



## Review

## Mumps outbreaks: A problem in need of solutions

Nicola Principi<sup>a</sup>, Susanna Esposito<sup>b,\*</sup><sup>a</sup> Professor Emeritus of Pediatrics, Università degli Studi di Milano, Milan, Italy<sup>b</sup> Pediatric Clinic, Department of Surgical and Biomedical Sciences, Università degli Studi di Perugia, Perugia, Italy

## ARTICLE INFO

## Article history:

Accepted 24 March 2018

Available online 18 April 2018

## Keywords:

Mumps

Mumps vaccine

Paediatric infectious diseases

Vaccine-preventable disease

Emerging viruses

## SUMMARY

**Objectives:** To discuss what is presently known about recent mumps outbreaks and what solutions can be suggested to ensure more complete protection against mumps.

**Methods:** PubMed was used to search for all of the studies published over the last 15 years using the key words “mumps” or “mumps virus” or “mumps vaccine”. More than 1500 articles were found, but only those published in English or providing evidence-based data were included in the evaluation.

**Results:** Prevention of mumps remains an unsolved problem. Available vaccines are effective but the protection they evoke declines over time. The use of booster doses can control outbreaks but it is not precisely defined whether they can prevent them. The rapid decline of antibody levels could limit the impact of the introduction of a third dose in the recommended immunization schedule. Furthermore, in most of the areas, mumps viral strains that are genetically different from those included in the vaccines are emerging and this might favour vaccine escape. However, also for this problem, its real relevance in favouring outbreak development is not precisely defined.

**Conclusions:** The true reasons for the development of mumps outbreaks in people with very high vaccination coverage are not clearly understood. The use of a booster dose or the preparation of vaccines containing the emerging serotypes are possible solutions, but both have some limitations. Further studies mainly devoted to improve our knowledge of the immune response to mumps vaccines are needed before long-term effective mumps vaccines can be prepared and outbreaks can be avoided.

© 2018 The British Infection Association. Published by Elsevier Ltd. All rights reserved.

## Introduction

Mumps is a highly contagious infectious disease caused by a single-stranded, negative-sense RNA virus that is a member of the *Paramyxoviridae* family, subfamily *Paramyxovirinae*, genus *Rubulavirus*. The M virus (MuV) genome includes 15,384 nucleotides that encode seven proteins.<sup>1</sup> Among these proteins, the putative membrane-associated small hydrophobic (SH) protein and the surface protein haemagglutinin-neuraminidase (HN) are used to generate a global sequence database and define MuV genotypes. Twelve MuV genotypes have been identified and named with letters A to N, except for E and M.<sup>1</sup>

In absence of any preventive measure, mumps is a childhood disease that mainly occurs in children that are 5–9 years old, although this disease can also occur in adolescents and adults. The average annual incidence of mumps in the pre-vaccination era was 100–1000 cases/100,000 of the general population. About 30% of MuV infections remains asymptomatic or causes only non-specific symptoms, including low-grade fever, particularly in patients <2 years.<sup>2</sup> In the great majority of remaining patients, characteris-

tic unilateral or bilateral parotid gland swelling develops. This swelling persists for 2–10 days and later resolves spontaneously without any permanent alteration. However, in some cases, sometimes in absence of parotitis, complications can develop. Death is exceptional (1/10,000 cases).<sup>2</sup> However, more than 50% of the patients have cerebrospinal fluid alterations. In most cases, pleocytosis remains asymptomatic, but approximately 1–10% and 0.1% of them develop signs and symptoms of aseptic meningitis and encephalitis, respectively.<sup>2</sup> Neurological sequelae, among which sensorineural deafness is the most common (5/100,000), can occur.<sup>2</sup> Postpubertal males suffer from orchitis in 20% of cases. Oophoritis and mastitis are significantly less frequent. In both cases, reproductive problems are rare. MuV infection during the first 12 weeks of pregnancy can lead to abortion. Fortunately, later infection does not seem to be associated with the development of malformations.<sup>2</sup>

No treatment for mumps is available and immune globulins have poor protective effects. To reduce mumps-related clinical, social and economic problems, vaccines were developed. An inactivated MuV vaccine was first licensed in 1948. However, it only had short term effectiveness [and, starting from the 1960 s, it was substituted with preparations based on live attenuated virus strains, including the Jeryl-Lynn, RIT 4385, Leningrad-3,

\* Corresponding author.

