A Million Dollar Measles Outbreak: Epidemiology, Risk Factors, and a Selective Revaccination Strategy

SUSAN E. ROBERTSON, MD, MPH, MS
LAURI E. MARKOWITZ, MD
DENNIS A. BERRY
EUGENE F. DINI, MPA
WALTER A. ORENSTEIN, MD

At the time of the investigation, Dr. Robertson was with the Division of Immunization, National Center for Prevention Services (NCPS), Centers for Disease Control (CDC), Atlanta, GA. She is currently with the Expanded Programme on Immunization, World Health Organization, Geneva, Switzerland. Dr. Markowitz and Dr. Orenstein are with the Division of Immunization, NCPS. Mr. Berry is with the Arkansas State Department of Health, (ASDH) Little Rock. Mr. Dini is currently with the Georgia Department of Human Resources, Atlanta, GA. At the time of the investigation, he was with the ASDH.

Stuart Fitzhugh, MD, ASDH, requested and facilitated this investigation. Ruby Jones, Virginia Hockett, RN, and Marie Tucker, RN, ASDH; Lee Cole, RN, and Hazel Mabry, RN, Washington County Health Unit; Linda Mabry, RN, Rogers School District; and Robert Wirag, MD, University of Arkansas Student Health Services, provided guidance and assistance in data collection.

Tearsheet requests to Technical Information Services, National Center For Prevention Services, Mail Stop E 07, Centers for Disease Control, Atlanta, GA 30333.

Synopsis

Between February 8 and April 4, 1986, an outbreak of measles occurred in the State of Arkansas. A total of 489 suspected measles cases were reported from 53 counties; 86 schools statewide reported suspected measles cases. There were 284 cases confirmed in 18 counties; 23.6 percent among students in one university and 41.2 percent among students in kindergarten through 12th grade in 32 schools.

An epidemiologic investigation was carried out to evaluate risk factors for vaccine failure and to assess the effectiveness of a selective revaccination strategy in the outbreak setting. A cohort study conducted at a junior high school showed that, compared with students vaccinated against measles at ages 15 months or older, those vaccinated at ages 12-14 months had a three-fold increased risk of measles (relative risk 3.2, 95 percent confidence interval 1.5, 6.9).

For schools reporting measles, the Arkansas Department of Health and the Department of Education jointly required reimmunization of students vaccinated at ages younger than 15 months and the exclusion of students not vaccinated at ages 15 months or older until they were vaccinated or until 2 weeks after the last rash onset. To implement these recommendations, more than 100,000 doses of combined measles-mumps-rubella vaccine were distributed at a cost greater than $1 million.

SINCE MEASLES VACCINE was introduced in the United States in 1963, the reported incidence of measles has decreased 99 percent, and indigenous measles transmission has been eliminated from most of the country. Of the cases reported annually between 1981 and 1988, there was a low of 1,497 in 1983 and a high of 6,282 in 1986 (*1*). In 1985 and 1986, of 152 measles outbreaks in the United States, 101 (66.4 percent) occurred primarily among school-age persons (*2*). Many of the school-age measles cases occurred among persons who had previously received measles vaccine.

The efficacy of the vaccine in persons receiving it at ages 15 months or older has been calculated to be above 90 percent; in persons vaccinated at ages 12 to 14 months, however, the efficacy of measles vaccine has been found to be lower (*3*). The extent of measles transmission among highly vaccinated school-age populations suggests that additional strategies, such as selective or mass revaccination of prior vaccine recipients may be necessary to prevent outbreaks. Selective revaccination of persons vaccinated prior to age 15 months was first implemented as an outbreak control strategy in 1985 (*4*).

Our report is of an outbreak of measles that occurred in Arkansas in the spring of 1986.

In the State of Arkansas, all children attending kindergarten through grade 12 are required by State law to present evidence of measles immunity

as a condition for school attendance. This consists of documentation of (*a*) adequate immunization with live measles vaccine on or after the first birthday or (*b*) physician-diagnosed measles. The law allows medical and religious, but not philosophic, exemptions; all exemptions must be certified by the Director of the State Immunization Program.

Immunization surveys in Arkansas in 1982-83 and 1984-85 indicated measles immunization levels of 99 percent among kindergarten and first grade students and 94 percent among children attending day care centers, according to unpublished data of the Arkansas Department of Health. The State was measles-free in 1982 and 1985. There were only 25 measles cases reported in 1981, 8 in 1983, and 13 in 1984.

