Measles Outbreak in a Vaccinated School Population: Epidemiology, Chains of Transmission and the Role of Vaccine Failures

BENJAMIN M. NKOWANE, MD, SANDRA W. BART, BBA, WALTER A. ORENSTEIN, MD, AND MICHAEL BALTIER

Abstract: An outbreak of measles occurred in a high school with a documented vaccination level of 98 per cent. Nineteen (70 per cent) of the cases were students who had histories of measles vaccination at 12 months of age or older and are therefore considered vaccine failures. Persons who were unimmunized or immunized at less than 12 months of age had substantially higher attack rates compared to those immunized on or after 12 months of age. Vaccine failures among apparently adequately vaccinated individuals were sources of infection for at least 48 per cent of the cases in the outbreak. There was no evidence to suggest that waning immunity was a contributing factor among the vaccine failures. Close contact with cases of measles in the high school, source or provider of vaccine, sharing common activities or classes with cases, and verification of the vaccination history were not significant risk factors in the outbreak. The outbreak subsided spontaneously after four generations of illness in the school and demonstrates that when measles is introduced in a highly vaccinated population, vaccine failures may play some role in transmission but that such transmission is not usually sustained. (*Am J Public Health* 1987; 77:434–438.)

Introduction

Widespread use of measles vaccine in the United States has led to a dramatic decline in the number of reported cases of measles. Since 1979, over 95 per cent of school enterers have had histories of receipt of measles vaccine.[1] Measles vaccine is highly effective; most studies have shown that at least 90 per cent of vaccine recipients are protected and many studies indicate a protection level of 95 per cent or higher.[2–5] However, since the vaccine is not 100 per cent effective, there will always be some proportion of vaccinees (10 per cent or less) who remain susceptible to the disease. A major concern in the measles elimination effort is whether this small proportion of vaccine failures could sustain measles transmission.

Between March 3 and April 18, 1984, an outbreak of measles occurred in a high school in Massachusetts with a documented school immunization level of 98 per cent. This setting allowed us to address the question of whether measles transmission could be sustained in a highly vaccinated population and to assess the role of vaccinated individuals in the transmission of the disease.

Background

Waltham, a city nine miles west of Boston, MA with a land area of 12 to 41 square miles, contains 11 elementary schools (Kindergarten–5th grade), three junior high schools (Grades 6–8), and one senior high school (Grades 9–12). In addition, there is a college with an enrollment of 5,000 and a university with an enrollment of 3,000. The outbreak senior high school has an enrollment of 2,098 students. Students come to school by either school bus or personal cars. The school buses are shared by both elementary and high school students. In the outbreak school, intermingling of students from different grades typically occurs in the hallways before each class session and during lunch in the school cafeteria. There were no competitive sporting events involving other schools during the period of the outbreak.

Address reprint requests to Technical Information Services, Centers for Prevention Services, Centers for Disease Control, Atlanta, GA 30333. From the Division of Immunization, Centers for Prevention Services, CDC, and the Massachusetts Department of Public Health, Boston. This paper, submitted to the Journal January 28, 1986, was revised and accepted for publication September 4, 1986.

Methods

Case Definition

A case of measles was defined as an individual with: 1) generalized maculopapular rash of ≥ 3 days duration; 2) fever (≥101°F if measured); 3) at least one of the following: cough, coryza or conjunctivitis.

Surveillance

Regular daily contact was maintained throughout the outbreak period with school nurses, physician offices, and hospital emergency rooms in the county. Each patient with rash illness was interviewed, investigated, and attempts were made to determine the possible source of infection or exposure. School bus schedules were reviewed and bus drivers were also interviewed. School absentee registers covering the period February 1–April 30, 1984 were reviewed and any students absent from school for three or more consecutive days or the first and last days of the school week were interviewed to determine the reasons for absence. Students who were sick during Spring Break (April 13–April 23, 1984) were also interviewed to determine the nature of the illness.

