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Shift within age-groups of mumps incidence, hospitalizations and severe complications in a highly vaccinated population. Spain, 1998–2014

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ABSTRACT

The mumps vaccine (Jeryl-Lynn-strain) was introduced in Spain in 1981, and a vaccination policy which included a second dose was added in 1995. From 1992–1999, a Rubini-strain based vaccine was administered in many regions but later withdrawn due to lack of effectiveness. Despite high levels of vaccination coverage, epidemics have continued to appear.

We characterized the three epidemic waves of mumps between 1998 and 2014, identifying major changes in susceptible populations using Poisson regression.

For the period 1998–2003 (P1), the most affected group was from 1 to 4 years old (y) [Incidence Rate (IR) = 71.7 cases/100,000 population]; in the periods 2004–2009 (P2) and 2010–2014 (P3) IR ratio (IRR) increased among 15–24y (P2 = 1.46; P3 = 2.68) and 25–34y (P2 = 2.17; P3 = 4.05).

Hospitalization rate (HR), complication rate (CR) and neurological complication rate (NR) among hospitalized subjects decreased across the epidemics, except for 25–34y which increased: HR ratio (HRR) (P2 = 2.18; P3 = 2.16), CRR (P3 = 2.48), NRR (P3 = 2.41).

In Spain mumps incidence increased, while an overall decrease of hospitalizations and severe complications occurred across the epidemics. Cohorts born during periods of low vaccination coverage and those vaccinated with Rubini-strain were the most affected populations, leading to a shift in mumps cases from children to adolescents and young adults; this also reveals the waning immunity provided by the mumps vaccine. Despite not preventing all mumps cases, the vaccine appears to prevent serious forms of the disease.

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1. Introduction

Mumps is a vaccine-preventable disease caused by the mumps virus (MuV, *Paramyxoviridae* family), which commonly appears in childhood in unvaccinated populations or those with low vaccination coverage. The main clinical manifestations of mumps are fever and swelling of the parotid glands. The incubation period for mumps ranges between 15 and 24 days. The main vectors of transmission are salivary droplets, direct contact or contaminated fomites. Complications associated with mumps among children are rare and usually mild; nonetheless, it can lead to complications

such as meningitis (1–10% of all infections), encephalitis, orchitis (15–30% of adult men with infection)/oophoritis (5% of adult women with infection) or sensorineural deafness, especially in adults or babies [1–3]. However, up to 30% of mumps cases could be asymptomatic or present with non-specific respiratory symptoms with or without parotitis [2].

Neurological complications due to the MuV may be underestimated, since up to 50% of the meningitis due to MuV comes about without swelling of the parotid gland. A recent study among patients with meningitis or encephalitis without clinical symptoms of parotitis, and in the context of mumps epidemics, detected MuV in cerebrospinal fluid (CSF) in 3.8% of cases (6/158) [4].

Based on data reported to the World Health Organization (WHO), 385,648 cases of mumps were estimated worldwide in 2015 [5]. In Europe, mumps cases have decreased from 243,344 in 2000 to 9939 in 2015 [6], coinciding with high vaccination coverage using Measles Mumps Rubella vaccine (MMR) in most

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European countries [7]. In the Region of the Americas, 43,840 cases of mumps were reported in 2000 and 19,115 cases in 2015 [8]. Despite sustained high vaccination coverages, there is a resurgence in mumps cases and outbreaks of mumps are still occurring [9–14]. This could be explained by low vaccine effectiveness, caused by a waning of vaccine induced immunity [15,16], a decrease in the capacity of the antibodies induced by the vaccine to protect against circulating wild-type MuV, an incomplete cross-reaction between genotypes [17], or antigenic drift [18]. In addition, improvements in diagnostic techniques may also have boosted the reported figures [13,19].

In Spain, the mumps vaccine is delivered as a component of the MMR jab, introduced to the national childhood immunization schedule in 1981 for children aged 15 months. In 1995, a second dose was added at age 11 (y), and it was brought forward to 3–6 years in 1999. In 2012, an update of the national childhood immunization schedule was approved, and set the first dose of MMR at 12 months and the second at 3–4 years [20]. Different vaccine strains have been used as the mumps vaccine antigen. The Jeryl-Lynn strain (JLs) has been administered since MMR vaccine was introduced, but it coexisted with the Urabe strain (1981–1992) and the Rubini strain (1992–1999) in most autonomous regions. The Urabe strain was withdrawn due to adverse effects, and the Rubini strain because of low effectiveness. Since 2000 only the JLs and RIT 4385 strain (obtained from JLs) are administered nationwide [21] (Fig. 1).

