Explosive School-based Measles Outbreak

Intense Exposure May Have Resulted in High Risk, Even among Revaccinees

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Even high levels of measles vaccination coverage have not always prevented outbreaks of measles spread by airborne transmission. It has been suggested that a large inoculum might increase vaccine failure risk. Airborne transmission might occasionally entail a large measles inoculum. The epidemiologic relevance of measles among properly vaccinated persons (i.e., those vaccinated after 15 months of age and with live attenuated virus) is increased when they become contagious. The authors studied inoculum intensities as measured by proxy variables and the contagiousness of properly vaccinated persons who contracted measles among 51 measles patients infected in one school, at home, or elsewhere, utilizing preexisting records of measles cases and 214 healthy controls from an explosive school outbreak that occurred in a rural Finnish municipality in 1989. One “super-spreader” infected 22 others in one day, including eight once-vaccinated students and one twice-vaccinated student, probably during an assembly of 144 students in a poorly ventilated hallway with no sunlight. Those infected later at home had high measles risk, even if they were revaccinees. When siblings shared a bedroom with a measles case, a 78 percent risk (seven out of nine children) was observed among vaccinees. Vaccinees had approximately 2 days' shorter incubation time than unvaccinated persons. Vaccinated and unvaccinated students were equally able to infect their siblings. Total protection against measles might not be achievable, even among revaccinees, when children are confronted with intense exposure to measles virus. Am J Epidemiol 1998;148:1103–10.

communicable diseases; disease outbreaks; disease transmission; immunization; measles; measles vaccine; measles virus; vaccination

The extreme contagiousness of measles creates problems with its control, and ultimately its eradication (1). Outbreaks have occurred among highly vaccinated schoolchildren, especially after documented airborne transmission, even in groups with close to 100 percent vaccination coverage (2–5). Case reports from physicians’ offices (6–9) also suggest that measles is transmissible by small droplet nuclei (<5 μm in diameter) that can remain unprecipitated from indoor air for several hours (10). The overall importance of the airborne transmission of measles is not fully understood (1, 5). Some clarification may be afforded by a theory (11) which postulates that a large measles inoculum can cause vaccine failure, since airborne transmission might occasionally entail a massive inoculum. Theoretical vaccination coverage calculations for herd immunity assume a person-to-person contact model and lifelong immunity after successful vaccination (12).

Vaccinees receiving their first measles vaccination after 15 months of age are considered properly immunized, as the mother’s antibodies no longer interfere with the process. The epidemiologic relevance of vaccine failure increases if properly vaccinated persons become truly contagious and participate in the chain of transmission (13).

We examined whether differences in measles inoculum intensity affected measles risk among vaccinees and whether properly vaccinated measles patients became contagious during an explosive school outbreak in Honkajoki, a small rural Finnish municipality, in 1989.

MATERIALS AND METHODS

Vaccination

In Finland, children are vaccinated free of charge by public health nurses at child health care centers.

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Abbreviations: MMR vaccine, trivalent live attenuated measles–mumps–rubella vaccine (M-M-R® II or Virivac®); Mo vaccine, monovalent live attenuated measles vaccine (Rimevax®).

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Vaccination is voluntary. Each vaccination is registered on the individual’s health card, which is kept at the health care center, and on a vaccination card kept at home. The health card, which also includes any history of measles, is transferred from the health center to the school nurse when the child begins school. All children born between 1973 and 1981 should have received the monovalent live attenuated Schwarz strain (Mo) measles vaccine (Rimevax®; SmithKline Biologicals, Rixensart, Belgium). This program started in 1975, and children at least 14 months old were targeted. Preschool children born before 1973 also occasionally received Mo vaccine. Since 1982, the trivalent measles–mumps–rubella (MMR) vaccine (M-M-R® II (Merck and Company, Inc., West Point, Pennsylvania), distributed in Finland as Virivac® (SBL Vaccine AB, Stockholm, Sweden)) containing the More Attenuated Enders-Edmonston strain of measles virus has been used exclusively; it has been administered first at 14–18 months of age and again at 6 years according to a comprehensive national vaccination program (14, 15). Children born between 1975 and 1981 were covered by both the Mo and the MMR vaccination programs, receiving Mo vaccine at 14 months of age and, with rare exceptions, the first MMR vaccination at 2–5 years of age. After October 31, 1982, children older than 18 months of age were allowed to become vaccinated with MMR whenever they visited public health nurses. These children were to receive a third measles vaccination routinely at 6 years of age. The interval required between successive measles vaccinations was at least 6 months. No routine evaluation of vaccination coverage was done prior to the outbreak in Honkajoki.