Classification of Cases

A person was considered to have adequate evidence of immunity if he/she received live measles vaccine on or after the first birthday or had a prior history of physician-diagnosed measles. Those who received vaccine at less than 12 months of age were considered inadequately immunized. A case was considered preventable if the individual was born after 1956, lacked adequate evidence of immunity to measles, had no medical contraindication to receiving vaccine, and had no religious or philosophical exemption under state law. All other cases were considered non-preventable. For all the analyses regarding adequacy or inadequacy of vaccination, unimmunized individuals were included in the group termed inadequately vaccinated.

Health Record Review

The school health records of all the cases were reviewed for evidence of measles immunizations. In order to estimate the overall immunization level in the school, a random sample of 480 school records was taken by arbitrarily picking a record in the drawer and reviewing every fourth record thereafter.

Data Analysis

Information from the school records that was analyzed included age of student, date(s) of measles vaccination, age at vaccination, number of vaccinations, and time elapsed since vaccination. Attack rates for measles were computed assuming uniform exposure among all students in the school. Denominators for calculation of the estimated attack rates by date of vaccination, age at vaccination, number of vaccinations, and time elapsed since vaccination were calculated by multiplying the number of students in a particular group determined by the health record review by 4.37 (2098/480). Analyses for attack rates by age at vaccination, number of vaccinations, and time elapsed since vaccination were done only for those immunized with measles vaccine on or after the first birthday. Separate analyses were also done for those vaccinated under 12 months of age and those vaccinated at 12 to 14 months of age. For the comparisons of clinical features of illness, cases immunized at less than 12 months of age were included in the inadequately vaccinated group. Vaccine efficacy was calculated using the formula:

$$VE = [(ARu\text{-}ARv/ARu] \times 100 = [(1\text{-} (ARv/ARu)] \times 100$$

Where VE = Vaccine efficacy (%)
ARu = Attack rate among unvaccinated
ARv = Attack rate among vaccinated.

95% confidence intervals were computed using the formula described by Orenstein, *et al.*[6]

Statistical Tests

Statistical testing on all the attack rates and the estimation of vaccine efficacy was done using denominators from the random sample. Ninety five per cent confidence intervals (CI) were computed for comparisons of epidemiologic features among adequately and inadequately immunized persons.

Epidemiologic Studies

A case-control study, using one randomly picked control for each case in the high school, matched by grade, was conducted to evaluate risk factors associated with the outbreak. Cases and controls were interviewed and asked questions regarding any illnesses, contact with sick persons with rash, history of travel, classroom schedules, school bus schedules, and activities they participated in during the period February 1 through April 30, 1984. The school immunization histories in the school records were verified by contacting the parents of the child and obtaining the provider's name and address. The provider was then contacted and requested to provide the date(s) vaccine was given. The school immunization record was considered provider-verified if the date in the school record matched the provider's date and the provider confirmed that he or she gave the vaccine. Comparisons between the cases and controls were done by computing 95% CI of the differences observed.

Results

Between March 3 and April 18, 1984, a total of 27 cases of measles were reported in Waltham, Massachusetts. Acute and convalescent serum specimens were available for testing from 10 (37.0 per cent) of the patients. The diagnosis was serologically confirmed in seven cases [by a greater than four-fold rise in hemagglutination inhibition (HI) antibodies in five cases and by presence of measles specific IgM antibodies in two cases]. The remaining three patients with serum specimens tested all had convalescent HI antibodies of 1:64 or greater.

Twenty four of the 27 cases occurred in students attending the senior high school (enrollment 2,098, attack rate 1.1 per cent). Of the remaining three cases, two were siblings of the source case (one elementary school attendee and the other a junior high school attendee). The third patient, who also attended the junior high school, had onset of illness while on spring break in Florida. No other cases were reported from the schools these three cases attended or from any other schools in the city.

