-age children and adolescents, including college students, were the sectors of the US population most affected by measles during the early 1980s,[2] the large measles outbreaks from 1989 until the present involved predominantly preschool-age children. The driving force of the current epidemic is the low level of immunization coverage among these preschoolers.[16] Following the Milwaukee measles outbreak of 1989-1990, we confirmed that only 64% of Milwaukee 2-year-olds had been vaccinated against measles. Given such low immunization rates in Milwaukee and presumably elsewhere in the United States, the outbreaks of measles and other vaccine preventable diseases that occurred during the late 1980s could have been expected.[17,18]

An important finding of this study was the highly significant correlation between increasing immunization coverage and decreasing measles transmission. In particular, our analysis suggests a threshold of immunization coverage above which widespread measles transmission does not appear to occur. As shown in Fig 3, the increase in average measles immunization rate from 50% to 60% was associated with a reduction in the median MAR by more than half (from 11.6 to 5.0 cases per 1000 persons). With 70% immunization coverage, measles incidence was lower by 86% (from 11.6 to 1.6 cases per 1000 persons). At 81% immunization coverage, the median MAR was zero.

These results are similar to those of a recently completed CDC study comparing vaccine coverage and measles incidence for eight US cities that suggests that a level of immunity of 70% to 80% among 2-year-old children in inner cities may be protective against disease outbreaks.[4] Measles epidemiology studies in Baltimore, Md, in the 1930s showed cyclical outbreaks paralleling a population of susceptible subjects that varied between 30% and 50%.[19] This work served as the basis for the concept of herd immunity thresholds, which created the expectation that nationwide immunization would lead to the eradication of measles in the United States by 1967.[20] The herd immunity, ie, immunization coverage, threshold required to prevent disease transmission within schools has been found to be quite high, exceeding 95%.[21] Empirical immunization thresholds that apply to the general population, however, have not been previously documented.

Mathematical models of disease outbreaks have been used to estimate immunity thresholds necessary to prevent disease transmission, but generally they require that populations mix randomly.[22] Natural populations, such as Milwaukee's, have much more complex mixing structures, driven by the special dynamics of subpopulations based on age, race, neighborhoods, schools, etc, and are affected by changing external forces, such as the economy and the seasons. Thus, to fully understand disease transmission to lay the groundwork for appropriate disease prevention strategies, theoretical models must be informed by empirical studies. By geographically matching MARs with immunization rates in Milwaukee, we have quantified the association between the two variables and have established the protection conferred by different levels of immunization in one urban community.

Our data suggest that the resurgence of measles in the United States is not necessarily the result of a more virulent virus or a less efficacious vaccine.[23] Rather, it is apparent that we have yet to achieve the required herd immunity threshold within a critical population. We have been overly optimistic about vaccine coverage of the preschool population that, in Milwaukee as elsewhere, has proven to be the engine of the current epidemic. The data also show, however, that we are not so far away from the herd immunity threshold of this hard-to-reach group that we should despair. Even among Milwaukee's black minority, in which racial segregation and greater population density increased the risk of measles transmission, modestly increased immunization levels remained strongly correlated with decreased MARs.

The substantial additional protection generated by relatively modest improvements in immunization coverage is the silver lining of this dark cloud. Moreover, our data suggest that immunization coverage of 2-year-olds of 80% or less may be sufficient to prevent sustained measles outbreaks in urban communities. Our challenge is to apply the human and financial resources necessary to achieve such coverage. Additionally, it is hoped that similar ecological studies will be performed in other urban and nonurban populations to establish locally relevant thresholds and to further define and quantify the concept of herd immunity.

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