ORIGINAL ARTICLE

Mumps Outbreak in Orthodox Jewish Communities in the United States

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ABSTRACT

BACKGROUND

By 2005, vaccination had reduced the annual incidence of mumps in the United States by more than 99%, with few outbreaks reported. However, in 2006, a large outbreak occurred among highly vaccinated populations in the United States, and similar outbreaks have been reported worldwide. The outbreak described in this report occurred among U.S. Orthodox Jewish communities during 2009 and 2010.

METHODS

Cases of salivary-gland swelling and other symptoms clinically compatible with mumps were investigated, and demographic, clinical, laboratory, and vaccination data were evaluated.

RESULTS

From June 28, 2009, through June 27, 2010, a total of 3502 outbreak-related cases of mumps were reported in New York City, two upstate New York counties, and one New Jersey county. Of the 1648 cases for which clinical specimens were available, 50% were laboratory-confirmed. Orthodox Jewish persons accounted for 97% of case patients. Adolescents 13 to 17 years of age (27% of all patients) and males (78% of patients in that age group) were disproportionately affected. Among case patients 13 to 17 years of age with documented vaccination status, 89% had previously received two doses of a mumps-containing vaccine, and 8% had received one dose. Transmission was focused within Jewish schools for boys, where students spend many hours daily in intense, face-to-face interaction. Orchitis was the most common complication (120 cases, 7% of male patients ≥12 years of age), with rates significantly higher among unvaccinated persons than among persons who had received two doses of vaccine.

CONCLUSIONS

The epidemiologic features of this outbreak suggest that intense exposures, particularly among boys in schools, facilitated transmission and overcame vaccine-induced protection in these patients. High rates of two-dose coverage reduced the severity of the disease and the transmission to persons in settings of less intense exposure.

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N Engl J Med 2012;367:1704-13.
DOI: 10.1056/NEJMoa1202865

In 1967, a live, attenuated mumps-virus vaccine (Jeryl Lynn strain) became available in the United States.[1] Ten years later, a single dose was recommended for children 12 months of age or older[2]; a second dose of measles–mumps–rubella (MMR) vaccine, which was licensed in 1971, was recommended for children 4 to 6 years of age, with the recommendation targeted for measles control in 1989[3] and for mumps control in 2006.[4] Single-dose MMR vaccine coverage among children 19 to 35 months of age during the period from 1995 through 2010 ranged from 90% to 93%, and two-dose MMR vaccine coverage among adolescents 13 to 17 years of age during the period from 2006 through 2010 ranged from 87% to 91%.[5] As a result, by 2005, the incidence of mumps in the United States had fallen by more than 99% from the incidence in the prevaccine era.[6]

During 2006, a nationwide outbreak of mumps occurred in a population of college-age persons in which the two-dose mumps vaccination coverage was 79% to 99%.[7-9] During subsequent years, outbreaks were reported in other countries in populations with high two-dose coverage,[10-12] whereas the reported number of cases declined to 400 in the United States during 2008 (similar to the annual number reported before 2006).[13] During 2009 and 2010, another outbreak occurred in the United States, this time affecting Orthodox Jewish communities.[14] Members of these communities did not generally oppose vaccination, and two-dose coverage among adolescents 13 to 17 years of age was not lower than the national average.[5] In the preliminary notice of this outbreak, we described 1521 provisional cases from June 2009 through January 2010[14]; this report includes 5 additional months of investigation, during which an additional 1981 cases were identified.

METHODS

CASE DEFINITIONS AND REPORTING

We used the case definition of mumps from the Council of State and Territorial Epidemiologists.[15] A clinical case of mumps was defined as an illness characterized by the acute onset of unilateral or bilateral tender, self-limited swelling of the parotid or other salivary glands lasting at least 2 days, without other apparent cause; a clinically compatible illness was an illness characterized by aseptic meningitis, encephalitis, hearing loss, parotitis or other salivary-gland swelling, orchitis, oophoritis, mastitis, or pancreatitis. Clinical cases and clinically compatible cases were reported to local health departments, which investigated them to gather demographic, clinical, laboratory, and vaccination data for the patients. These data were sent through state health departments to the Centers for Disease Control and Prevention (CDC).