Thirteen of the cases were male, and 14 female. Except for the non-senior high school cases, all the cases were aged 14 to 18 years of age. The immunization status for all the cases in the outbreak and the pattern of transmission are shown in Figure 1. Overall, eight cases (30 per cent) were preventable, three with no history of vaccination and five who had been vaccinated at less than 12 months of age. The remaining 19 cases were non-preventable and had all received at least one dose of vaccine at 12 months of age or older.

The source case for the senior high school outbreak was a 16 year-old male 12th grade student who worked part-time in the dining room of the nearby college, where there had been an outbreak of measles; he was epidemiologically linked to cases that had been reported at the college. The student had onset of rash illness on March 3, 1984 but did not attend school during the major communicable period of illness (the prodrome and the first four days after onset of rash). The two siblings of the source case developed rash illness seven and ten days thereafter and attended school during their infectious period. No spread was recognized in the schools they attended, however.

The outbreak was introduced into the senior high school by a female 16 year-old 11th grade student who rode on the same school bus as the junior high sibling of the source case. This adequately immunized patient transmitted disease to at least five other students in the senior high school. For the cases after the introduction in the senior high school, adequately immunized persons were identified sources for 11 cases (48 per cent) and inadequately immunized persons for 10 cases (44 per cent). Adequately immunized persons gave rise to a median of zero cases (mean = 1.9, range 0 to 5) while for inadequately immunized persons the median was 1.5

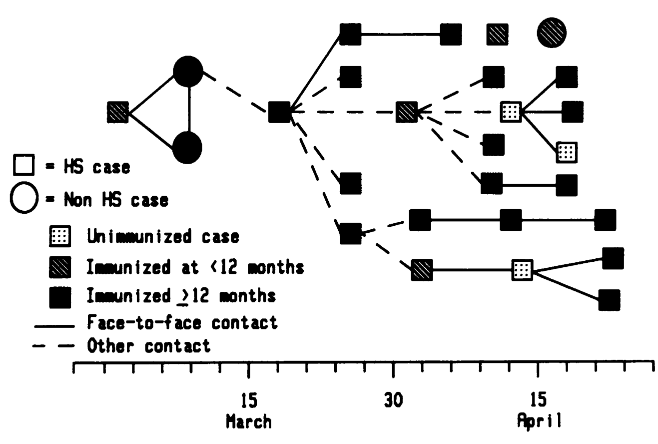

FIGURE 1—Pattern of Measles Transmission, Waltham, Massachusetts, March–April 1984

TABLE 1—Comparison of Clinical Features of Illness by Vaccination Status, Waltham, Massachusetts, March–April 1984

Variables	Immunization Status: Adequate	Inadequate*	Difference**	95% CI of Difference
Number Cases	19	8		
Mean number days absent	6.2	7.5	1.3	−0.7, 6.5
Mean number days of rash	5.5	5.6	0.1	−0.8, 1.7
Mean number days fever	4.6	7.0	2.4	−1.3, 5.6
Mean number days cough	4.6	4.5	−0.1	−1.2, 1.7
Median number cases resulting***	0.0	1.5	1.5	−0.3, 2.3

*Includes unvaccinated cases and cases vaccinated prior to first birthday.
**Inadequate minus Adequate.
***Only for the cases in senior high school, excludes siblings of the source case.

cases, the mean 1.7, range 0 to 4. One junior high school case could not be epidemiologically linked to the other cases in the outbreak. Four generations of spread occurred and no cases occurred more than 46 days following onset of the source case in the outbreak.

Seven (26 per cent) of the 27 patients were hospitalized for the illness. These included all three unimmunized patients, one of those immunized at less than 12 months of age, and three adequately immunized persons. Thus half of the unimmunized and inadequately immunized cases were hospitalized versus 3/19 of those adequately immunized (difference 34 per cent–95 per cent CI −4.4 per cent, 72.4 per cent). The reasons for hospitalization included high fever, severe cough, and pneumonia in two of the adequately vaccinated students. Further indices for severity of illness among the cases by vaccination status are presented in Table 1. In general, only minor differences were observed between the two groups.

