The epidemiology of mumps in Italy

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1. Introduction

Mumps is an acute contagious disease which is endemic worldwide [1]. Infection typically occurs in childhood, though it can also occur in adults, among whom some complications can be more frequent than among children. Infection, even if asymptomatic, induces a long-lasting immunity [2].

The disease is usually benign, and 30% of paediatric cases are asymptomatic. Severe complications, though rare, include hearing loss in children (5/100,000), and encephalitis (incidence of <2/100,000 cases, of which 1% are fatal). Adults have a greater risk than children of meningitis and encephalitis. When acquired after puberty, mumps can be related to orchitis, testicular atrophy and even sterility in males, and to mastitis and oophoritis in males. Mumps infection in the first 12 weeks of pregnancy may result in foetal loss [3]. Other important characteristics of mumps are the occurrence of asymptomatic forms, allowing many countries to achieve near-elimination of the disease, preceding the clinical onset, and the lack of a specific antiviral therapy.

The epidemiological impact of mumps and its possible sequelae have prompted the development of a vaccine, which represents the best option for preventing the disease and its complications.

The mumps vaccine contains live attenuated virus and is available as a single-antigen preparation, as a trivalent combination with measles, rubella vaccines (MMR) [4], or as a quadrivalent combination with measles, rubella and varicella vaccine [5]. More than 10 different live attenuated viral strains are included in mumps vaccines worldwide.

In Italy, for many years the Rubini strain has been widely used. The poor effectiveness in preventing mumps and its nationwide use has contributed to the failure of control of this disease in the 1990s [6]. In June 2001 in order to contain the Rubini strain, the registration of products containing this specific vaccine strain was revoked [7] and since then widely used live attenuated mumps vaccines have included or include the Jeryl Lynn, Urabe and RIT4385 strains.

The adoption of a single dose schedule has led to a significant decrease in the incidence of mumps, yet outbreaks continue to occur in school settings [8–10]. A two-dose schedule has proved even more effective in decreasing mumps incidence, allowed many countries to achieve near-elimination of the disease.
2. Materials and methods

2.1. Incidence data

In Italy, mumps is subject to mandatory notification [18], and all reported cases are recorded by Italy’s National Census Bureau (ISTAT). The clinical case definition is sufficient for a case to be reported; laboratory diagnosis is not required. The clinical case definition is a mono or bi-lateral swelling of salivary glands (parotitis or others glands) lasting at least 2 days and absent/moderate fever, without other concomitant pathologies.

We calculated the incidence for the period 1991–2004 for the entire country and for three main geographical areas (northern Italy, central Italy, and southern Italy and the islands), based on mandatory notifications, using as reference the Italian population included in the national census (for the years 1991 and 2001) or estimates provided by ISTAT (for the remaining years). We also calculated the trend in incidence for the periods 1991–1995, 1996–2000 and 2001–2004, by age class: 0–14, 15–24, 25–64, and ≥65 years. For each of these periods, the trend in incidence by geographical area and the percentage of notifications in different age groups were also determined.

2.2. Analysis of other databases

Given that mandatory notification is affected by underreporting, we analysed data from other databases with information on mumps. In particular, we considered the incidence data for the years 2000–2004 provided by Italy’s Paediatric Sentinel Surveillance System of Vaccine-Preventable Diseases (SPES), a network of paediatricians located throughout Italy and co-ordinated by the Istituto Superiore di Sanità (Italy’s National Health Institute). We also examined the National Hospital Discharge Database, created in 1994, which collects information on all hospitalisations recorded in Italy [19]. For the analysis of this latter database, we considered the main reason for hospitalization, which is codified using the ICD9-CM code (0072 for mumps). The analysis was performed on data for the period 1999–2004.

2.3. Seroprevalence study

A national cross-sectional population-based seroprevalence study of mumps antibodies was performed on samples collected in the period from January 2003 to October 2004 in each of Italy’s 19 Regions and 2 Autonomous Provinces. Assuming an overall mumps prevalence of 70%, a sample size of 2017 sera was required to show that the trend in incidence was statistically significant.
Table 1
Incidence of mumps per 100,000 children 0–14 years, Italy, 2000–2004

