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Mumps outbreak among vaccinated university students associated with a large party, the Netherlands, 2010

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ABSTRACT

We investigated a mumps outbreak within a highly vaccinated university student population in the Netherlands by conducting a retrospective cohort study among members of university societies in Delft, Leiden and Utrecht. We used an online questionnaire asking for demographic information, potential behavioural risk factors for mumps and the occurrence of mumps. Vaccine status from the national vaccination register was used. Overall, 989 students participated (20% response rate). Registered vaccination status was available for 776 individuals, of whom 760 (98%) had been vaccinated at least once and 729 (94%) at least twice. The mumps attack rate (AR) was 13.2% (95%CI 11.1–15.5%). Attending a large student party, being unvaccinated and living with more than 15 housemates were independently associated with mumps ((RR 42 (95%CI 10.1–172.4); 3.1 (95%CI 1.7–5.6) and 1.8 (95%CI 1.1–3.1), respectively). The adjusted VE estimate for two doses of MMR was 68% (95%CI 41–82%). We did not identify additional risk factors for mumps among party attendees. The most likely cause of this outbreak was intense social mixing during the party and the dense communal living environment of the students. High coverage of MMR vaccination in childhood did not prevent an outbreak of mumps in this student population.

1. Introduction

The Netherlands introduced mumps vaccination into the National Immunisation Programme in 1987 using the measles, mumps and rubella vaccine (MMR). The MMR vaccine used contains the Jeryl-Lynn mumps virus strain and is administered in a two-dose schedule at 14 months and nine years of age. Nationally, the MMR vaccination coverage at 10 years of age for the second MMR dose has been consistently above 90% since the programme's inception [1]. Nevertheless, in recent years the Netherlands has experienced localised outbreaks of mumps: in 2004 (genotype G5) among students at an international university of hospitality management (105 cases reported, of whom 62 of 64 (97%) with known vaccination status were vaccinated with a least one MMR dose) [2]; and between 2007 and 2009 in the so-called Bible Belt (genotype D4) [3], an area traditionally associated with low vaccine uptake and outbreaks of vaccine-preventable diseases [4–6]. Whereas the occurrence of mumps in communities religiously opposed to vaccination can be anticipated, mumps in highly vaccinated adult populations is concerning and warrants investigation, particularly as the rate of certain complications of mumps increases with age [7].

Mumps became a notifiable disease in the Netherlands in December 2008. From 1 December 2009 to 20 April 2010, 172 mumps cases were notified to municipal health authorities across the country, a marked increase from the 65 cases notified in the eleven preceding months in 2009. Seventy-nine cases were notified to Municipal Health Service (MHS) Zuid-Holland West (including the city of Delft), 44 were notified in the Leiden region (MHS Hollands-Midden), 11 were notified to MHS Utrecht and 38 were notified in other regions across the country. The majority of cases (70%; n = 114/164 cases with known vaccination status) had received at least one dose of MMR. Overall, 65% of cases (n = 112) were students, of whom 27 (24%) reported having attended at least one evening of a large four-day party in Leiden (23–26 February,

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week 8). This party was organised and hosted by students in nine rooms spread across several floors of a members-only student association building. It was attended by 1175 Leiden students and 1850 students from other cities. The majority of cases reported to MHS Hollands-Midden occurred in week 11, one incubation period after the party, further implicating the event as a source of transmission, described in earlier communication about this outbreak [8].

Outbreaks of mumps in educational settings such as schools and colleges have been previously reported [9–12]. Explanations for this include the close contact environment that facilitates transmission and possibly a particular susceptibility for mumps in adolescents who were vaccinated in childhood [12,13]. The 2009–2010 mumps outbreak in a highly vaccinated student population provided an opportunity to assess risk factors for mumps in this population and to investigate factors associated with mumps vaccine failure among vaccinated party attendees.

2. Methods

We conducted a retrospective cohort study among students from the three university cities most affected by the outbreak: Delft, Utrecht and Leiden. Within these cities the study was restricted to student associations invited to the party in Leiden to permit investigation of party-related risk factors. Student associations in the Netherlands are similar to North American fraternities and sororities in that membership is applied for and approved after an initiation period. Members have close social ties: they typically live together and social events are frequently organised and attended by members only. Each of the eight student associations of this type in the Netherlands hosts a three- or four-day party once a year which is open to members of the other associations. In May 2010, all 4988 members of the four selected student associations in Delft ($n = 356$ women; $n = 1044$ men), Leiden ($n = 1400$; sex breakdown of members not provided but estimated by society to be an approximately equal sex ratio) and Utrecht (two societies: $n = 1288$ women; $n = 900$ men) were invited to the study by email. Invitation and reminder emails (sent one week later) were circulated via the society's mailing list and contained a link to the online questionnaire (Questback, Oslo, Norway).

