

# Characteristics of a large mumps outbreak: Clinical severity, complications and association with vaccination status of mumps outbreak cases

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In recent years, large mumps outbreaks, involving mainly adolescents and young adults, have re-emerged in several countries. We investigated a large mumps outbreak, evaluated the association between mumps clinical severity (complications, hospitalization) and vaccination status (number of previous measles, mumps and rubella - MMR vaccine doses), and assessed vaccine effectiveness. The first mumps cases emerged in an ultra-orthodox boys' school in Jerusalem and were epidemiologically linked to the mumps outbreak in New York. Overall, 3130 mumps cases were notified in the Jerusalem district during September 2009–August 2011 (median age 13y, 64% males). Most cases were reported from community clinics. Patients with systemic symptoms and/or complications (419, 13.4%) were either hospitalized ( $n = 79$ ) or treated in an emergency medical center ( $n = 340$ ). The main complications included orchitis (3.8% males > age 12y) and meningoencephalitis (0.5%). The mumps virus genotype was G5. The distribution of previous MMR vaccine doses ( $n = 0,1,2$ ) was: 24.8%, 28.3% and 46.9%, respectively. The number of previous vaccine doses was inversely associated with clinical severity. Adjusted values for MMR vaccine effectiveness against complications were estimated as 52.1% (95% CI  $-4$ –78%) for one vaccine dose and 62.7% (95% CI 25.7–81.3%) for 2 doses. The outbreak was characterized by predominance of male students; the majority of whom had been previously vaccinated. The reported complication rate was relatively low. Vaccination status was associated with age and disease severity. The combination of limited mumps vaccine effectiveness and the specific school setting (dense learning and living conditions) probably contributed to the disease spread.

## Introduction

Mumps is an acute viral illness, classically characterized by swelling of one or more salivary glands. Complications include orchitis (post-pubertal), meningoencephalitis, oophoritis, pancreatitis, sensorineural deafness, nephritis, arthritis, thyroiditis, myocarditis and rarely death.<sup>1,2</sup>

The measles, mumps and rubella (MMR) vaccine was introduced into many national immunization programs in the 1970s–80s; with adequate vaccination coverage, mumps incidence declined considerably. Subsequent implementation of a 2-dose schedule aimed to cover primary failure, provide boosting and improve coverage.<sup>1–4</sup>

In Israel, the mumps vaccine was introduced into the schedule in 1984 and halted in 1985. In December 1988, the MMR vaccine was instituted at 15 months. A two dose MMR vaccination schedule was implemented in 1994, first dose (MMR1) at age 12 months and the second dose (MMR2) at age 6 y in the first school grade.<sup>5</sup> Routine vaccinations are provided free of charge in community well-baby

clinics for infants and toddlers, and by school health services for schoolchildren. The MMR vaccine used in Israel contains the mumps Jeryl-Lynn strain. The measles mumps rubella and varicella (MMRV) vaccine replaced the MMR vaccine in 2008.<sup>6</sup>

In recent years, large mumps outbreaks, involving mainly adolescents and young adults, have re-emerged in several countries.<sup>4</sup> In June 2009 a mumps outbreak emerged in New York, among ultra-orthodox Jewish children, through mumps virus importation from the UK.<sup>7</sup> In September 2009, the first mumps cases that were epidemiologically linked to the New York cases, were notified in Jerusalem. A large mumps outbreak spread among male students in religious schools in Jerusalem.<sup>8,9</sup>

The Jerusalem district's population in 2009 was 950,000 (30% Arabs, 70% Jews and others). About 40% of Jews are ultra-orthodox (the rest are traditional or secular). The mean socio-economic status of the district is 4 (on a Likert scale of 1 to 10). The neighborhoods are homogenous and each group keeps its own educational system.<sup>10</sup>

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During 2009 – 2010 the mumps outbreak extended to other districts in Israel, and later spread to the military sector, with over 5200 reported mumps cases country-wide.<sup>9,11</sup>

We characterized the cases of mumps in Jerusalem that occurred during this outbreak, evaluated the association between the clinical severity of mumps (defined by mumps complications and hospitalization) and vaccination status (number of MMR vaccine doses received prior to the outbreak); and assessed the MMR vaccine effectiveness.