The estimated attack rates by age at vaccination for students who had received a single dose or more than one dose of measles vaccine in the senior high school are presented in Table 2. The attack rates were highest (15 per cent) for persons immunized at less than 12 months of age and lowest for those immunized after the first birthday (1.3 per cent). Among the 274 students in the random sample who had received more than one dose of measles vaccine, 170 (62.0 per cent) had received their first dose of measles vaccine at less than 12 months of age. Among those who had received their first dose on or after 12 months of age, the second or

TABLE 3—Measles Attack Rates (AR)* of Single Dose Recipients by Years since Vaccination, Waltham (Massachusetts) Senior High School March–April 1984

Years since Vaccination	Cases	Sample	AR
0–4	0	18	0.0
5–9	1	21	1.1
10–16	10	158†	1.4
Total	11	197	1.3

*Cases/estimated total students from random sample.

third immunization was given as measles-mumps-rubella (MMR) vaccine when the school laws required evidence of immunity to mumps and rubella.

In all, persons who received one dose of measles vaccine at 12 months of age or older had almost three times the risk of developing measles than persons who had received two doses (relative risk = 2.6, 95 per cent CI 0.9, 7.8). The estimated vaccine efficacy computed using the sample of immunization records as denominators for calculation of attack rates was 94.4 per cent (95 per cent CI 90.6 per cent, 97.0 per cent) for single dose recipients immunized on or after 12 months of age.

The risk of disease by time passed since vaccination was evaluated for single dose recipients of measles vaccine who had been vaccinated on or after their first birthday (Table 3). The estimated attack rates by time elapsed since vaccination varied from zero for those immunized 0 to 4 years previously to 1.4 per cent for those immunized 10 or more years previously. ($p = 0.28$, chi-square test for trend). The attack rates of subjects who received more than one dose were not analyzed in this way since the subsequent doses were administered more recently.

The results of the case-control study are presented in Table 4. Cases of measles were more likely to have had face-to-face contact with another case, to have attended the same classes, shared common activities, and have a case as a friend. History of revaccination or provider verification of the immunization history were not risk factors in this outbreak.

Outbreak Control

During the outbreak period, a complete review of all school immunization records was conducted and 23 students were identified with inadequate evidence of immunity to measles. Measles vaccine was given to 15 of the students. The remaining eight had religious or philosophical objections to vaccination and were therefore excluded from school until

TABLE 2—Measles Attack Rates (AR)* by Doses Number and Age at Vaccination, Waltham (Massachusetts) Senior High School March–April 1984

Age at Vaccination	One Dose: Cases	Sample	AR	Two or More Doses**: Cases	Sample	AR
No Vaccine	3	3	22.9	0	0	0.0
<12 months	4	6	15.3	0	0	0.0
12–14 months	1	49	0.5	0	0	0.0
≥15 months	10	148	1.5	6	274	0.5
Total	18	206	—	6	274	0.5

*Cases/estimated total students projected from random sample.
**Age at second dose was 15 months or older.

TABLE 4—Results of Case-Control Study, Waltham (Massachusetts) Senior High School March–April 1984

Risk Factors	Cases n = 24 (%)	Controls n = 24 (%)	Percentage Difference*	95% CI of Difference
Face-to-face contact with cases	7 (29.2)	3 (12.5)	16.7	−5.8, 39.8
Revaccination	6 (25.0)	8 (33.3)	8.3	−16.4, 34.4
Provider verified immunizations	19 (79.2)	20 (83.3)	4.1	−18.2, 26.2
Attending classes with cases	10 (41.7)	6 (25.0)	16.7	−8.1, 44.1
Sharing activities with cases	10 (41.7)	7 (29.2)	12.5	−13.8, 39.8
Having a case as friend	5 (20.8)	4 (16.7)	4.1	−18.2, 26.2

*Absolute difference (per cent of cases minus per cent of controls).

May 10, 1984, 21 days after the last case was reported. In addition, two infants who were siblings of cases were given immune globulin prophylaxis.