To investigate risk factors associated with mumps among these student associations the questionnaire asked about demographic characteristics including current living arrangements, MMR vaccination history, and history of mumps infection. Informed consent was sought to verify MMR vaccination status using the national vaccination register. A case was defined as a student with self-reported mumps (swelling of one or both cheeks with symptoms lasting at least two days) since 1st September 2009. To investigate risk factors associated with vaccine failure among vaccinated party attendees, additional information was requested from party-attendees; specifically, the day(s) of party attendance, locations visited at the party (from a list of nine rooms or areas within the student association including several bars, themed rooms with DJs and two smoking rooms), contact with shared items including food, drinks and cigarettes, and close personal contact (kissing) during the party or at an after party.

Questionnaire responses were downloaded from the password-protected website and imported to STATA 10 for analysis [14]. Individuals with a history of mumps prior to September 2009 ($n = 13$) or whose MMR vaccination status could not be determined from the vaccine register ($n = 30$) were excluded from the analysis. Associations between risk factors and self-reported mumps were first explored in univariable analysis. Variables with a p-value <0.25 (from the univariable analysis), as well as age and sex, were entered into the multivariable regression model. When we found evidence of collinearity among explanatory variables we selected the variable which gave the best model fit (based on the Bayesian Information Criterion – BIC) into the final model. We estimated vaccine effectiveness (VE) as 1 minus the relative risk (RR) (VE = 1-RR), using the adjusted RR for mumps in vaccinated compared to unvaccinated participants.

Persons who were not susceptible to mumps at the time of the party (mumps with date of onset prior to the minimum incubation time of 12 days after the first day of the party (23rd February)) were excluded from the analysis of party-related risk factors associated with mumps failure. Cases arising after the maximum incubation time (25 days after the last day of the party (26th February)) were included as non-cases so risk factors associated with the party could be investigated.

3. Results

3.1. Study population

Overall, 989 individuals responded to the questionnaire (response rate = 20%; 10% among male students, 31% among female students) and reported studying in Delft ($n = 212$), Utrecht ($n = 517$) or Leiden ($n = 195$). For 65 respondents, the city of study was not available. Respondents were aged between 17 and 28 years (median age 21 years) and were predominantly female (75%; $n = 738$). The median age of the invited population of society members in these cities was also 21 years, 47% were female.

MMR vaccination status was verified for 91% (776/853) of consenting survey respondents: 94% ($n = 729$) had received two doses of MMR vaccine, 4% ($n = 31$) were vaccinated with one dose of MMR and 2% ($n = 16$) had never been vaccinated with MMR (Table 1).

Overall, 946 of the 989 survey respondents answered questions about mumps disease, of whom 125 reported having had mumps (attack rate 13.2%, 95%CI 11.1–15.5%). Half the cases (54%) reported visiting their GP, of whom seven were diagnosed with complications, specifically meningitis (1; 0.8% of cases), pancreatitis (2; 1.6%), orchitis (3; 8% of male cases) and deafness (4; 3.2%). One additional individual was admitted to hospital for one night due to the severity of symptoms but had no complications.

Date of symptom onset ranged from 25th December 2009 to 1st June 2010 ($n = 110$) (Fig. 1). The number of cases peaked in mid-March (week 11), about one incubation period [15] after the party.

3.2. Risk factors associated with mumps

The attack rate among men was higher than among women (17% vs. 12%, $p = 0.06$). Age-specific attack rates, did not significantly differ ($p = 0.12$) and there was no difference in the mean number of years since last vaccination between cases

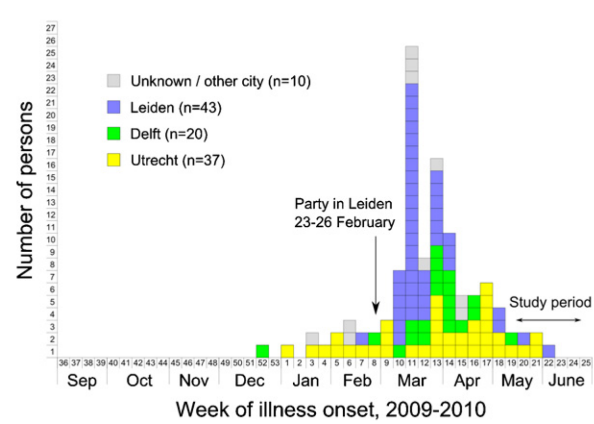

Fig. 1. Epidemic curve showing the number of mumps cases by week of symptom onset and city of study, December 2009–June 2010, the Netherlands ($n = 110$).