Cases meeting the criteria for probable or confirmed cases were included in the analysis. A case was classified as probable if it met the clinical case definition for the illness but was not confirmed by laboratory testing and if it was epidemiologically linked to a clinically compatible case; a case was classified as confirmed if it met the clinical case definition or was associated with a clinically compatible illness and if it was either confirmed by laboratory testing or was epidemiologically linked to a confirmed case.[15]

VACCINATION STATUS AND COVERAGE

The vaccination status of case patients was verified (in hierarchical order) by health care providers, immunization registries, or personal vaccine cards. The status of unverified cases was classified as unknown. Estimates of two-dose MMR vaccine coverage among adolescents 13 to 17 years of age in affected states were obtained from the National Immunization Survey — Teen.[5]

LABORATORY TESTING

Standard confirmatory diagnostic testing included detection of mumps IgM antibodies, primarily with the use of commercially available enzyme immunoassays or immunofluorescence assays; detection of mumps RNA by means of real-time reverse-transcription–polymerase-chain-reaction (RT-PCR) assays[16]; and isolation of mumps virus in cell culture. Testing was performed at commercial, public health, and CDC laboratories. To classify viral isolates according to genotype, genetic analysis of mumps viruses was performed at the CDC, with the use of standard methods.[17,18]

STATISTICAL ANALYSIS

Proportions were compared with the use of chi-square and Fisher's exact tests, and medians were compared with the use of Wilcoxon rank-sum tests. All analyses were performed with the use of SAS software, version 9.2.

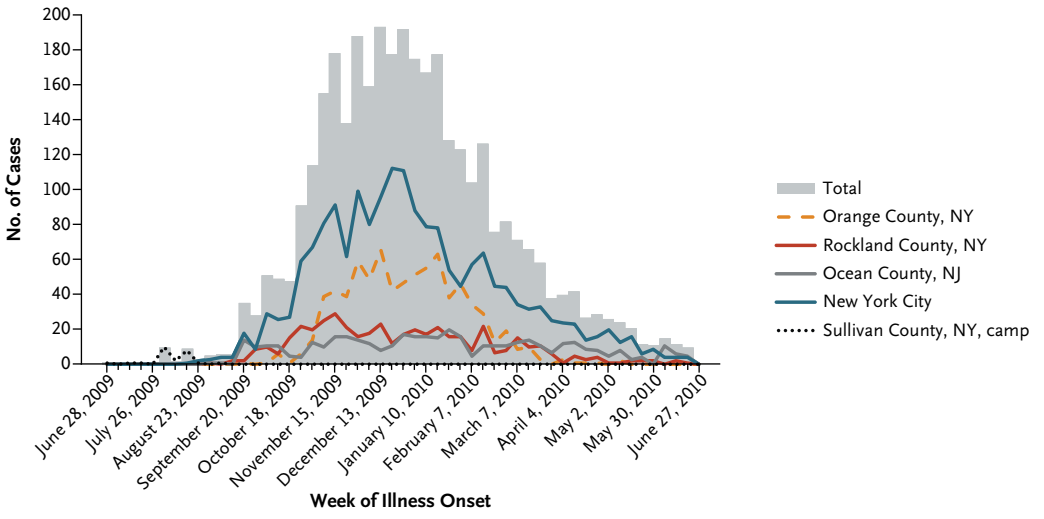

Figure 1. Confirmed and Probable Outbreak-Associated Cases of Mumps in the Northeastern United States, June 28, 2009, through June 27, 2010.

The weekly total numbers of outbreak-associated cases of mumps according to the week of onset of the illness are shown for all locations combined and for each individual location.