Discussion

This outbreak of measles occurred in a highly vaccinated population and 70 per cent of the cases were vaccine failures. The overall attack rate of 0.8 per cent in the school, among presumably adequately vaccinated students, was below the expected 2–10 per cent primary vaccine failure rate for measles vaccine.[5,7,8] Vaccine failures in this setting also played some role in the spread of disease.

Although there was a tendency to more severe illness among the inadequately vaccinated patients, as evidenced by the higher hospitalization to case ratio in this group, this was not impressive. The failure to find large differences in other potential indices of severity of illness such as number of days absent from school, duration of fever, and duration of rash may have been due to the inclusion of persons immunized prior to 12 months of age in the inadequately immunized group. However, since primary vaccine failure (most never responded to initial vaccination) is known to be high in this inadequately vaccinated group, the failure to observe differences suggests that overall illness patterns are similar in vaccine failures and in the unvaccinated.

The finding that inadequately and adequately immunized students gave rise to a similar number of cases on average indicates that vaccine failures in this outbreak played some role in the spread of disease. The likely reason for the fact that measles transmission subsided spontaneously and no cases occurred beyond the fourth generation in the high school, is that in a highly vaccinated population, the few vaccine failures do not come into frequent contact with students capable of transmitting the virus. The lack of spread in the junior high school and the elementary schools attended by the siblings of the source cases suggests that this may be the case. The closure of school for spring break may also have reduced the risk of contact. Nevertheless, depending on how they are dispersed in the population, and the extent of exposure, vaccine failures may serve to perpetuate an outbreak even in a highly vaccinated population. Clearly, the low overall attack rate among vaccinated students in the senior high school, given the expected failure rate of 2–10 per cent, suggests that not all susceptibles were exhausted.

The possible causes of vaccine failures can be divided into two major categories: primary, due to lack of initial seroconversion; and secondary, due to loss of immunity after initial seroconversion. Since seroconversion is rarely documented after vaccination, these two types of vaccine failure are difficult to distinguish. The primary failure rate for measles vaccine has been shown to be less than 5 per cent under field trial conditions.[2–4] It has been suggested that in clinical practice it may be somewhat higher, as much as 10 per cent.[1] Nevertheless, one serologic study using a sensitive Elisa test showed a failure rate of only 1.7 per cent.[5]

Primary vaccine failure can be due to either inactive vaccine or inadequate host response. In this outbreak we were unable to show clustering of cases by time, place, or provider of vaccine which would have suggested a potential problem with vaccine handling. We were able to provider verify immunization histories for both our case and controls to a similar extent, suggesting that the school vaccine histories for both cases and controls were accurate. The finding of significantly higher attack rates among persons immunized at less than 12 months is consistent with previous reports that have shown lower vaccine efficacy when compared to those immunized after 12 months of age.[9–11] The second possibility, inadequate host response to vaccine, could not be ruled out among the vaccine failures.

The analysis of attack rates by time elapsed since vaccination suggests that waning immunity among the vaccine failures was not a major problem in this outbreak. This finding is consistent with other similar epidemiologic studies which have failed to show any significant differences in attack rates when the interval from vaccination to exposure varied from 0–3 years to 10–12 years.[7–9,12] In addition, multiple serologic studies have shown that immunity induced by measles vaccine is long lasting.[8,11,13,14] Measles specific antibodies have been shown to persist up to 16 years after vaccination and although about 13 per cent of individuals lose detectable antibodies, these individuals show a secondary or anamnestic response when they are revaccinated, suggesting that they are still probably immune.[14]

This outbreak demonstrates that while measles transmission can occur in a highly vaccinated population and vaccine failures may play some role in the spread of disease, such transmission is usually not sustained.

ACKNOWLEDGMENTS

We thank J. Egan, J. Ferolito, B. Obrys, M. Regan, R. Mailloux, Dr. J. McManama, Dr. N. Fiumara, and V. Beraldi for their part in the investigation.