Setting

Honkajoki is a small agricultural municipality in southwestern Finland with 2,398 inhabitants, 749 living in the central village. Seven elementary schools (grades 1–6) are scattered around Honkajoki. In 1989, the town’s lone high school had three junior classes (grades 7–9; n = 76) and three senior classes (grades 10–12; n = 68) occupying a single, poorly ventilated building. This building had been efficiently heat-insulated after the 1974 energy crisis, and ventilation was particularly poor in the hallway, which also had no sunlight penetration. Every school day began with a student assembly in the hallway (figure 1).

Vaccines were brought to Honkajoki from a refrigerator 16 miles (25 km) away approximately once or twice per month. They were transported via automobile by the public health nurse, who carried 5–10 doses per journey in her handbag. They were refrigerated after arrival in Honkajoki and were removed from the refrigerator only for vaccination. Against this background, it is possible that vaccines were exposed temporarily to heat exceeding 30°C for 15–30 minutes during local transportation.

The local outbreak of the present study was part of the last large outbreak season in Finland in 1988–1989, when 1,749 cases of measles were serologically confirmed (14). No cases of measles had been detected in Honkajoki since 1979 prior to February 4, 1989, when an 18-year-old male nonvaccinee at the high school developed symptoms. We could not base the dates of measles onset on the onset of rash, because the local nurse had asked each person who contracted measles the date on which he or she “came down with
measles," which is a less precise definition (16, 17).

The 18-year-old index case was unvaccinated because he did not belong to the birth cohorts included in the official vaccination programs, nor had he been exposed to live virus in the sparsely populated rural areas covered by the Mo vaccination program beginning in 1975. After the index case became ill, 21 13- to 15-year-old junior high school students and one senior high school student developed measles in one generation during days 8–14 of the epidemic (figure 2). In the first class (grade 10) of the senior high school, two measles cases, neither sharing a home with an index case, were identified on days 19 and 23. Two vaccinated cases soon appeared in elementary schools during epidemic days 5 and 6. Secondary cases within families appeared an average of 10 days after those in the high school. All vaccinees who contracted measles had received their first vaccination after 15 months of age. Emergency vaccination with the MMR vaccine was targeted at senior high school students, both with \( n = 26 \) and without \( n = 23 \) a recorded measles history, who had previously received only Mo vaccine. On February 28, 20 students were vaccinated; on April 1–3, 13 students were vaccinated; and on April 10, 16 students were vaccinated. The outbreak was contained within 3 weeks.

![Diagram](https://academic.oup.com/aje/article-abstract/148/11/1103/123185)

**FIGURE 2.** Course of the measles outbreak in Honkajoki, Finland, by setting, February 4–March 18, 1989.
Data on cases and controls

The diagnosis of measles was serologically confirmed in 34 (67 percent) of 51 patients, including the index case. The public health nurse collected data on age, sex, vaccination history, and the date of disease onset. The cases were divided into primary cases (infected outside the home) and secondary cases (infected at home by a sibling) according to modified (i.e., disease onset was not based on onset of rash) US Centers for Disease Control and Prevention criteria (16, 17). A case was deemed secondary when symptoms and signs commenced 7–18 days after the onset of symptoms in another case in the same household.

History of measles and measles vaccination was checked for both cases (n = 25) and healthy controls (n = 119) in the high school, and for the secondary cases (n = 15) and all healthy family members (n = 23) within the families of primary cases. Data were also collected from a systematic sample of healthy younger preschool children (n = 36) and from healthy children in seven elementary schools (n = 36)—six individuals from each annual birth cohort in the central health card register of Honkajoki, which includes all of the town’s residents. All vaccination and measles data were abstracted from official health cards. The nurse also checked whether the bedroom of the primary case in the family was shared with one or more siblings. Bedroom data were incomplete.

Since the nurse was familiar with the detailed living conditions in most families, it was possible to separate the secondary cases occurring in the older, more air-permeable wooden houses from those occurring in the well-insulated, poorly ventilated newer homes. Homes built of brick after the 1974 energy crisis were virtually sealed against the movement of air because of the newer construction standards, and were considered airtight.

Statistical methods

The statistical significance of the difference in mean incubation times between vaccinated and unvaccinated individuals was assessed by t test.

Measles attack rates were calculated directly for the high school and for the homes of primary cases, as all contact information regarding these settings was available. For preschoolers and elementary school children, denominators for calculation of attack rates were estimated from the total number of children in each age group, multiplying this by the proportion of each measles and vaccination history category in the control series.

The vaccination status of the primary case in the family and the airtightness of the home and shared bedroom were both considered factors potentially affecting the subsequent measles attack rate in the families. Relative risks and their 95 percent confidence intervals were calculated by the method of Greenland and Robins (18).