RESULTS

CHRONOLOGY OF THE OUTBREAK

From June 28, 2009, through June 27, 2010, a total of 3502 cases of mumps were reported: 3381 (97%) confirmed cases and 121 (3%) probable cases. The index case patient in this outbreak was a twice-vaccinated 11-year-old boy who returned to the United States on June 17, 2009, from the United Kingdom, a country that was experiencing a large mumps outbreak at that time.[19] Parotitis developed in the boy on June 28 while he was attending a camp in Sullivan County, New York, with approximately 400 Orthodox Jewish boys. Camp ended on August 27; a total of 25 cases of mumps developed among 22 campers and 3 adults who were exposed there. Mumps virus spread within Brooklyn (a borough of New York City), and Rockland County, New York, after the return of several infected campers to these communities. Mumps then spread to residents of Ocean County, New Jersey, and Orange County, New York, from ill contacts in Brooklyn. There were 25 cases reported from the Sullivan County camp, 1813 in New York City, 449 in Rockland County, 425 in Ocean County, and 790 in Orange County (Fig. 1).

CHARACTERISTICS OF THE PATIENTS

The majority of cases — 71% (2479 of the 3502 cases) — occurred among males. The highest proportion of cases (27%, 962 cases) occurred among adolescents 13 to 17 years of age (Fig. 2). A total of 78% of the patients 13 to 17 years of age (748 of the 962 patients in that age group) were male. The age and sex distributions shifted over time. Before February 2010, a total of 33% of the cases occurred among adolescents 13 to 17 years of age and 74% of the cases occurred among males, but after January 2010, these percentages declined to 14% and 61%, respectively.

A total of 3405 cases (97%) occurred among Orthodox Jewish persons. In New York City, most of the cases occurred in one of three Orthodox Jewish neighborhoods (Fig. 3). In Ocean County, Orange County, and Rockland County, the cases were concentrated in one or two villages. The remaining 97 cases (3%) were epidemiologically linked to Orthodox persons because the patient worked in one of the communities or at a business frequented by members of the communities. Orthodox case patients differed significantly from non-Orthodox case patients with respect to median age (15 years vs. 28 years, $P<0.001$) and the