## Results

Overall, between September 6th 2009 and August 12th 2011, 3130 mumps cases were notified in the Jerusalem District (mean age  $14.8 \pm 10$  years, median age 13 years; 98% Jews, 73% ultra-orthodox). The first 5 cases were 4 male students in a single ultra-orthodox school in Jerusalem and the fifth was a student's sister. Epidemiologic investigation revealed recent contact with students from New York. The mumps epidemic peaked in February 2010, with 646 notified cases. The cases were mainly male students in religious schools. In 485 schools (of 900 in the district), at least one mumps case was reported; attack rates in the schools ranged between 0.1% and 10%.

Most mumps cases were reported from community clinics in the district. General characteristics of the mumps cases are presented in **Table 1**. Patients with severe symptoms (419, 13.5%) were either hospitalized ( $n = 79$ ) or treated in an emergency care center ( $n = 340$ ). The clinical symptoms and signs included: swelling of one or more salivary glands (94.4%), fever (55%),

malaise (28.8%), headache (15.4%), abdominal pain (6.9%), nausea (6.6%), vomiting (5%), orchitis (3.8% of males aged > 12 years), meningoencephalitis (0.5%) and pancreatitis (0.03%).

Case ascertainment included clinical features and mumps IgM antibody ( $n = 211$ ), IgM and IgG ( $n = 151$ ), IgG ( $n = 82$ ) and RT-PCR ( $n = 6$ ). Laboratory confirmation was performed in the beginning of the outbreak, with further cases defined by clinical features and epidemiological linkage. The virus genotype was classified as G5.

Vaccination status: the overall distribution of the number of previous MMR vaccine doses (0,1,2) was 24.8%, 28.3% and 46.9%, respectively (**Table 1**). The MMR vaccination coverage among the mumps cases (age-appropriate) was 86.2% (first dose, age 1–5 years) and 79.1% (second dose, age 10–14 y). The distribution of the number of previous MMR vaccine doses according to the cases' age is presented in **Figure 1**. Most mumps patients aged 6–21 y (1649/1890, 87.2%) had received at least one MMR vaccine dose previously (1377, 72.9% received 2 doses), compared with 25.6% of those aged 22 y and older (8.1% received 2 doses).

The final logistic regression model included mumps complications and locus of medical care by the number of previous MMR vaccine doses, adjusted for age and gender (except orchitis). Mumps patients treated in hospital or emergency care center were significantly less likely to be previously vaccinated (**Table 2**).

Vaccine effectiveness was assessed by 2 methods.<sup>12</sup> Calculated by the basic formula, according to attack rates in vaccinated (1 or 2 previous vaccine doses) and unvaccinated cases, vaccine effectiveness (VE) was 48.3%, 73.2%, 50.6% and 72% for mumps hospitalization, orchitis, meningitis and all complications, respectively. The estimated values for vaccine effectiveness against mumps complications (derived from adjusted odds ratios, **Table 2**) for one previous MMR vaccine dose were: 28%, 49.3%, 74% and 52.1%; and for 2 vaccine doses: 43.7%, 77.1%, 43.5% and 62.7%, for mumps hospitalization, orchitis, meningitis and all complications, respectively.

**Table 1.** General characteristics of mumps cases in the Jerusalem district during September 2009 – August 2011 (n=3130)

Characteristic	N (%)
Age groups (years)	
<1	23 (0.7%)
1–4	363 (11.6%)
5–9	626 (20%)
10–14	895 (28.6%)
15–19	540 (17.3%)
20–24	284 (9.1%)
25–29	155 (5%)
30+	244 (7.8%)
Male gender (%)	1998 (63.8%)
Year of the outbreak	
2009	523 (16.7%)
2010	2,488 (79.5%)
2011	119 (3.8%)
Vaccination status: Number of mumps vaccine doses	
0	775 (24.8%)
1	886 (28.3%)
2	1,469 (46.9%)
Locus of medical care	
Hospital	79 (2.5%)
Emergency care center	340 (10.9%)
Community clinic	2,711 (86.6%)
Attended an educational facility	2,291 (73.2%)
>1 mumps case in the household	876 (28%)

## Discussion

The mumps outbreak described herein was the largest in Israel in the last 2 decades.<sup>8,9</sup> Of the 3130 cases reported in Jerusalem, 60.4% were children and adolescents aged 6–21 y. The cases' age - appropriate vaccination coverage was 86.2% and 79.1% (for MMR1 and MMR2), lower than the mean coverage rates in the Jerusalem district during the past decade of 93% and 95%, respectively.<sup>8</sup> The first mumps cases in Jerusalem were epidemiologically linked to New York cases. Between June 2009 and June 2010, 3502 cases were reported in New York and New Jersey; 97% were orthodox Jews, mainly male adolescents. Most cases were appropriately vaccinated; 89% of the mumps cases aged 13–17 y had received 2 previous vaccine doses.<sup>7,13</sup>