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Methods

Case definition. In the Arkansas outbreak, clinical, epidemiologic, and programmatic case definitions were modeled after recommendations of the Centers for Disease Control (CDC) (*5*). A clinical case of measles was defined as an illness characterized by a generalized maculopapular rash lasting 3 or more days; a fever of 101 degrees Fahrenheit or higher, if measured; and at least one of the following symptoms: cough, coryza, or conjunctivitis. Three epidemiologic case definitions were used.

1. A suspected case was defined as a person with a febrile rash illness.
2. A probable case was defined as a patient meeting the standard CDC clinical case definition or, during the initial weeks of the outbreak, a patient diagnosed by a physician to have measles.
3. A confirmed case was defined as a case that was serologically confirmed or, where serologic data were not available, a probable case epidemiologically linked to another probable or confirmed case, for example, rash onset 7-18 days after rash onset in the linked case. Serologic confirmation was defined as either a four-fold rise in measles antibody titer between acute and convalescent sera or a single positive measles-specific immunoglobulin M titer.

Measles cases were classified programmatically as preventable or nonpreventable. A case was considered preventable if the illness occurred in an American citizen at least 16 months of age, born after 1956, lacking adequate evidence of immunity to measles (documentation of vaccination with live vaccine on or after the first birthday, physician-diagnosed measles, or laboratory evidence of measles immunity), without a medical contraindication to receiving vaccine, and with no religious exemption.

Surveillance. A total of 11 public health nurses trained in communicable disease control routinely investigate rash illnesses in Arkansas within 48 hours after they are reported. During the outbreak, active surveillance consisted of regular contact with schools, colleges, day care centers, physicians' offices, and hospital emergency rooms throughout the State. Each patient with febrile rash illness was interviewed, investigated, and attempts were made to determine the possible source of infection or exposure.

Cohort study. A retrospective cohort study was conducted at junior high school A to examine the risk of acquiring measles by age at vaccination, number of doses of vaccine received, and time since vaccination. School health records of 627 students in grades seven to nine were examined for age at measles vaccination. Age at vaccination (in months) was defined as the number of complete calendar months attained (for example, a person vaccinated on or after the first birthday but before the 13th month interval would have an age at vaccination of 12 months). Because a revaccination program was administered at the school on February 25, 1986, the study included as cases only students whose rash onset occurred by that date. This provision eliminated the potential bias of students whose vaccination status changed during the course of the outbreak. Vaccine efficacy (*VE*) was calculated by the following equation:

$$VE\ (percent) = [(ARu - ARv) \div ARu] \times 100,$$

where ARu is the attack rate in the unvaccinated and ARv is the attack rate in the vaccinated (*6,7*).

Figure 1. Comparison of suspected measles cases with confirmed cases by county in Arkansas, 1986