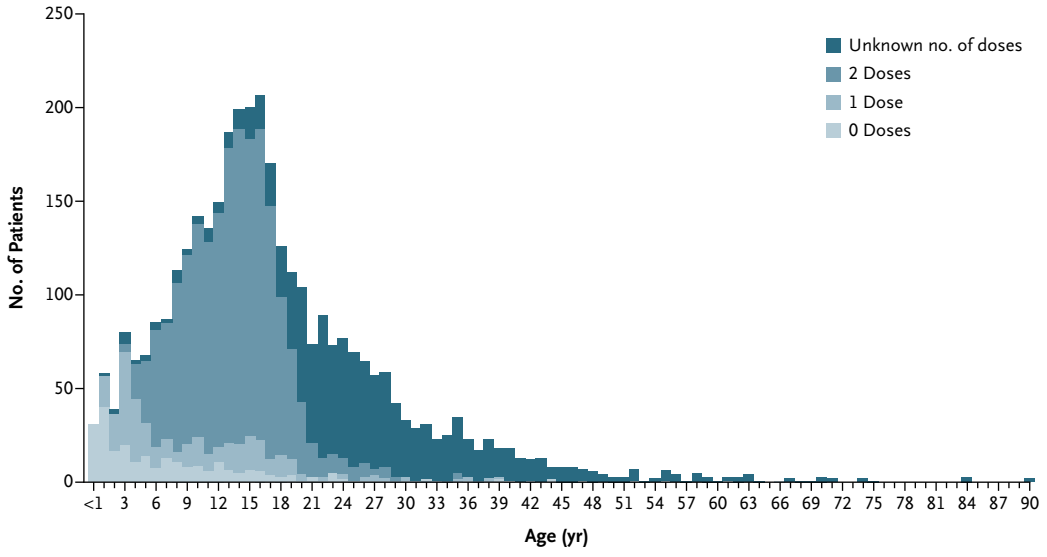

Figure 2. Mumps Vaccination Status of Patients with Outbreak-Associated Mumps, According to the Age of the Patients.
The number of patients with a case of mumps associated with the outbreak in the northeastern United States between June 28, 2009, and June 27, 2010, is shown, according to the age of the patient and the number of doses of measles–mumps–rubella vaccine received before the exposure to mumps.

proportion of males (71% vs. 57%, P=0.003), but not with respect to the proportion who had been vaccinated (89% vs. 81%, P=0.18). No reported cases were spread by non-Orthodox patients.

VACCINATION STATUS AND COVERAGE

A total of 3419 cases (98%) occurred among persons for whom vaccination is recommended (i.e., persons ≥12 months of age and born after 1956) (Fig. 2). Among the 2317 patients (68%) in this population who had verified vaccination status, 10% were unvaccinated, 14% had received one dose of MMR vaccine, and 76% had received two doses of MMR vaccine; 78% of the males had received two doses, as compared with 72% of the females (P=0.003). Among the 884 case patients 13 to 17 years of age with verified vaccination status, 3% were unvaccinated, 8% had received one dose of MMR vaccine, and 89% had received two doses; there was no difference in vaccination profile with respect to sex. The two-dose coverage among case patients was similar to that in 2009 among adolescents 13 to 17 years of age in New Jersey (91%), New York State excluding New York City (94%), and New York City (89%).[5]

COMPLICATIONS

A total of 140 complications were identified. Orchitis was the most common complication, occurring in 120 of 1771 male patients 12 years of age or older (7%). Meningitis, oophoritis, pancreatitis, deafness (temporary or permanent), mastitis, and facial Bell's palsy were reported at lower frequencies (Table 1). A total of 41 patients (1%) were hospitalized for mumps-related conditions, with orchitis (16 patients [39% of the total number of patients hospitalized]) and painful parotitis (5 patients [12%]) the most common conditions leading to hospitalization. No deaths or cases of encephalitis were reported. Among male case patients 12 years of age or older, orchitis occurred less frequently among patients who had received two doses of MMR vaccine than among unvaccinated case patients (4% vs. 11%, P=0.04). Case patients who had received two doses of MMR vaccine were also less likely to report deafness, meningitis, and oophoritis (which was assessed in female patients ≥12 years of age) than were unvaccinated persons or persons who had received one dose, but the differences were not significant (Table 1). Case patients who were 18 years of age or older, as com-