E-mail address: [susanna.esposito@unimi.it](mailto:susanna.esposito@unimi.it) (S. Esposito).

Leningrad-Zagreb, Urabe Am9, S79, Rubini, and others. Although single preparations are available, generally MuV vaccines are administered in combination with measles and rubella (MMR) vaccines or, more recently, with measles, rubella, and varicella (MMRV) vaccines.<sup>3</sup> The inclusion of a single dose of Mu vaccine in the national immunization schedules of children rapidly led to a significant reduction in the incidence of mumps. However, years later, several outbreaks among vaccinated populations have been reported, which indicates that high coverage with a single dose of mumps vaccine does not always prevent disease transmission. This has led health authorities to recommend a second dose of the vaccine. Presently, two-dose schedules are implemented in most countries.<sup>4,5</sup> The first dose is usually given at 12–18 months. The second is given at least one month later, most children receive the second dose by the time they enter school. However, despite high vaccination coverage with two vaccine doses, several MuV outbreaks continue to occur worldwide. The reasons for this trend are not precisely defined. The main aim of this paper is to discuss what is presently known about this trend and what solutions can be suggested to ensure more complete protection against mumps. PubMed was used to search for all of the studies published over the last 15 years using the key words “mumps” or “mumps virus” or “mumps vaccine”. More than 1500 articles were found, but only articles published in English or providing evidence-based data were included in the evaluation.

### Epidemiology of mumps in the post-vaccination era

Two doses of MuV vaccine are 88% (66–95%) effective for protecting against mumps. This effectiveness explains why, after the two-dose schedule has been adopted and vaccination coverage was well above the estimated herd immunity threshold of 75–86%,<sup>6</sup> reported cases of mumps have declined by 99%. This vaccination schedule limited the disease incidence rate to less than 1/100,000 population and reached the World Health Organization (WHO) control target.<sup>7–10</sup> However, despite high vaccination coverage, outbreaks have occurred worldwide.<sup>11–18</sup> Adolescents, young adults and, generally, people in close-contact settings, such as people on college campuses, are at increased risk of exposure and have been mainly involved in these outbreaks. In some outbreaks, most of the cases were diagnosed in patients who had already received  $\geq 2$  doses of the MuV vaccine. This occurred in the USA, where outbreaks occurred in 2006 in the Midwest states and in 2009 in the Northeast states with 63% and 75% of patients, respectively, that had been vaccinated according to official recommendations.<sup>19</sup> Similar data were collected during the most recent USA outbreak. In Arkansas in 2016, there were 4975 mumps cases, which represented 78% of all cases identified in the USA during that year, and patients were diagnosed with an incidence rate of 1.9/100,000. In this outbreak, 73% of mumps cases occurred in subjects that were vaccinated with  $\geq 2$  doses.<sup>20</sup> In Europe, in several states with an immunization schedule that includes two doses of MuV vaccine and high vaccination coverage, notable increases in mumps notification rates that suggested an outbreak were observed, although these increases occurred in different years. For example, in Slovakia from 2013 to 2014 reported cases increased from 4.0/100,000 to 28.8/100,000.<sup>21</sup> Similarly, in Ireland, the rates varied from 4.8 in 2013 to 16.0/100,000 in 2014.<sup>21</sup> Previously, transient, although very significant, increases in mumps incidence rates occurred in Belgium and Spain.<sup>21</sup>