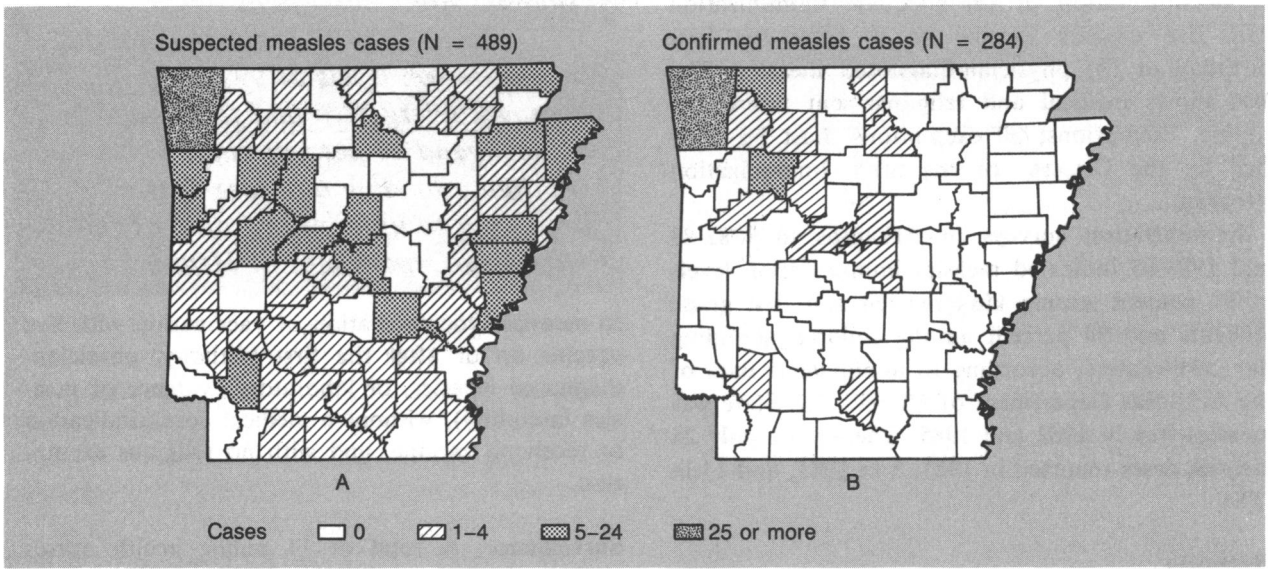


Table 1. Classification of confirmed measles cases, Arkansas, February–April 1986

Classification	Number	Percent
Nonpreventable:		
Persons younger than 16 months of age	21	7.4
Persons born before 1957	10	3.5
History of vaccination:		
At 12–14 months	47	16.5
At 15 months or older	106	37.3
Exemption	1	0.4
Prior physician diagnosis	2	0.7
Preventable	97	34.2
Total	284	100.0

Time since vaccination was calculated as the duration between the date of vaccination and the first rash onset of the outbreak (February 8).

Case-control study. To evaluate the validity of school records and to examine other risk factors for measles, a case-control study was conducted at school A. In all, 41 students who had rash onset by February 25 were selected for the study. Controls were randomly selected from students who had no signs or symptoms compatible with measles; they were frequency matched by grade in a 1:1 ratio to cases. Parents were interviewed and the health care providers identified by parents were contacted by telephone to obtain information on the patient's measles vaccination. School record vaccination date and provider vaccination date were compared. A school record was considered verified if it had the same month and year of vaccination as the provider record.

Statistical analysis. Statistical analysis was performed on a microcomputer using Epi-Info, an epidemiologic software package developed by the Epidemiology Program Office, CDC (*8*). Taylor series approximations of 95 percent confidence intervals for vaccine efficacy were obtained by calculating the confidence interval around the relative risk according to the method described by Orenstein and colleagues (*6,7*). The case-control study was analyzed in an unmatched fashion.

Results

Descriptive epidemiology. From February 8 to April 30, 1986, the Arkansas Department of Health received reports from local health departments of 489 suspected measles cases. Suspected cases were reported from 53 (70.7 percent) of the 75 counties in Arkansas; the measles outbreak appeared to have spread throughout the State (fig. 1).

Following complete investigation, 284 (58.1 percent) of the 489 suspected cases were confirmed as measles. Fifty-six cases were serologically confirmed. All cases occurred in Arkansas residents. Cases were confirmed in 18 (24 percent) of the 75 counties in Arkansas; most confirmed measles cases were localized to the northwest portion of the State (fig. 1).

Rash onsets for the 284 confirmed cases occurred from February 8 through April 4, 1986. An index

Table 2. Risk of measles by doses of vaccine and age at vaccination based on school vaccination records of 627 students, junior high school A, Arkansas, 1986

Doses	Cases		Students		Attack rate (percent)	Relative risk	95 percent confidence interval
	Number	Percent	Number	Percent			
0 doses	3	7.3	5	0.8	60.0	20.2	8.0, 50.9
1 dose at —							
Younger than 12 months	10	24.4	56	8.9	17.9	6.0	2.7, 13.5
12–14 months	16	39.0	167	26.6	9.6	3.2	1.5, 6.8
15 months or older	11	26.8	371	59.2	3.0	1.0	
2 doses —							
1 at younger than 12 months	1	2.4	6	1.0	16.7		
Both at 12 months or older	0	0.0	22	3.5	0.0		
Total	41		627		6.5		