Table 1
Characteristics and risk factors for mumps among the entire study population ($n = 946$).

	N	No. (%) mumps[a]	Univariable relative risk (95%CI)	Multivariable relative risk (95%CI)
Gender				
Male	231	39 (16.9)	1.4 (1.0–2.0)	1.1 (0.7–1.6)
Female	713	86 (12.1)	Ref.	Ref.
Age				
17–19	188	30 (16.0)	Ref.	Ref.
20–21	397	42 (10.6)	0.7 (0.4–1.0)	0.7 (0.4–1.1)
22 and over	357	52 (14.6)	0.9 (0.6–1.4)	0.8 (0.5–1.3)
Vaccination status[b]				
Unvaccinated	16	7 (43.8)	3.4 (1.9–6.0)	3.1 (1.7–5.6)
Vaccinated (twice)	706	92 (13.0)	Ref.	Ref.
Attended party				
Yes	267	61 (22.9)	2.4 (1.7–3.3)	1.8 (1.2–2.6)
No	674	64 (9.5)	Ref.	Ref.
Number of housemates				
<5	352	34 (9.7)	Ref.	Ref.
5–15	470	65 (13.8)	1.4 (1.0–2.1)	1.3 (0.8–2.0)
>15	122	26 (21.3)	2.2 (1.4–3.5)	1.8 (1.1–3.1)

[a] $n = 125$, all mumps cases since September 2009 (excluding 3 cases with past infections).
[b] Confirmed with vaccination records. 776 records were verified out of 853 consenting participants. Not all individuals with confirmed vaccination status provided information on whether or not they had had mumps. Of 735 individuals vaccinated at least once, 706 were vaccinated twice. The 29 once-vaccinated individuals are excluded from analysis.

(12.2 years) and non-cases (12.5 years), $p = 0.54$. The attack rate was higher among respondents from Leiden (25%) than among those from Delft (12%) and Utrecht (9%) ($p = 0.05$) and was also higher among party-attendees than non-attendees (23% vs. 10% respectively) (Table 1). The attack rate increased with the number of household contacts, with individuals living with fifteen or more housemates (large society houses of up to 40 students, not dorms) twice as likely to have had mumps than those living with fewer than five other people (p-trend = 0.001) (Table 1). Among cases, attending the party and studying in Leiden was closely correlated: 93% of cases in Leiden attended the party, compared with 29% in Delft and 14% in Utrecht. After adjusting for age and sex and observing that party attendance gave a better model fit than city of study, not being vaccinated, having more than 15 housemates and attending the party were independently associated with developing mumps (Table 1).

When restricting the cases to those who were susceptible at the time of the party ($n = 35$), and including cases that arose more than one incubation time after the party as non-cases, the relative risk of acquiring mumps associated with party attendance was 42 (95%CI 10.1–172.4; $p < 0.0001$).

3.3. Vaccine effectiveness

In total, 92 of 101 (91%) mumps cases with known vaccination history had been twice-vaccinated with MMR. Among individuals with known vaccination history and known mumps disease status ($n = 751$), the attack rate was 44% (7/16) among unvaccinated individuals and 7% (2/29) and 13% (92/706) among once and twice-vaccinated individuals respectively. The adjusted VE estimate for two doses of MMR was 68% (95%CI 40.6–82.2%).

3.4. Factors associated with vaccine failure among vaccinated party-attendees

Analysis was restricted to vaccinated party-attendees with known mumps disease status ($n = 206$). The attack rate among party-attendees was similar among men (14.2%) and women (11.6%) ($p = 0.54$) and across all age groups ($p = 0.66$). Two thirds (67%) of students who attended the party were from Leiden (the host city), 21% from Utrecht and 12% from Delft. The majority of Delft and Utrecht students (84% and 98%, respectively) bought a one-day ticket, typically attending on the third day. Conversely, Leiden students more frequently bought four-day tickets: 87% of students from Leiden attended on at least three evenings. The attack rate was higher among students who attended the party on the third day (14.1%) than those who did not attend on this day (4.6%) but this difference was not statistically significant (RR 3.1; 95%CI 0.8–12.4, $p = 0.08$). We found no association between any of the specific behaviours at the party or other potential risk factors studied and the occurrence of mumps.