The main complications reported in the current study were 3.8% mumps orchitis in males >12 y old and 0.5% meningoencephalitis (higher in under-vaccinated cases), comparable to

7% and 0.2% complication rates in the New York outbreak, and to 6.1% and 0.3% in England and Wales, respectively.<sup>7,14</sup>

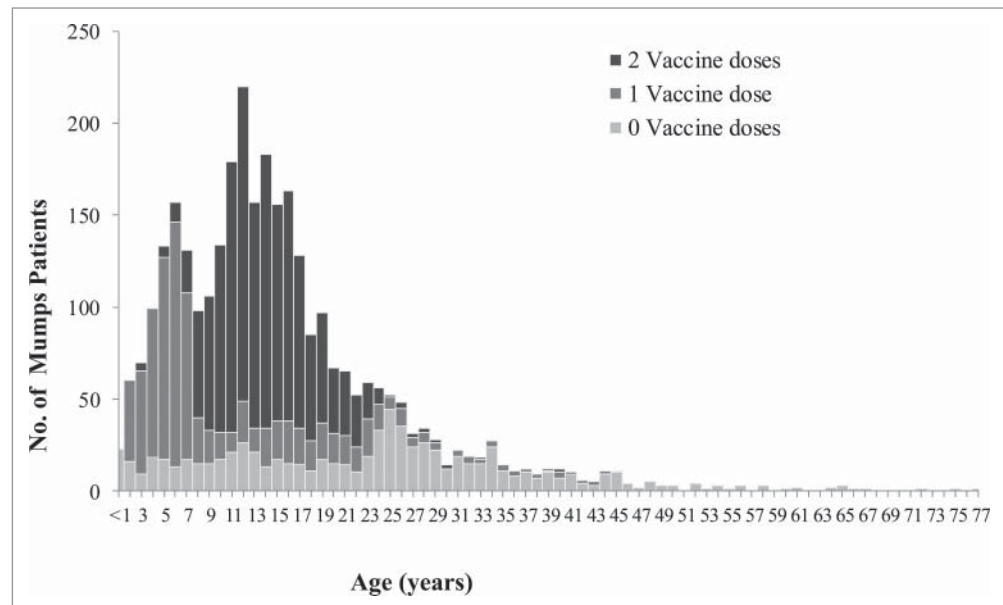
In 2010, mumps notifications from Israel accounted for about one fifth of all the European Region cases.<sup>15</sup> The mumps virus genotype G (identified in the described outbreak) has been prevalent in the WHO European Region during 2005–2011.<sup>16</sup> A European sero-survey revealed lower mean geometric mumps antibody titres in mumps outbreak countries. MMR1 vaccination coverage  $\geq 95\%$  and a 4–8 y interval between vaccine doses were found protective.<sup>17</sup> Vaccine effectiveness of Jeryl-Lynn containing MMR in children and adolescents was estimated as 64–66% for one vaccine dose and 83–88% for 2 doses.<sup>18</sup>

Declining immunity over time may contribute to mumps outbreaks in previously vaccinated population groups.<sup>19</sup>

We report inverse association of both mumps complications and hospitalization with number of previous MMR vaccine doses. The adjusted VE for 2 vaccine doses were 43.7% and 77.1% for hospitalization and orchitis, respectively. A UK study showed reduced risk for hospitalization, orchitis and meningitis for one MMR vaccine dose (OR 0.54, 0.72 and 0.28, respectively) and 2 doses (OR 0.45, 0.64 and 0.17, respectively).<sup>14</sup> In a study of a recent large mumps epidemic in the Netherlands, receipt of 2 vaccine doses reduced risks for orchitis (most frequent complication), overall complications and hospitalization

(VE of 74%, 76% and 82%, respectively).<sup>20</sup> In a smaller outbreak in Germany, VE was calculated as 91.9% for 2 vaccine doses in children (mean age: 9 y) and 50.0% for one dose in adults (mean age: 26 y).<sup>21</sup>

This study assessed VE during a mumps outbreak, which is naturally an uncontrolled and unplanned phenomenon. The study has several potential limitations. First, it was conducted in a district with a population characterized by relatively low socioeconomic status and high density in the educational system (especially the religious boys' high schools) and in housing. Additionally, while the district's average immunization coverage may be adequate, the coverage among specific ultra-orthodox



**Figure 1.** The mumps vaccination status of patients with outbreak-associated mumps in the Jerusalem district (September 6th 2009 - August 12th 2011), according to the age of the patients and the number of doses of measles–mumps–rubella (MMR) vaccine received before the outbreak.

