Outbreak of mumps in a vaccinated child population: a question of vaccine failure?

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Abstract
In Belgium, children are immunized against measles–mumps–rubella (MMR) in a two-dose schedule at the age of 15 months and 11 years. Despite these recommendations, epidemics of mumps still occur. During an outbreak of mumps in Bruges (Belgium), 105 cases were registered in seven schools (age group 3–12 years). Lower than optimal vaccination coverage, inadequate vaccination schedule and a combination of primary and/or secondary vaccine failure are considered as possible reasons for the outbreak as described in the article. The role of secondary vaccine failure is highlighted.

Keywords: Outbreak; Mumps; Vaccination

1. Introduction
Prior to vaccination, mumps was an infectious disease that occurred frequently among primary schoolchildren (5–9 years of age). In Belgium, the first mumps vaccine, licensed in 1967, was recommended for general use at the age of 15 months (boys only) in 1980. Since 1985, a first dose of trivalent measles–mumps–rubella (MMR) vaccine was recommended for all 15-month-old toddlers (boys and girls), followed by a second dose at the age of 11 years (fifth grade in primary school) since 1995. From the onset of the MMR-vaccination program Pluserix® (Urabe strain; GlaxoSmithKline) was used in Belgium, which was systemati-
cally replaced by MMR Vax II® (Jeryl Lyn strain; Aventis Pasteur MSD) in the year 1993 (withdrawal of Pluserix® from the market). In the years following general vaccina-
tion a sharp decline of reported mumps cases was noted in Belgium (Personal communication of Van Casteren, Scientific Institute of Public Health, Belgium) and in several other countries [1–3]. During the last decade, several outbreaks of mumps have occurred in Belgian schoolchildren. Before the introduction of a second dose of MMR in the US in 1989, county or state-wide outbreaks of mumps occurred mainly among junior high school students, despite high vaccination coverage (95–98%) [1–3]. Primary and secondary vaccine failure have been put forward as possible explanations for the outbreaks, but evidence for waning vaccine-induced immu-
nity was found in only two of the three outbreaks that looked for secondary vaccine failure [1,2].

In this study, we describe a mumps outbreak in several kindergarten and primary schools in the region of Bruges (Belgium) and try to define underlying causes.

2. Materials and methods

The study population consists of all pupils from seven kindergarten and primary schools in Bruges, having re-
ported at least one case of mumps to the school health service between 01/09/1995 and 30/06/1996. All pupils in the affected schools were given a questionnaire on the symp-
toms of mumps, visits to health care providers, possible contacts with other mumps cases, and history of vaccina-
tion and mumps disease. The questionnaire was to be filled in by the parents retrospectively and returned by the end of June 1996. Vaccination data were thoroughly checked and compared against immunization data from the medical files...
of the school health service. In agreement with the CDC definition, cases of mumps were defined as any illness with unilateral or bilateral painful self-limited swelling of the parotid or any other salivary gland for at least 2 days and without other apparent cause [4]. The CDC case definition, when used within the context of an outbreak of parotitis and supported by serologic confirmation for a number of the reported cases, is generally considered to be very suggestive for mumps.

The vaccine efficacy (VE) was calculated as the attack rate in the unvaccinated population (ARU), minus the attack rate in the vaccinated population (ARV) divided by the ARU, thus VE (%) = (ARU – ARV/ARU) x 100, as described by Orenstein et al. [5].

The data were analyzed with the SAS system for windows version 8.01 (SAS Institute, NC, USA). The categorical outcome of groups was compared with a chi-square test or Fisher’s exact test when appropriate. Disease prevalence according to the number of years since the last dose of mumps vaccine was administered, was modeled with logistic regression analysis using SAS proc. GENMOD.

3. Results

By the end of the study period, 1843 out of 2204 distributed questionnaires (83.6%, distributed as 47.6% boys and 52.4% girls) were returned. Immunization data, checked against the school health records, were obtained from 1825 subjects (99% of the respondents). Table 1 presents the local vaccination coverage at the start of the outbreak in each school. The overall vaccination coverage (at least one dose of MMR) before the outbreak was 91.8% (n = 1675) of 1825 children with documented vaccination records and increased to 94.1% by the end of the school year.

From November 1995 to June 1996, 105 (5.7%) children were clinically diagnosed as having mumps based on reported symptoms, of which 12 cases had serological confirmation of a recent mumps infection. A painful swelling of the parotid was reported for 103 children (98.1%). One child had a swelling of the submandibular salivary glands. One child experienced fever without parotid swelling, but mumps was diagnosed through a blood sample. Major complications included one vaccinated child with both orchitis and meningitis, and persistent unilateral deafness in an unvaccinated child. Forty-seven children experienced mumps in the past.

For the calculation of the odds ratios (OR), we excluded all children without reliable vaccination data (n = 18) and 45 children who had a history of mumps prior to the outbreak. In the remaining group 85 out of 1641 vaccinated children (5.2%) and 20 out of 139 unvaccinated children (14.4%) developed mumps during the outbreak. The odds ratio for developing mumps of the vaccinated versus the unvaccinated children was 0.33 (95% confidence interval (CI): 0.19–0.55), and the overall vaccine efficacy in this particular outbreak was 64.0% (CI: 43.2–77.2%). The proportion of vaccinated children with mumps increased progressively by increasing time lapse since the last dose of mumps vaccine was administered, was modeled with logistic regression analysis using SAS proc. GENMOD.