Although two doses of MuV vaccine do not fully protect against mumps, available data indicate that double vaccination has a protective effect against the severity of the disease. Mu occurring in patients who have received two MuV vaccine doses was generally less severe than compared to patients who were partially vaccinated or not immunized. In a UK study, it was found that the

risk of hospitalization, orchitis and meningitis were reduced by 46%, 28% and 72% by one MuV vaccine dose and by 55%, 36%, and 83% by two doses compared to unvaccinated patients.<sup>22</sup> Similar results were obtained in Israel,<sup>23</sup> the Netherlands,<sup>24</sup> Spain,<sup>25</sup> and the USA.<sup>26</sup>

### Suggested reasons for mumps outbreaks

Epidemiological studies carried out in the pre-vaccination era have led to the conclusion that a natural infection from the wild type MuV typically conferred lifelong protection against the virus, although cases of re-infection have been reported.<sup>27</sup> Natural boosters due to continuous exposure to the circulating virus maintained protection. With the introduction of the MuV vaccine and the achievement of a high vaccination coverage, natural boosters were significantly reduced, and protection was assured only by vaccine. The occurrence of mumps outbreaks revealed the limitations of the MuV vaccine. Several factors have been suggested to explain outbreak development. Some of them, such as waning immunity and immune escape by circulating MuV strains are strongly supported by epidemiological and research data. Some others, such as a decline in vaccine coverage, can be easily debunked. As already reported, the herd immunity threshold is estimated to be 75–86%,<sup>6</sup> and most outbreaks occurred in geographic areas where mumps vaccination coverage was higher.<sup>19–21</sup> However, the contribution of each factor is not precisely defined, and this uncertainty has caused problems for defining the best strategies to reduce or eliminate outbreaks.

### Waning of vaccine-induced immunity

A large amount of evidence seems to suggest that waning of vaccine-induced immunity is one of the causes of mumps outbreaks. During outbreaks, most cases were diagnosed in adolescents and young adults, unlike the pre-vaccination era when most of the mumps cases were diagnosed in children in primary school. The shift within age-groups for mumps incidence in highly vaccinated populations has been repeatedly reported.<sup>11–18,25</sup> Research has shown that the risk of mumps in fully vaccinated subjects increased by 10% for every year that passed since the second MuV dose (adjusted odds ratio [aOR]: 1.10; 95% confidence interval [CI]: 1.02–1.19;  $p = 0.02$ ).<sup>28</sup> In some studies, it was demonstrated that the risk of mumps development during outbreaks was significantly higher in subjects that were given the second dose more than 10 years prior than in more recently vaccinated individuals.<sup>29,30</sup> Finally, the protection offered by the vaccine was clearly time-dependent. Cohen et al. established that the effectiveness of two doses of the MuV vaccine, along with the second dose administered at 3–5 years of age, was 99% (95% CI: 97–99.5) in 5- to 6-year-old children and was reduced to 86% (95% CI: 74–93) in 11- to 12-year-old subjects ( $p < 0.001$ ).<sup>31</sup> Serological studies seem to further support this hypothesis. Fully vaccinated mumps patients generally have lower pre-outbreak mumps antibody levels than subjects that, despite exposure to the virus, remain healthy.<sup>32</sup> Although a precise correlate of protection has not been defined, high antibody levels do not exclude infection because of the possibility of immune escape, low or no antibody concentrations indicate either poor or no protection. On the other hand, the role of cell-mediated immunity in protection from MuV infection, despite what has been suggested by some studies, has not been clearly established. However, no strict correlation between the nature and magnitude of cell-mediated immunity and protection has been demonstrated,<sup>33</sup> which suggests that details of the immune response made by the host to stimulation by the MuV are not known.

Download English Version:

<https://daneshyari.com/en/article/8740384>

Download Persian Version:

<https://daneshyari.com/article/8740384>

[Daneshyari.com](https://daneshyari.com)