**Table 2.** Association between mumps complications, hospitalization and MMR vaccination status, mumps cases in the Jerusalem district during September 2009 – August 2011 (n = 3,130)

complication	No. MMR Vaccine doses received	No cases with complications /total (%)	Adjusted* Odds Ratio (95%CI)	p value	Adjusted Vaccine Effectiveness (95% CI)
Hospitalization	0	163/775(21)	Ref	Ref	Ref
	1	107/886 (12.1)	0.72 (0.53–0.97)	0.03	28 (3.1–46.5)
	2	149/1,496 (10.1)	0.56 (0.43–0.73)	0.0001	43.7 (26.9–56.6)
Orchitis	0	26/336 (7.7)	Ref	Ref	Ref
	1	7/194 (3.6)	0.51 (0.21–1.24)	0.13	49.3 (–24.3–79.4)
	2	9/579 (1.6)	0.2 (0.095–0.55)	0.001	77.1 (45–90.5)
Meningitis	0	6/775 (0.8)	Ref	Ref	Ref
	1	2/886 (0.2)	0.26 (0.05–1.4)	0.12	74 (–44–95.3)
	2	7/1,469 (0.5)	0.56 (0.17–1.8)	0.34	43.5 (–82 –82.4)
All complications	0	30/775 (3.9)	Ref	Ref	Ref
	1	11/886 (1.2)	0.48 (0.22–1.04)	0.063	52.1 (–4 –78)
	2	16/1,469 (1.1)	0.37 (0.19–0.74)	0.005	62.7 (25.7–81.3)

\*Adjusted for age (as continuous variable) and gender except orchitis which was adjusted only for age among males > 12 years.

communities is inadequate. The outbreak indeed emerged in Jerusalem in ultra-orthodox communities (probably post mumps virus importation) and spread to other districts in Israel. A similar situation was observed previously with measles outbreaks in ultra-orthodox communities in Jerusalem.<sup>22-24</sup> Despite the overall similarity with the national surveillance data, further studies in other populations could reveal different findings. Second, variables that might have been associated with mumps were unavailable in the health records, such as mumps exposure history and specific school and boarding conditions. Finally, although the mumps clinical case definition in Israel is general, increased physicians' awareness in the Jerusalem district may have affected mumps notification rates.

In this outbreak, mumps transmission was associated with intense contact among students in religious schools, similar to the preceding outbreak in New York.<sup>7,25</sup> Nevertheless, the clinical disease was significantly milder among vaccinated cases. Probable contributing factors to the outbreak include insufficient vaccine effectiveness and less than optimal vaccination coverage. The roles of these and other factors need to be further explored.

## Methods

A case was defined as a person reported on with mumps during the period September 6th 2009 and August 12th 2011 in the Jerusalem District. Mumps is a modifiable disease in Israel; physicians and laboratories notify cases to district health offices. Cases are notified based on clinical presentation. The mumps clinical case definition is of an acute illness with parotid (or other salivary gland) swelling. Laboratory tests include specific mumps IgG and IgM antibodies, and virus detection by RT-PCR. The Ministry of Health Central Virology Laboratory performs virus genotyping.

The case investigations included interviews (with patients, parents and physicians), hospital files and health records. The variables collected by a case questionnaire included demographic

and clinical characteristics, mumps complications, locus of medical care (hospital, emergency care center, community clinic), laboratory tests, other cases in the household and the patient's vaccination status (defined by the number of MMR vaccine doses received prior to the outbreak: 0,1,2). The vaccination status of the mumps cases was validated by collecting individual vaccination certificates and additionally by searching the database of electronic health records.

Data analysis was performed with the SPSS software version 21.0 (SPSS Inc., Chicago, IL). The Odds Ratio (OR) and the 95% confidence intervals (95% CI) are presented. A multiple logistic regression model was utilized for mumps complications and vaccination status adjusted for age and gender (except orchitis). Vaccine effectiveness (VE) was calculated by the basic formula  $VE = (ARU - ARV) / ARU \times 100$

(ARU = attack rate in unvaccinated cases, ARV = attack rate in vaccinated cases).<sup>12</sup>

Vaccine effectiveness was also estimated by  $VE = (1 - \text{adjusted OR})$  from the logistic regression model. We used the adjusted OR as an approximation of relative risk. A p value < 0.05 was considered significant for all comparisons.

The study was conducted in accordance with the relevant Ministry of Health ethical regulations.

## Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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