case was not identified for the outbreak. The probable setting of transmission for the first generation of cases was a basketball game at a university in Washington County, on January 25. Within 2 weeks after the basketball game, 15 university students and 2 junior high school students who attended the game were diagnosed as having measles. Over the next week, measles spread among the university student body. Eventually, 21 students with measles were admitted to the university health center. A total of 67 confirmed cases occurred among students at the university. The attack rate at the university was 0.5 percent (67 of 13,000 students); the attack rate was higher for on-campus residents (0.8 percent) than off-campus residents (0.4 percent) ($\chi^2 = 6.3$, $P = 0.01$). In addition to the 67 cases at the university, 48 other cases occurred in Washington County. Benton County, the county immediately north of Washington County, had 113 confirmed cases. In one town in Benton County there were 71 confirmed cases. In that town, measles spread rapidly at junior high school A, the school attended by two students who most likely acquired measles at the January 25 university basketball game. The attack rate at junior high school A was 7.9 percent (50 of 627 students).

Of the 284 confirmed cases in this outbreak, 34.1 percent were preventable and 65.9 percent were nonpreventable (table 1). Persons who had received measles vaccine at ages 12 months or older accounted for 53.8 percent of all the cases, including 47 cases (16.5 percent); these were persons vaccinated between ages 12 and 14 months. Patients in this outbreak ranged in age from 5 months to 38 years; the majority (75 percent) were between ages 10 and 24, 16.5 percent were younger than age 10, and 8.5 percent were between ages 25 and 38. A total of 117 cases (41.2 percent) occurred in primary and secondary school students who attended 32 different schools (16 elementary schools, 8 junior high schools, 7 high schools, and 1 private school). There were 67 cases (23.6 percent) among students at a single university. None of 33 other colleges and universities in Arkansas reported confirmed measles cases.

Cohort study. Among the cohort of 627 students at junior high school A, 5 (0.8 percent) had not been vaccinated, 594 (94.7 percent) had received a single dose of measles vaccine, and 28 (4.5 percent) had received two doses of measles vaccine (table 2). Compared with students vaccinated once at ages 15 months or older, those who had not been vaccinated had a 20-fold increased risk of measles; those who received a single dose of measles vaccine before age 12 months had a 6-fold increased risk; and those who received a single dose of vaccine at ages 12-14 months had a 3-fold increased risk. None of the 22 students who received two doses of measles vaccine at ages 12 months or older became ill.

The clinical efficacy of one dose of measles vaccine received before age 12 months was 70.2 percent (table 3). The clinical efficacy of a single dose of measles vaccine at ages 12 months or older was 91.6 percent. For a single dose of measles vaccine received at ages 12-14 months, clinical efficacy was 84.0 percent; for a single dose received at ages 15 months or older, 95.1 percent.

The risk of disease by years since vaccination was evaluated for single dose recipients of measles vaccine who had been vaccinated on or after age 12 months. The attack rate was 0 percent among students vaccinated 0-4 years before the outbreak, 1.4 percent for those vaccinated 5-9 years before, 5.4 percent for those vaccinated 10-14 years before, and 9.5 percent for those vaccinated 15-19 years

Table 3. Efficacy of measles vaccine by age at vaccination, based on school vaccination records, junior high school A, Arkansas, 1986

Age at vaccination	Vaccine efficacy (percent)	95 percent confidence interval
Younger than 12 months	70.2	21.6, 88.0
12 months or older	91.6	81.3, 96.3
12–14 months	84.0	62.5, 93.2
15 months or older	95.1	87.6, 98.0

Table 4. Years since measles vaccination for students with a single dose administered at 12 months or older, based on school vaccination records, junior high school A, Arkansas, 1986

Cases and students by age at vaccination	Period when vaccinated			
	1982–86	1977–81	1972–76	1967–71
Years since vaccination	0-4	5-9	10-14	15-19
Total number of cases	0	1	24	2
Vaccinated at 12–14 months	0	0	14	2
Vaccinated at 15 months or older	0	1	10	0
Total number of students	2	74	441	21
Vaccinated at 12–14 months	0	0	149	18
Vaccinated at 15 months or older	2	74	292	3
Total attack rate (percent)	0.0	1.4	5.4	9.5
Vaccinated at 12–14 months	0.0	0.0	9.4	11.1
Vaccinated at 15 months or older	0.0	1.4	3.4	0.0

before. There was a trend toward increasing risk of disease with increasing time since vaccination (chi-square test for linear trend, 1-tailed, $P = .04$). However, when stratified by age at vaccination (12–14 months and 15 months or older), age at vaccination and time since vaccination were shown to be highly confounded, with vaccinations at 12-14 months occurring primarily in the earlier years (table 4). Data were insufficient to assess these factors further.