![Fig. 1. The percentage of children with mumps according to the number of years between vaccination and the outbreak and a logistic regression model with intercept −4.22 (−4.81 to −3.62; P < 0.001) and coefficient 0.24 (0.15–0.32; P < 0.001), model goodness of fit: likelihood ratio chi-square 31.6 on 1 d.f., P < 0.001.](image-url)
4. Discussion

In the school year 1995/1996, an outbreak of mumps occurred in a population of primary schoolchildren in Bruges (Belgium). Different hypotheses were considered as to why this outbreak occurred: (i) low vaccination coverage; (ii) primary and/or secondary vaccine failure; (iii) an inadequate vaccination schedule.

In 1990, Anderson and May [6] considered a vaccination coverage of 90–92% at 2 years of age to be high enough to prevent circulation of the virus. In 1999, the overall vaccination coverage for one MMR vaccine at the age of 24 months was as low as 83.4% for the whole of Flanders, ranging from 65.6 to 92.8% according to province. In the province of West-Flanders, where Bruges is situated, the vaccination coverage was limited to 79.8% [7]. Even though the overall vaccination coverage was 91.8% in the whole population of the schools where the outbreak occurred, the circulation of wild mumps virus in the surrounding area cannot be excluded. The actual force of infection might have been a lot higher than would be expected on the basis of the vaccination coverage in the different schools. In this situation, a local coverage with one MMR-vaccine close to 95% in some schools was not enough to prevent an outbreak.

The efficacy of the live attenuated vaccine against mumps (Urabe and Jeryl Lynn, which were the two vaccines used in our study population) as measured in pre-licensure studies was 95% [8], which however in several outbreak reports appeared to be notably lower and ranged from 61 to 91% [1–3,8]. In this study, the efficacy estimate was as low as 64.0%, and clearly related to the time lapse since the vaccine was administered (Fig. 1). The efficacy of a vaccine is determined by (i) case definition; and (ii) case ascertainment; (iii) determination of vaccination status; and (iv) comparability of exposure [5]. Kim-Furley et al. [9] outlined possible pitfalls in the determination of vaccine efficacy in case of a mumps outbreak. Methods of case ascertainment and determination of vaccination status may greatly influence vaccine efficacy calculations. In our study, the case definition was outlined before the questionnaire was taken from the parents and in agreement with CDC-guidelines. In addition, the epidemic character of the parotitis was extremely suggestive for mumps especially since serologic confirmation was obtained for 11.4% of the cases [9]. Case detection is the weak point in this survey, because of its retrospective nature. However, the high proportion of respondents of the survey limits the likelihood of a significant bias in the case reporting between vaccinated and unvaccinated children. The determination of vaccination status was carried out thoroughly, since all vaccination data reported by the parents were checked with the medical school records. And last but not least, the comparability of exposure was considered to be equal among both vaccinees and non-vaccinees because of the relatively high incidence rate (5.7%) during the outbreak [5]. By carrying out this study, we also detected 47 pupils who experienced mumps in the past. This is probably an underestimation of the actual number, since mumps can present as a disease with non-specific or primarily respiratory symptoms in as many as 40–50% of the cases [8].

The calculated very low vaccine efficacy suggests that next to primary vaccine failure and less than optimal vaccination coverage, another factor might be involved. Waning immunity, the so-called secondary vaccine failure, might have increased over the years the number of susceptible children in the observed age group. In this study, the contribution of waning immunity was estimated with a logistic regression model. In this model, the odds to develop mumps increased rapidly with increasing time interval between the last vaccination and the outbreak. Similar results were obtained when birth cohort or school grade were used in the logistic regression model. The subjects who were immunized 10 years prior to exposure had a lower risk to develop mumps than children with shorter intervals. All of these pupils were born in 1985, which was the begin period of free MMR-immunization in Belgium. It is likely that during this start-up phase, mumps-virus was still circulating widely in Belgium. Many children of this age group might have had contact with the wild mumps virus. For two other outbreaks, described in the literature, the contribution of waning immunity in vaccine failure was investigated, but could not be proven with the available data [1,2].

Narita et al. [10] showed that in a group of 14 children with recent mumps infection despite one vaccination (≥2 years ago) 12 children developed antibodies with high avidity immediately after infection. This indicates that secondary vaccine failure is a risk factor to be taken into account. Seven of these 12 individuals also showed IgM antibodies despite high avidity antibodies, which would misclassify them otherwise as primary vaccine failures. The age of the children varied between 5 and 11 years of age. To date, immunity to mumps was believed to be life long, regardless whether it was acquired by natural infection or by immunization. The results of our logistic regression model and the results of avidity testing reported by Narita show that this is not always the case after one dose of vaccine. Most probably, the driving force of the outbreak described in our study is the low surrounding vaccination coverage in Flanders, but probably facilitated by a combination of primary and secondary vaccine failure. In addition, the interval between both recommended MMR vaccinations in Belgium (at the ages of 15 months and 11 years) might be too large to compensate for the risk for outbreaks. A shift of the second dose of MMR vaccine to a younger age (i.e. 4–6 years, as was the case in several other European countries) would result in a better control of circulation of the mumps virus and preclude further outbreaks. Although Finland was able to eradicate measles, mumps and rubella with the same vaccination schedule used in Belgium, they reached this goal by means of a considerably higher vaccination coverage (>95%) for both doses [11]. A shift of the second vaccine dose to younger age holds several advantages: (i) better control of the diseases (measles and mumps); (ii) less build-up of sus-
ceptible individuals; and (iii) higher vaccination coverage
[12].

We think to have shown that secondary vaccine failure is
a possible risk factor in the development of outbreaks of
mumps in countries with a lower than optimal vaccination
coverage, and a two-dose schedule with the second dose
administered at the age of 11 years.

References