4. Discussion

We report a large mumps outbreak with a self-reported attack rate of 13% among a university student population of whom 94% was fully vaccinated. Our findings suggest that, together with reduced vaccine effectiveness at student age, the most likely cause of this outbreak is a combination of intense social mixing during a student party in Leiden and the dense communal living environment of the students. The shape of the epidemic curve is consistent with a point-source exposure at the party: one third of reported cases arose about one incubation period after the party, and party attendance was found to be an independent risk factor for mumps. Among students who attended the party, no specific risk factor was identified. It seems plausible that the circumstances of this party – taking place over four days and attended by students from multiple cities at a time when mumps was known to be circulating – provided an environment that promoted transmission. Considering that the number of cases in the period after the peak following the party quickly declined may suggest that sustained mumps transmission in this population is unlikely. However, increased transmission at other social events or in the winter season could prove this assumption too optimistic.

Living with a large number of housemates increased the risk of mumps. This is consistent with results found elsewhere [16]. In addition to the number of housemates, dormitory residence has also been associated with an increased risk of mumps among students [2,17]. However, student dormitories do not exist in the Netherlands.

In addition to the above-discussed risk factors for exposure to the mumps virus, risk factors for vaccine failure should also be considered when studying an outbreak of a vaccine preventable disease in a highly vaccinated population [17–19]. Precise estimation of vaccine effectiveness in this setting is not feasible due to the low numbers of unvaccinated cases as reflected in the wide confidence interval around the VE estimated in our study. However, even with the large confidence interval, our estimated VE supports the growing body of evidence that two doses of MMR do not confer long-term protection against mumps [12,13,18]. Potential reasons for vaccine failure include primary vaccine failure, waning immunity over time (secondary vaccine failure) and the possibility that the vaccine strain (genotype A) affords lower than optimal protection against heterologous genotypes such as the G genotypes which caused this outbreak and outbreaks in other countries [13,18,20–24]. Unfortunately we could not assess the effect of either of these factors in this outbreak, as it was a single genotype outbreak affecting a group of individuals within a narrow age-range and a long time has elapsed since vaccination.

The key limitation we faced in this study was the relatively low response rate, although in a large, multi-centre study of web-based surveys in student populations in the USA, the response rate was similar (20%) [25]. The low response rate may not necessarily have introduced bias into our study [26]. While we had no specific information on non-respondents, student association members invited to participate were a socio-demographically homogenous group. It is unknown how in this context, non-respondents' behaviour might differ and what impact, if any, this would have on the risk of disease.

Non-responders were more frequently male (53% of invitees were male compared with 25% of respondents), again not atypical in survey research [25]. It is also possible that those who attended the party and people with mumps were more likely to have responded to the survey. This may have caused an overestimation of the attack rate and the risk of acquisition of mumps among respondents.

As nearly all cases in Leiden attended the party we were unable to disentangle the effect of living in Leiden from that of attending the party. We believe selective participation of students with other risk factors is unlikely, suggesting all other measures of association are not biased by non-response. The slight delay between the party and the study could have affected recall of party-related risk factors but it is unlikely that recall would have been associated with mumps disease status.

National recommendations to control the mumps outbreak among university students in the Netherlands have included the advice to ensure students have received two doses of MMR. The importance of this is underlined by the observation that vaccinated individuals with mumps are less likely to develop complications than unvaccinated individuals with mumps [27,28]. Even though individuals with asymptomatic mumps virus infection are still infectious, the potential for transmission may be reduced by recommending students suffering from mumps not to attend large indoor social gatherings. Cancellation of a party or large social event when mumps is known to be circulating in a population is also likely to be a useful control measure. Other options for control include delaying the age of the second MMR dose in the routine vaccination schedule or adding a third MMR [16,21,23,29]. The former is unlikely to be favourable, given that it would lead to an increase in measles, mumps and rubella susceptibility among children. A national outbreak control team convened in the Netherlands in January 2011, during which the addition of a third MMR dose to the vaccination schedule was discussed. It was advised that, given the cost, logistics and expected low vaccine uptake among students, and the low morbidity related to mumps, this intervention could not be justified based on the current available evidence and the uncertain effectiveness of a third dose.

Studies that can shed more light on the reasons for waning immunity are needed so that appropriate solutions can be developed and policy recommendations can be made.

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