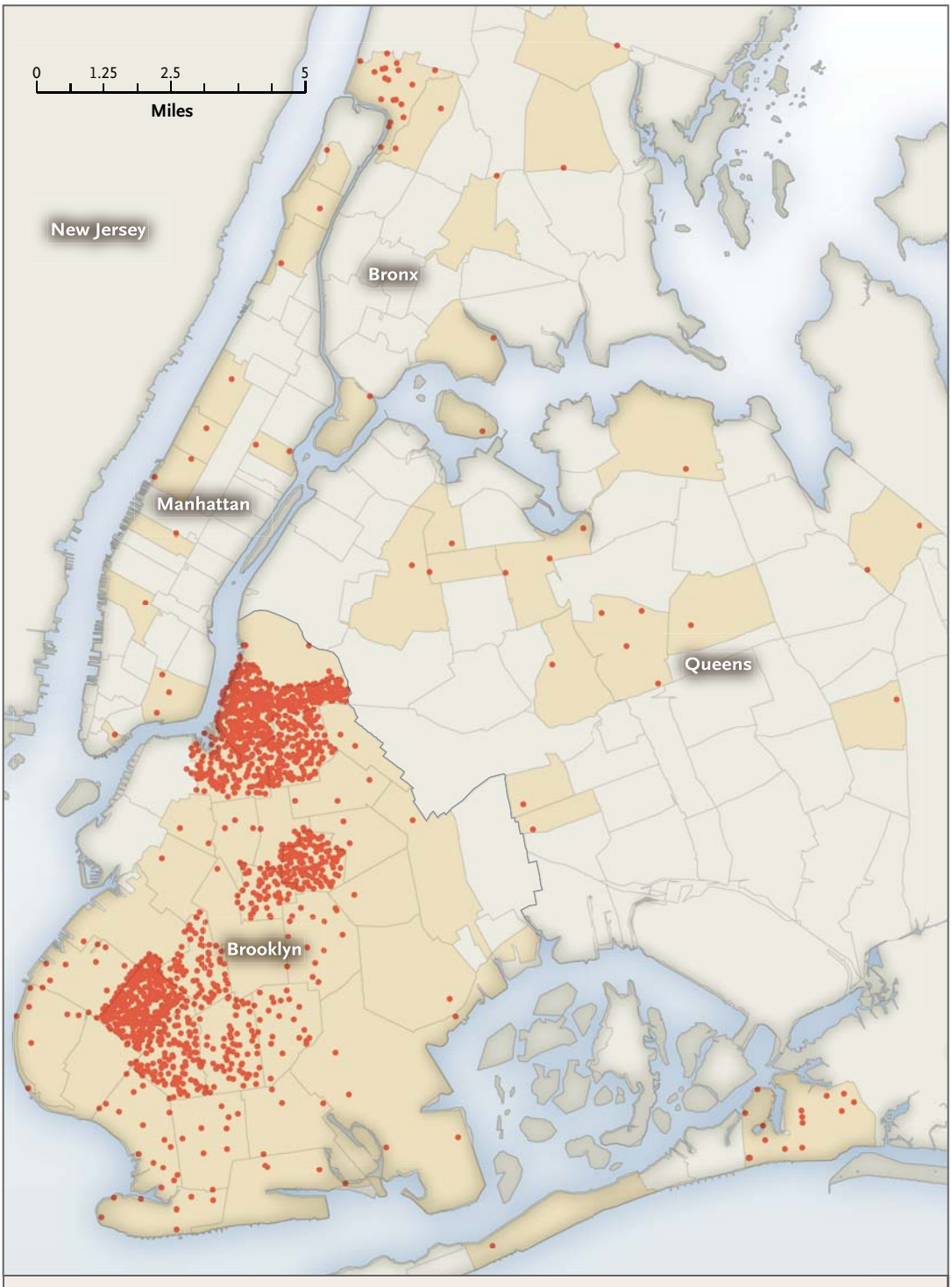

Figure 3. Location of Outbreak-Associated Cases of Mumps in New York City.

The geographic distribution of confirmed and probable outbreak-associated cases of mumps in New York City from June 28, 2009, through June 27, 2010, is shown. Each dot represents one case; dots are placed randomly within the ZIP Code areas (shaded) in which the patients lived.

Table 1. Rates of Complications and Hospitalizations, According to Vaccination Status.*