Case-control study. Risk factors for measles were further examined in a case-control study conducted among 82 students at junior high school A, 41 in the case group and 41 in the control group. Inability to contact the health care provider and lack of provider verification of school vaccination records were not associated with an increased risk of measles. There was no difference in our ability to verify vaccination records of cases and controls, suggesting that school-based data demonstrating a risk of disease by age at vaccination in the cohort study were valid. School records were verified for 29 cases (70.7 percent) and 30 controls (73.2 percent), ($P = 0.81$).

Age at vaccination was found to be a risk factor. Based on provider-verified data, in the case-control study we found that students vaccinated at ages 12-14 months were 5.6 times as likely (as measured by the odds ratio) to acquire measles compared with students vaccinated at ages 15 months or older ($P = 0.02$) (table 5). This odds ratio is somewhat higher than the point estimate of relative risk in the cohort study (3.2), but it is well within the 95 percent confidence interval (1.5, 6.9) of the relative risk.

Outbreak control. The university did not have an immunization requirement for students or faculty prior to this outbreak. After the first measles cases were reported, university officials promptly organized an on-campus immunization clinic. Of 13,000 students, 6,000 (46.2 percent) voluntarily received measles-mumps-rubella (MMR) vaccine within the first 3 weeks of the outbreak. Students who did not attend the immunization clinic were requested to present evidence of immunity to measles. The university advised the National Collegiate Athletic Association that any out-of-State students visiting the campus for sporting events would be required to present evidence of immunity to measles.

When 50 schools statewide reported at least one suspected measles case, State health officials met with State education officials to formulate an outbreak control strategy. All primary and secondary schools in Arkansas were asked to audit student health records for dates of measles vaccination. Data from selected public schools throughout the State indicated that 8 percent to 10 percent of students in fourth grade and above were not in compliance with State measles immunization requirements. A general recommendation to revaccinate any child whose measles vaccination was received before age 15 months was widely publicized. Requirements for schools reporting probable cases of measles were (*a*) reimmunization of students vaccinated when they were younger than age 15 months and (*b*) exclusion of students not vaccinated at ages 15 months or older until they were vaccinated or until 2 weeks after the rash onset of the last case.

This outbreak control policy was announced on February 25, 1986. By March 31, 1986, a total of 111,442 doses of measles vaccine (primarily MMR) had been distributed in Arkansas. This amount

Table 5. Risk factors for measles, case-control study, junior high school A, Arkansas, 1986

Risk factor	Cases		Controls		Odds ratio	95 percent confidence interval	P value
	Number	Percent	Number	Percent			
Provider not contacted	10	24.4	8	19.5	1.3	0.4, 4.3	0.79
Provider contacted: not verified	2	4.9	3	7.3	0.7	0.1, 4.0	0.53
Verified unvaccinated:							
Religious exemption	1	2.4	0	...	...	...	
Physician-diagnosed measles	2	4.9	0	...	...	...	
Verified vaccinated:							
1 dose at younger than 12 months	7	17.1	1	2.4	[1]25.2	2.1, 1196.1	0.004
1 dose at 12–14 months	14	34.1	9	22.0	[1]5.6	1.3, 25.7	0.02
1 dose at 15 months or older	5	12.2	18	43.9	1.0		
2 doses	0	...	2	4.9			
Total	41	100.0	41	100.0			

[1] Compared with those who received 1 dose at 15 months or older.

exceeded the State's anticipated 1986 fiscal year MMR vaccine requirement (32,000 doses) by more than a factor of three. The cost of vaccine ($8.47 per dose of MMR, CDC contract price, February 1, 1986) and its administration (average $3.25 per vaccination in the public sector, CDC, February 1, 1986) totaled more than $1.3 million.

Impact of control measures. The outbreak subsided rapidly, and only six cases were reported more than 5 weeks after outbreak control measures were instituted. There was more than a single generation (2 weeks) of measles in only 5 of the 18 Arkansas counties with confirmed measles cases.

Events at two junior high schools in the same town in Benton County demonstrate the importance of prompt initiation of outbreak control activities. Measles attack rates at these schools showed a 15-fold difference, with 50 cases among 627 students (7.8 percent) at junior high school A compared with 4 cases among 739 students (0.5 percent) at junior high school B ($\chi^2 = 47.4$, $P < 0.01$).