RESULTS

The 18-year-old high school student in Honkajoki (the index case) probably infected 22 students by airborne transmission during the course of one day (2); therefore, a single, unimodal wave was expected, with a characteristic normal distribution on a logarithmic time scale due to the point-source nature of the exposure (19). Instead, vaccinated individuals contracted the disease earlier, on average, than unvaccinated individuals, and two incubation period distributions seemed to be superimposed on the first bimodal wave of high school cases (figure 2). The period since exposure was constructed for the secondary cases in the families (n = 15) and for the 22 cases following the index case in the school.

Only 4 percent (5/135) of vaccinated elementary school students and 1 percent (2/165) of recently MMR-vaccinated preschool children with no measles history were attacked when not exposed within the family (table 1). Including within-family exposures as well, the corresponding attack rates were 12 percent (16/135) and 3 percent (5/165). Thirty-six percent (9/25) of the vaccinated junior high school students and 8 percent (1/13) of the vaccinated senior high school students with no history of measles were attacked (table 1). Unexpectedly, the attack rate among unvaccinated senior high school students who had no record of previous measles was only 6 percent (2/33).

Measles risk was high among within-family exposed subjects, regardless of the number of vaccinations (table 2), and the risk was particularly high when the primary case in the family shared a bedroom with one or more siblings (table 3). The air permeability of the home also seemed to play a role (table 3). In relatively new and airtight buildings, the vaccine failure rate was 48 percent (10/21). In contrast, no cases occurred in the older, more air-permeable houses. At least 69 percent (18/26) of vaccine failures occurred after intense indoor exposure, either in the local high school or at home.

In the attacked families, one 8-month-old baby contracted measles, while four babies (<1 year old) remained healthy. When infants younger than 1 year of age were omitted, a high (83 percent [5/6]) attack rate was observed among the unvaccinated siblings within families; only one 13-month-old toddler did not develop clinical measles (table 2).

Because time since vaccination or between two sub-
sequent vaccinations or revaccinations did not alter measles risk, adjustments for these factors are not shown. Attack rates among once-vaccinated high school students who had been vaccinated <5 years, 5–9 years, and ≥10 years previously were 20 percent (1/5), 67 percent (2/3), and 25 percent (6/24), respectively.

### TABLE 1. Measles attack rates (%) in different population and vaccination groups, Honkajoki, Finland, 1989

<table>
<thead>
<tr>
<th>School attendance and age range</th>
<th>History of measles, with 0–2 previous vaccinations</th>
<th>No measles history</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 or 3 previous vaccinations</td>
<td>1 previous vaccination</td>
</tr>
<tr>
<td>Preschool, 1–6 years</td>
<td>0 (0/0)†</td>
<td>0 (0/36)</td>
</tr>
<tr>
<td>Seven elementary schools,</td>
<td></td>
<td>5 (5/106)</td>
</tr>
<tr>
<td>7–12 years</td>
<td>(1†/34)</td>
<td></td>
</tr>
<tr>
<td>Outbreak high school</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Junior classes, 13–15 years</td>
<td>0 (0/17)</td>
<td>25 (1/4)</td>
</tr>
<tr>
<td>Senior classes, 16–18 years</td>
<td>0 (0/22)</td>
<td>0 (0/3)</td>
</tr>
<tr>
<td>Total</td>
<td>1 (1/73)</td>
<td>4 (6/149)</td>
</tr>
</tbody>
</table>

* All vaccinations were properly administered, i.e., after 15 months of age.
† Numbers in parentheses, no. of cases/total number of children.
‡ Serologically confirmed case, in the daughter of the local public health nurse. The patient and her mother suffered from presumably genetically determined hypo-gamma-globulinemia and/or low complement level. This child was close to death, and she recovered only after receiving passive immunization in the hospital. She was unvaccinated because of repeated infections.

Vaccinated high school students had a 2 days' shorter mean incubation period than unvaccinated students ($p < 0.001$) (figure 2). Inclusion of measles cases contracted within families did not influence this disparity, although statistical significance was lost ($p < 0.1$) because of increased variance (figure 3).

Both properly vaccinated and unvaccinated primary patients were equally contagious within families: The attack rates among family members were 47 percent (9/19) and 43 percent (6/14), respectively.

### DISCUSSION

The basis for modern measles eradication is reliance on some type (20) of two-dose vaccination schedule, which minimizes the primary vaccine failures remaining after the first dose. The outbreak described here is unusual for its high risk of measles among those who had received two or three doses of vaccine when they were exposed to measles virus in the local high school or in the home of an infected sibling. Possible explanations include 1) a poor cold chain and 2) the impact of a large measles inoculum by airborne transmission.