Variable	0 Doses (N=263)		1 Dose (N=324)		2 Doses (N=1764)	Unknown No. of Doses (N=1151)	Total (N=3502)
	no./total no. (%)	*rate ratio (95% CI)†*	*no./total no. (%)*	*rate ratio (95% CI)†*		*no./total no. (%)*	
Orchitis‡	6/53 (11.3)	2.55 (1.13–5.74)§	3/94 (3.2)	0.72 (0.23–2.28)	40/900 (4.4)	71/724 (9.8)	120/1771 (6.8)
Meningitis	1/263 (0.4)	3.35 (0.31–36.86)	2/324 (0.6)	5.44 (0.77–38.51)	2/1764 (0.1)	1/1151 (0.1)	6/3502 (0.2)
Oophoritis¶	0/22	NA	1/33 (3.0)	4.02 (0.37–43.08)	2/265 (0.8)	2/384 (0.5)	5/704 (0.7)
Pancreatitis	0/263	NA	0/324	NA	1/1764 (0.1)	3/1151 (0.3)	4/3502 (0.1)
Deafness‖	0/263	NA	1/324 (0.3)	5.44 (0.34–86.82)	1/1764 (0.1)	1/1151 (0.1)	3/3502 (0.1)
Mastitis¶	0/22	NA	0/33	NA	0/265	1/384 (0.3)	1/704 (0.1)
Bell's palsy	0/263	NA	0/324	NA	0/1764	1/1151 (0.1)	1/3502 (<0.1)
Encephalitis	0/263	NA	0/324	NA	0/1764	0/1151	0/3502
Total complications**	7 (NA)	NA	7 (NA)	NA	46 (NA)	80 (NA)	140 (NA)
Hospitalized	4/263 (1.5)	2.24 (0.73–6.88)	2/324 (0.6)	0.91 (0.20–4.04)	12/1764 (0.7)	23/1151 (2.0)	41/3502 (1.2)

* NA denotes not applicable.
† The reference group is the group that received two doses.
‡ Orchitis was assessed in male patients 12 years of age or older.
§ P=0.04.
¶ Oophoritis and mastitis were assessed in female patients 12 years of age or older.
‖ One case of permanent deafness was reported in a patient who had received one dose of MMR vaccine, one case of temporary deafness was reported in a patient who had received two doses, and one case was reported in a patient with unknown vaccination history who was subsequently lost to follow-up.
** Two patients presented with two complications each: one patient who had received no MMR vaccine doses presented with orchitis and meningitis, and one patient with unknown vaccination history presented with pancreatitis and meningitis. The percentages for total complications could not be calculated because of different denominators for the sex-specific complications of orchitis, oophoritis, and mastitis.

pared with patients who were younger than 18 years of age, were significantly more likely to have orchitis (9% vs. 4%, P<0.001) and to be hospitalized (2% vs. 1%, P=0.001). There were no significant differences in the rates of complications or hospitalizations according to sex.

LABORATORY TESTING

Confirmatory testing was performed for 1648 of the 3502 cases (47%); of these, 831 (50%) were confirmed as positive by at least one method. The rates of positivity were 35% (550 of 1563) with the use of IgM assays, 68% (373 of 550) with the use of real-time RT-PCR assays, and 64% (283 of 443) with cell culturing. The results of real-time RT-PCR assays and cell culturing were positive for 75% and 72%, respectively, of specimens collected within 2 days after the onset of parotitis, with rates declining to 43% and 45% for specimens collected on days 3 through 6. Vaccinated case patients were significantly less likely to have a positive result on IgM assays than were unvaccinated case patients (26% vs. 76%, P<0.001), but the proportion of positive results on real-time RT-PCR assays and cell culturing did not differ significantly according to vaccination status.

Genetic analysis was performed on 221 samples obtained from case patients in all the affected communities. All specimens were genotype G and differed by no more than one nucleotide, a finding that pointed to a common source of the virus.

RESPONSE MEASURES

Response measures that were taken to control this outbreak varied by community, and since each community was unique, it was not possible to compare the effectiveness of the measures that were used. Active surveillance for mumpslike illness was implemented in certain yeshivas (Jewish religious schools) for boys, other private Jewish schools, health centers, and doctors' offices. Periodic health alerts informed providers about the outbreak and requested that they ensure that all their patients had received the appropriate vac-

cinations for their age group and that suspected cases of mumps were reported to the health department. School immunization records were reviewed, and students without proof of immunity were offered vaccination. Schools were instructed to exclude students who refused to be vaccinated until after the outbreak ended, but the numbers of persons who refused to be vaccinated or who were excluded from school are not known. Clinic sessions were held to vaccinate people who did not know whether they were completely immunized. Public guidance regarding the outbreak was presented through radio broadcasts and in periodicals serving the affected communities, particularly before Jewish holidays, when increased travel was expected. In one community in which there was a documented high rate of two-dose MMR vaccine coverage among schoolchildren and documented, ongoing mumps transmission within schools, a third MMR vaccine dose was offered under a protocol approved by an institutional review board.[20]