Based on risk factors identified in our investigations, the two schools had nearly identical potential to sustain an explosive measles outbreak. There was no significant difference in the proportion of students at each school who were out-of-compliance with State vaccination requirements (9.7 percent at junior high school A versus 8.4 percent at junior high school B), the proportion vaccinated at ages 12–14 months (26.6 percent versus 30.2 percent), or those who received measles vaccine at ages 15 months or older (59.1 percent versus 58.5 percent). The two schools enroll students from households in a town of 20,000 persons. The schools are similar single story concrete-block buildings, each with approximately 30 classrooms and 60 adult staff members. One school nurse covers both schools; health record maintenance and case reporting appeared to be identical.

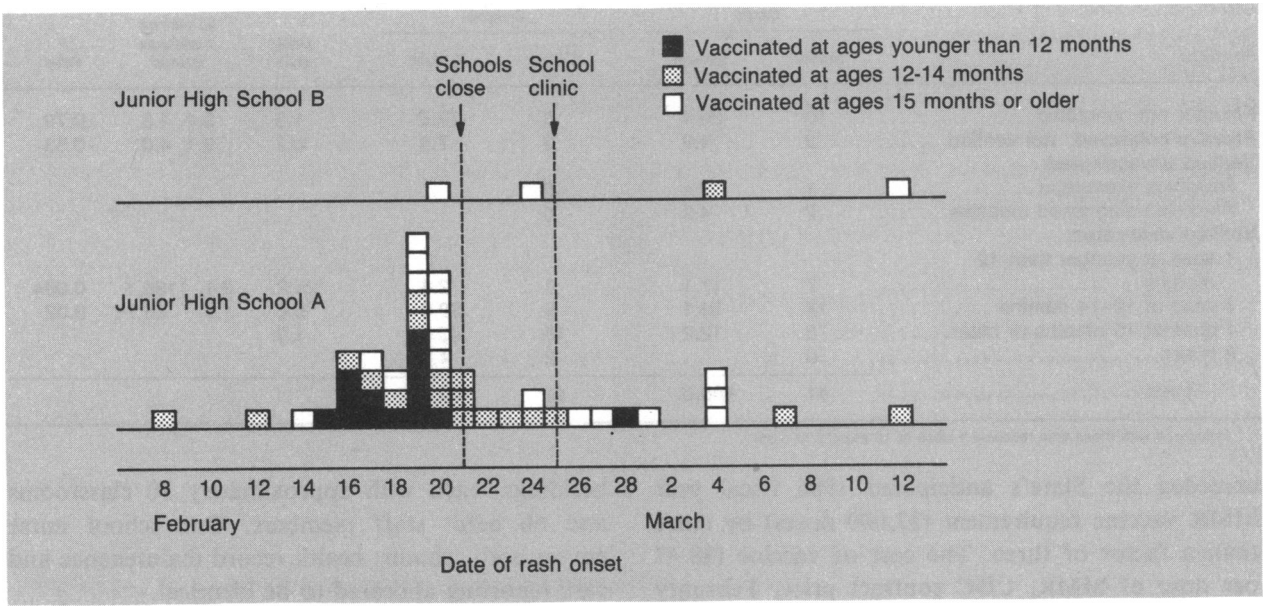
The only notable difference between the two schools was the interval between rash onset of the first case and institution of control measures (fig. 2). Outbreak control measures were not instituted until 13 days after the rash onset of the first case at junior high school A. In contrast, the first measles case at junior high school B had rash onset on February 20 and outbreak control began the following day. This suggests that significant delay in instituting outbreak control measures may have resulted in uncontrolled spread of measles at junior high school A. It is also possible that the index case at junior high school A was a more efficient transmitter of measles virus.

Discussion

This was the first time reimmunization was implemented for persons originally vaccinated at ages 12–14 months during an outbreak in the United States. The strategy for selective revaccination of persons who had been immunized at those ages was shown to be feasible, but costly. Important findings from this investigation include the higher than expected number of upper grade students not in compliance with State immunization requirements and the increased risk of measles in those vaccinated at ages 12–14 months.