In Spain, mumps has been a notifiable disease since 1982. All general practitioners and pediatricians must notify every clinically-suspected case to the National Epidemiological Surveillance Network (Red Nacional de Vigilancia Epidemiológica, RENAVE). In 1996, case-based reporting was implemented with the inclusion of basic epidemiological data (sex, age, case classification, and history of vaccination) and this reporting system became fully functional in 1998. Mumps cases are notified based on the definitions provided by the World Health Organization (WHO) and the European Centre for Disease and Control (ECDC) [21].

A case of mumps is defined as a person with fever and at least one of the following symptoms: sudden onset of swelling, painful to touch parotid or other salivary glands, orchitis. The laboratory criteria to confirm a suspected case should have at least one of these results: specific antibody response to a mumps virus (IgM or IgG seroconversion) in serum or saliva; detection of mumps viral RNA by RT-PCR in saliva, urine or CSF; and/or isolation of mumps virus in saliva, urine or CSF. The epidemiological criterion is defined as contact with a laboratory-confirmed mumps case between 14–25 days before the onset of symptoms [21].

Vaccination coverage in Spain has increased progressively since the introduction of MMR vaccine reaching 80% in 1985. The childhood vaccination schedule against mumps, which provides two separate doses of the MMR vaccine, was consolidated in the 1990s, with high vaccination coverages (>95% for the first dose

since 1999 and >90% for the second dose since 2003) [21,22]. Between 1985 and 2012, the mumps incidence rate (IR) decreased about 95%, in line with rates in other industrialized countries [2,23]. Nonetheless, five epidemic waves have occurred despite high vaccination coverage [21] (Fig. 2).

The aim of this study is to find out the reasons for this pattern of outbreaks in a highly-vaccinated population. For this purpose, we characterize the last three epidemic waves of mumps which occurred in Spain between 1998 and 2014, describing incidence rates globally, by age group and by epidemic period, as well as the hospitalization and complication rates, focusing on neurological complications. This will enable us to identify changes in susceptible population throughout the study period and lead to a better understanding the role of the current vaccination programme in providing protection.

2. Material and methods

Data related to mumps cases were obtained from RENAVE.

Data for hospitalizations and complications among hospitalized cases were obtained from the National Registry of Hospitalizations Discharge (CMBD) of the Ministry of Health, Social Services and Equality (MofH). Following the Ninth International Classification of Diseases (ICD-9CM) [24] we used these codes, recorded as the principal diagnosis, to analyze complications: 072.2 encephalitis, 072.1 meningitis, 072.0 orchitis, 072.3 pancreatitis, 072.71 hepatitis, 072.79 other complications, 072.8 mumps with unspecified complications, 072.9 mumps without mentioned complication. Data related to national vaccination coverage in Spain was obtained from the MofH [22]. Annual population data for the calculation of rates were obtained from the National Institute for Statistics [25].

We describe the overall mumps incidence rates (IR), the hospitalization rates (HR), complication rates (CR) and neurological complication rates in hospitalized cases (NR) due to mumps in Spain from 1998 to 2014. We have developed the variable “neurological complication” from the codes of meningitis and encephalitis taken together jointly. Data regarding complications are referred to those registered among hospitalized cases.

In order to analyze the evolution of the disease by period and age group, we have defined three periods (P) according to the three different epidemic waves observed between 1998 and 2014: P1 (1998–2003), P2 (2004–2009) and P3 (2010–2014); we also set seven age groups: <1 year, 1–4y, 5–9y, 10–14y, 15–24y, 25–34y and ≥35y.

2.1. Statistical analysis

To compare the epidemic waves, period rate ratios for incidence (IRR), hospitalization (HRR), global complications (CRR) and

Vaccine strain	Jeryl- Lynn																																	
	Urabe														Rubini																			
1 st dose	15 m																											12 m						
2 nd dose															11-13 y							3-6 y							3-4 y					
Year	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014

Source: Ministry of Health, Social Services and Equality

Fig. 1. MMR vaccine: strains of the mumps component and year of introduction of the 1st and 2nd dose. Spain, 1981–2014.

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