DISCUSSION

During 2009 and 2010, a mumps outbreak occurred in several communities in the northeastern United States. There were 3502 reported cases, primarily involving well-vaccinated, adolescent, Orthodox Jewish males. The demographic characteristics of the patients, with a disproportionate involvement of males 13 to 17 years of age, suggest that yeshivas (religious schools separated by sex in which Orthodox Jews study religious texts) for boys were foci of the transmission of mumps virus during this outbreak, just as colleges were foci of transmission during the 2006 mumps outbreak.[7-9]

The features of this outbreak are best explained by intense exposures, particularly among boys in schools, that overwhelmed the protection afforded by the vaccine. In general, Orthodox girls receive conventional schooling, whereas boys in yeshivas receive intense religious education starting at 12 years of age, with school days that are up to 15 hours long. Yeshiva study is typically interactive, involving a "chavrusa" (a study partner). Partners face each other across narrow tables or lecterns to study religious texts; the format is face-to-face, often with animated discussion. Frequently, several pairs of students study at a single table. A typical day involves several study sessions, with students changing partners for each session.

This chavrusa style of study may have allowed for particularly efficient transmission of mumps virus. Although mumps is a respiratory infection, it is spread through droplets and requires closer exposure than do more contagious respiratory infections transmitted by the airborne route, such as measles.[21] We postulate that chavrusa study, with its prolonged, face-to-face contact, resulted in high-inoculum exposures and that such exposures overcame vaccine-induced protection in individual students.[22] The role that the transmitted dose of a respiratory virus plays in the determination of vaccine effectiveness is difficult to study in humans, but challenge studies in animals that have been vaccinated with an avian influenza vaccine,[23] epidemiologic investigations involving patients with measles who had previously been vaccinated,[24,25] and biologic plausibility, as suggested from a comparison of challenge methods among volunteers who had been administered an inactivated mumps-virus vaccine,[26] all suggest that the risk of infection with mumps may be higher when the exposure dose of virus is large or intensely transmitted. This phenomenon can also explain why the efficacy of the mumps vaccine tends to be lower among household contacts than among school or community contacts.[27] If, in fact, the intensity of exposure reduced the effective protection provided by the mumps vaccine, the frequent daily changing of partners helps to explain why the disease spread in the yeshiva setting.

The finding that transmission of mumps to non-Orthodox persons in the affected communities occurred rarely and was not sustained in that population supports the conclusion that intense exposure is necessary to overcome an individual person's vaccine-induced immunity. Although Orthodox Jewish persons generally cluster geographically and socially, they often interact with their non-Orthodox neighbors and others who work within their communities or visit their communities. However, exposures in these settings would typically not be as intense as those in yeshivas. Notably, a large mumps outbreak in Jerusalem, Israel, during 2009 was linked to an importation from the U.S. outbreak. Orthodox Jewish adolescent boys, typically yeshiva students, were also disproportionately affected in that outbreak, even though their vaccination rates were high and

they mixed regularly with their non-Orthodox neighbors.[28]

Over time during the outbreak, transmission shifted from adolescent boys toward older and younger male and female contacts, as the infected boys introduced the virus into their homes. Although household exposures might not have been as intense as those in the yeshivas, transmission probably occurred in these settings too, particularly given the large families that are characteristic of Orthodox Jewish communities. Among Orthodox Jewish households in Brooklyn with at least one case of mumps, the median number of persons per household was 7 (range, 2 to 16),[29] as compared with an estimated aggregate household density for all of Brooklyn of 2.7 persons per housing unit.[30]