High vaccine failure rates have been associated with defective refrigerators (21, 22), and as there was some possibility of a cold chain disturbance in Honkajoki, it would be tempting to conclude that deficient primary serologic response was responsible for the observed high vaccine failure rate. The fact that time since vaccination did not explain vaccine failures may be taken to support this conventional interpretation. Cold boxes were not used in short local vaccine transportation, but no other weak point in the cold transport chain was detected. The small volume of vaccines carried during each local journey might have favored heat shocks, because the temperature of vaccines rises more readily when small numbers are transported.
On the other hand, certain facts reduce the likelihood of simple primary vaccine failures in this local outbreak. In ordinary settings, primary vaccine failure rates should be clearly below 10 percent (23). Revaccination effectively corrects primary vaccine failures (24). Even if we assume a high 25 percent primary failure rate in consecutive vaccinations of individuals, we would have expected failure rates of approximately 5 percent among revaccinees infected at home, instead of the observed 40 percent.

Measles did not spread markedly to preschool and elementary school children, although, according to the conventional explanation model, almost 80 percent of vaccinations could have been technically deficient, as seven out of nine failed when a sibling shared a bedroom with an index case. Furthermore, even if the division of vaccine failures into clearly either primary or secondary failure was accurate, an increased inoculum of measles would not have altered vaccine failure risk. Our findings seem to be congruent with a Danish theory (11) which postulates that a large measles inoculum resulting from within-family exposure increases vaccine failure risk. However, our vaccinated index cases were no less contagious than unvaccinated index cases, as was found in West Africa (11). Properly vaccinated children with measles have also been observed to become infectious in the United States (25).

In Honkajoki, the low attack rate among senior high school students probably results from unrecorded contact with wild measles virus during the 1970s, as these students were already 7–9 years of age by the time measles had disappeared from Honkajoki. Vaccinations are meticulously recorded in Finland, but the usual accuracy could not be achieved with measles, a disease previously regarded by mothers as trivial.

The reason why few (n = 7) unvaccinated preschoolers did not get measles when they were not exposed at home could be that they did not mingle with school-age children and/or that they were only casually in contact with older children other than their siblings. Most families with small children lived some distance from each other, which might also have protected the preschool-aged nonvaccinees.

A very similar explosive outbreak occurred in 1985 in a US (Illinois) high school, in which a common nonventilated hallway was also considered the crucial site of measles transmission (2). Almost 100 percent of the US students had been vaccinated, many even twice, but the revaccinated students were not better protected. The case students who had been exposed at school also appeared in one generation in that study, and it was unlikely that the index case had had close contact with all subsequent patients. The investigators concluded that measles was effectively spread by airborne transmission (2).

Other factors also may have accelerated the outbreak in Honkajoki: A complete lack of ultraviolet light in the hallway and low humidity during the winter months might have effectively prevented disinfection of indoor air (10, 26). Airborne transmission is uncommon in the literature, and its overall importance in measles outbreaks remains to be clarified (1–3, 5). In general, one has to be cautious when making generalizations from exceptional outbreaks (27), as they need something “unusual” in order to be triggered. In Honkajoki, it is probable that a hacking cougher in an unfavorable environment with high contact density triggered an explosive outbreak, which normally would occur rarely. Considering that measles transmission now appears to be blocked in Finland (14, 15), it is unlikely that airborne transmission poses a major obstacle for national measles control when a two-dose vaccination program with high coverage is maintained. Nevertheless, important lessons can be learned from outbreaks such as this one.

The more rapid onset of disease among vaccinees
compared with nonvaccinees could be explained by various mechanisms assuming an anamnestic response (28–33). The imprecise definition of measles onset used in this study should have made the difference between the incubation periods of vaccinees and nonvaccinees weaker, not created a difference. High and more rapid convalescent titers among vaccinees compared with nonvaccinees were observed in the late 1960s, which lends biologic credibility to our finding (33). To our knowledge, it has not been previously suggested that the incubation period among vaccinees may be shorter than that among nonvaccinees; therefore, this observation must be validated by additional studies. In the classic study of the Faroe Islands outbreak of 1846, rash appeared, on average, 14 days after inoculation (34). Interestingly, in the US high school, it took 12.5 days, on average (median, 12.0), for rash to appear in the vaccinees after the rash of the vigorously coughing index case appeared (2).

It is understandable that measles cases have been observed among fully vaccinated schoolchildren, since airborne transmission sometimes causes “astronomical” contact rates between the spreader and susceptible persons, and this mode of transmission effectively picks up the remaining few nonvaccinees and stochastic primary vaccine failures, who would enjoy herd immunity under conventional circumstances of person-to-person transmission. However, since airborne transmission might occasionally exceed the measles inoculum threshold, this could explain why revaccinated individuals get measles. It would thus appear that the presence of airborne transmission is one reason why eradication of measles has been much more difficult than originally anticipated.

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