REFERENCES

1. Centers for Disease Control: Measles Surveillance Report No. 11, 1977–1981. Atlanta: CDC, 1982.
2. Hilleman MR, Buynak EB, Weikel RE, Stokes J, Whitman JE, Leagus MB: Development and evaluation of the Moraten measles virus vaccine. JAMA 1968; 206:587–590.

3. Schwarz AJ: Immunization against measles: development and evaluation of a highly attenuated live measles vaccine. Ann Pediatr (Basel) 1964; 202:241–252.
4. Cooperative Study. Extensive clinical evaluation of a highly attenuated live measles vaccine. JAMA 1967; 199:26–30.
5. Brunell PA, Weigle K, Murphy MD, Shehab Z, Cobb E: Antibody response following Measles-Mumps-Rubella vaccine under conditions of customary use. JAMA 1983; 250:1409–1412.
6. Orenstein WA, Bernier RH, Dondero TJ, *et al:* Field evaluation of vaccine efficacy. Bull WHO 1985; 63:1055–1068.
7. Hayden GF: Measles vaccine failure: a survey of causes and means of prevention. Clin Pediatr 1979; 18:155–167.
8. Weibel RE, Buynak EB, Mclean AA, Hillerman MR: Follow-up surveillance for antibody in human subjects following live attenuated measles, mumps and rubella vaccines. Proc Soc Exp Viol Med 1979; 162:328–332.
9. Marks JD, Halpin TJ, Orenstein WA: Measles vaccine efficacy in children previously vaccinated at 12 months of age. J Pediatr 1978; 62:955–960.
10. Lerman SJ, Gold E: Measles in children previously vaccinated against measles. JAMA 1971; 216:1311–1314.
11. Shasby DM, Shope TC, Downs H, Herrmann KL, Polkowski J: Epidemic measles in a highly vaccinated population. N Engl J Med 1977; 296:585–589.
12. Shelton JD, Jacobson JE, Orenstein WA, Schulz KF, Donnell HD: Measles vaccine efficacy: influence of age at vaccination vs duration of time since vaccination. Pediatrics 1978; 62:961–964.
13. Krugman S: Present status of measles and rubella immunization in the United States: a medical progress report. J Pediatr 1977; 90:1–12.
14. Krugman S: Further attenuated measles vaccine: characteristics and use. Rev Infect Dis 1983; 3:477–481.

NCHSR Solicits Proposals for Research in Medical Practice Variations and Patient Outcomes

The National Center for Health Services Research and Health Care Technology Assessment (NCHSR) encourages researchers to submit grant proposals for studies of variations in the patterns of medical practice and their effects on patient outcomes and the costs of care. The program is designed to provide research information to address important clinical questions as well as immediate health policy concerns.

Proposals should focus on medical conditions which have particular relevance to the Medicare program. Treatments and procedures to be studied should be those which are significant in terms of Medicare beneficiaries' use of health services, length of hospitalization, costs and risks, and for which data indicate highly varying patterns of use.

NCHSR seeks to stimulate research designed to provide better guidance to clinicians about the outcomes and the costs of alternative practice patterns, and to identify feasible and acceptable methods for reducing variations due to factors such as physician convenience, perceptions about malpractice, peculiarities in payment schemes, or other considerations not related to the quality of care. Areas of particular interest include:

- Model evaluations of patient outcomes
- Assessments of admission and treatment criteria
- Improvements in research methods and data sources

Investigators are encouraged to discuss research ideas with NCHSR staff members prior to submitting a proposal. Additionally, staff members can offer suggestions about whether support should be requested through the usual NCHSR grants program or through the Small Grants Program. They should be contacted through:

Director
NCHSR Division of Extramural Research
18A-19 Parklawn Building
Rockville, MD 20857; 301/443–2345.

The submission and review schedule is:

NIH/DRG submission	Study section review	Council review	Earliest start
June 1	October	February	March 1
October 1	March	June	July 1
February 1	June	September	September 30