Although intense exposures within households, and especially within yeshivas, may have facilitated this outbreak, other factors may also have played a role. Results from outbreak settings suggest that vaccine-induced protection against mumps may wane,[8,9,31] and neutralizing antibody titers, which may correlate with protection against mumps,[32,33] decline after vaccination,[34] although they remain sufficiently high to effectively neutralize mumps virus.[35] However, the burden of mumps in this outbreak was not increased among the oldest vaccine recipients, who would have experienced the most waning since their childhood vaccinations. Evidence suggesting that waning immunity contributed to this outbreak may have been difficult to discern because of differences in exposure risk according to age and the strong correlation between age and time since vaccination. Another possible factor is reduced vaccine effectiveness against the outbreak genotype. The virus in this outbreak was genotype G, the genotype identified in the 2009 U.K. outbreak and the 2006 U.S. outbreak.[7,36] Mumps vaccine in the United States includes the genotype A Jeryl Lynn strain, and antibody induced by this vaccine effectively neutralizes genotype G viruses, albeit at a lower titer.[33,35]

Nonetheless, neither waning nor reduced heterotypic protection alone would explain why an outbreak would affect particular communities while sparing broader adjacent communities. Although correlates of protection for mumps are not well defined, there is some evidence that lower titers before exposure to mumps may increase the risk of clinical disease after exposure.[32,33] However, the high rate of infection among females in dormitories during the mumps outbreaks in 2006[9,17] and the high proportion of cases among males attending yeshivas in this study suggest that a high-density setting, in which there are certain behaviors that facilitate transmission of the virus, may overwhelm existing antibody levels. When a recent study did not identify an antibody-titer cutoff point for protection, it was suggested that the level of immunity required to protect against clinical mumps may depend on the inoculum of virus to which one is exposed, so that protection at a particular titer is not absolute.[33]

This study had several limitations. Some true cases of mumps were probably not included because some ill persons did not seek medical care, some properly diagnosed or suspected cases were not reported to the health department, some cases were misdiagnosed, and some cases were subclinical. Attack rates could not be calculated because the size and age distribution of the specific affected communities were mostly unknown. Vaccination histories were often incomplete among adults, since documentation was rarely available for patients who were no longer in school. Clinical specimens were tested at a variety of laboratories with the use of a variety of assays, and therefore, the results that were reported reflect a range of sensitivities and specificities. Although only 50% of cases with an available specimen were laboratory-confirmed, those with a negative test result had a clinically compatible illness (almost always parotitis) and were epidemiologically linked to an affected community, thus reducing the likelihood of overreporting.

The fact that the outbreak did not spread to surrounding communities highlights the effectiveness of the two-dose MMR vaccine schedule in most settings. Previous studies have shown that two doses of mumps vaccine have an effectiveness of approximately 88% (range, 79 to 95) in preventing clinical mumps,[8,31,37] and this schedule has been successful in controlling mumps in the general U.S. population[6]; a similar schedule has resulted in the elimination of mumps in Finland.[38] Since this outbreak, rates of mumps in the United States have been at near-record low levels, with only 370 provisional cases reported by the end of 2011.[39] Other outbreaks have occurred in populations that had high rates of vaccination (as did the population in the 2009–2010 outbreak), but they

were limited to specific settings with opportunities for intense exposures[7-12] and did not spread to other communities, despite numerous opportunities. Finally, vaccination appeared to limit the severity of cases; complication rates were lower than rates reported during the prevaccine era.[40] Nonetheless, although the current vaccination schedule has been successful, there remains an ongoing threat of imported infections and of endemic transmission of mumps virus. The outbreak reported here highlights the importance of maintaining a high rate of two-dose MMR vaccine coverage in all communities.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention, Department of Health and Human Services.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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