Several factors may have contributed to the 8 percent to 10 percent of Arkansas school children in the fourth grade and above who were out-of-compliance with State immunization requirements for measles vaccination on or after the first birth-

Figure 2. Comparison of confirmed measles cases at two junior high schools by date of rash onset and age at vaccination among children vaccinated at different ages, Arkansas, 1986



'The ACIP now recommends that a routine two-dose schedule be implemented and that during outbreaks all persons who have not received two doses of measles vaccine be revaccinated...The routine two-dose vaccination strategy should eventually lead to the prevention of outbreaks among school-age populations.'

day. These children were born in 1975 and earlier. The immunization law was instituted in 1967 in Arkansas, but it was not strictly enforced until the late 1970s. The Arkansas School Immunization Law is enforced by local school officials, who transcribe information provided by the parent onto a standardized form provided by the department of health. Only information documented by a physician's signature or a health department stamp is accepted.

The law requires all schools to submit summary reports annually to the Arkansas Department of Health. To assess the validity of these reports, the health department audits the records of a 10 percent sample of kindergarten programs each year, but does not audit records of students in upper grades. The statewide school record audit of all grades conducted during this outbreak provided an important opportunity to address any deficits.

In 1976, based on data indicating that vaccine effectiveness was higher when measles vaccine was given at age 15 months compared with age 12 months, the Immunization Practices Advisory Committee (ACIP) raised the recommended age for routine measles vaccination from 12 to 15 months (*9*). Since the efficacy of measles vaccine administered at age 12 months was still high (greater than 80 percent), children vaccinated at ages 12-14 months were considered to have adequate evidence of immunity and routine revaccination was not recommended. In this study we found that persons vaccinated at ages 12-14 months were at higher risk for measles than persons vaccinated at ages 15 months and older. This is similar to the results of most other studies (*3*).

Data from this study showed higher attack rates with increasing time since vaccination; however, this trend was confounded by age at vaccination. Most measles cases occurring in persons previously vaccinated are thought to be due to primary vaccine failure. Secondary vaccine failure due to waning vaccine-induced immunity has not been felt to be a major problem. However, the findings from this study taken together with results from other epidemiologic studies suggest waning immunity may be contributing to vaccine failures although it appears to be less of a risk factor than primary vaccine failure (*10*). Whether measles vaccine-induced immunity does decrease with time since vaccination requires further evaluation.

Because of the increased risk of measles in persons vaccinated at ages 12–14 months in this outbreak, revaccination of such persons in the outbreak setting was recommended. While this strategy may have contributed to the rapid control of this outbreak, the cost of implementation was more than $1 million. One of the reasons outbreak control was so expensive was that revaccination was implemented in many counties, including those in which rash illnesses were later confirmed not to be measles. Laboratory confirmation of measles was often not available until several weeks after rash onset. This highlights the need for an accurate, rapid diagnostic test for measles which could facilitate decisions about outbreak control. In addition, revaccination in the outbreak setting was confusing and disruptive for medical personnel, school staff, students, and parents.

The effects of the selective revaccination that occurred in 1986 continue to be monitored in Arkansas through vigilant surveillance. No indigenous measles cases were reported in the first 2 years following the outbreak; in 1988, one imported case was reported. In 1989, 3 indigenous and 19 imported measles cases were reported. In 1990, 18 indigenous and 31 imported cases were reported. All the indigenous cases were nonpreventable, since they occurred in persons ages 15 months or younger, persons born before 1957, or persons with a religious exemption. Despite several instances of introduction of measles virus into schools by individual students, there have been no reports of school-based outbreaks.

After this outbreak, this selective revaccination strategy was used in other outbreaks, according to unpublished CDC data. In 1987, the ACIP recommended that revaccination of persons vaccinated at ages 12–14 months be considered in outbreak settings and that local officials establish a geographic zone of risk and limit revaccination to persons in this area (*11*). However, because of the prominent role that persons with primary vaccine failure have continued to play in measles transmission and because the majority of cases in school-age children have occurred in those vaccinated at ages 15 months or older, the ACIP issued revised recommendations for measles outbreak control in 1989 (*12*). The ACIP now recommends that a routine two-dose schedule be implemented and that during outbreaks all persons who have not received two doses of measles vaccine be revaccinated. While this outbreak control strategy will be costly, it represents an interim measure. The routine two-dose vaccination strategy should eventually lead to the prevention of outbreaks among school-age populations.

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