<table>
<thead>
<tr>
<th>Year</th>
<th>Northern (Italy)</th>
<th>Central (Italy)</th>
<th>Southern (Italy)</th>
<th>Italy</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>1917</td>
<td>2274</td>
<td>1830</td>
<td>1939</td>
</tr>
<tr>
<td>2001</td>
<td>1518</td>
<td>665</td>
<td>761</td>
<td>1039</td>
</tr>
<tr>
<td>2002</td>
<td>302</td>
<td>206</td>
<td>150</td>
<td>220</td>
</tr>
<tr>
<td>2003</td>
<td>215</td>
<td>81</td>
<td>116</td>
<td>149</td>
</tr>
<tr>
<td>2004</td>
<td>109</td>
<td>65</td>
<td>54</td>
<td>79</td>
</tr>
</tbody>
</table>

Data from paediatric sentinel surveillance (SPES).

the three areas and that there was a clear north–south gradient, with the highest incidence consistently found for northern Italy, followed by central and southern Italy (Fig. 1).

3.2. Analysis of other databases

In the period 2000–2004, 11,697 cases of mumps were reported to SPES, with the annual incidence progressively decreasing from 1939 per 100,000 children (0–14 years) (2000) to 79 per 100,000 children (2004). In general, incidence rates were higher in northern and central Italy than in southern Italy (Table 1).

According to the National Hospital Discharge Database, in the period 1999–2004 there was an annual mean of 363 hospitalizations and 247-day-hospital admissions for mumps, 619 and 325 hospitalizations and day hospital admissions, respectively. The mean duration of stay was 2.54 days.

3.3. Seroprevalence study

Overall, 3094 blood samples were analysed: 2276 were positive, 621 were negative, and 197 were equivocal. The seroprevalence showed a typical pattern. In the first year of life (when children are passively protected by the mother), 25.4% of individuals 0–11 months old were seropositive; among 12–23-month olds, the seroprevalence was 30.8% (difference not significant compared to 12–23-month olds); it continued to increase though not always significantly: 65.0%, 78.8%, 92.8%, respectively, for the age classes 5–9, 10–14, and >40 years (Fig. 2). Of note was the finding that the percentage of seronegative individuals was greater than 20% in the age groups 2–4, 5–9 and 10–14 years and greater than 10% in the age classes 15–19 and 20–39 years.

No statistically significant difference was found in seroprevalence when comparing males and females (Fig. 2). The trend in seroprevalence was basically uniform when considering the three geographic areas, with no significant difference.
The GMT progressively increased up to 10–14 years and then significantly \( p < 0.01 \) decreased in the age class 15–19 years. There were no significant differences when comparing males and females, except for the age group 15–19 years \( p < 0.01 \).

### 3.4. Comparison of seroprevalence data from 1996 and 2004

Only in the age group 2–4 years was the seroprevalence in the survey conducted in 2004 statistically higher than that in 1996 \( p < 0.01 \). No significant differences were detected in other age classes (Fig. 4).

### 4. Discussion

Before vaccination was introduced, mumps was a common infectious disease in all parts of the world, with the highest annual incidence among 5–9-year olds. In many countries, the availability of safe and efficacious vaccines has led to a rapid decrease in morbidity. According to WHO, in 2004, mumps vaccination was included in the vaccine schedules of 109 countries, which constitutes a marked increase with respect to the 74 countries in 1999. In 2004, a two-dose vaccination schedule, mainly with the MMR vaccine, was extensively adopted (in 82% of the 109 countries) [22].

In countries where it was possible to implement vaccination and to rapidly achieve and maintain high VC, there was a consistent decrease in morbidity [3].

In Italy, mumps vaccination was introduced in the beginning of 1980s and in 1982 the Ministry of Health recommended vaccination of susceptible males, both in pre- and post-puberty. The availability of combined MMR vaccines permitted to start the immunization of both males and females in the second year of life and MMR vaccination has been included in the national vaccine schedule since the beginning of 1990s. At that time the vaccines commercially available contained at least one of the following mumps strains: Jeryl Lynn and Rubini. The impact of vaccination on mumps was inadequate; notifications changed from 62,000 per year in the period 1980–1989 to 45,000 in the period 1990–1997. Epidemic peaks were registered every 3–4 years and over 80% of cases involved children up to 15 years of age. During 1990s the observation of mumps cases in already vaccinated subjects prompted some studies on the efficacy of commercially available vaccines; the result was that the Rubini strain had a very low efficacy level (23–31%) and that its wide use could be related to the unsatisfactory control of mumps at national level [23–25]. For these reasons, in July 2001 products containing Rubini strain were withdrawn [7].

However, VC is still not sufficient because the control and/or eradication/eradication of an infectious disease can only be achieved by reaching and maintaining a 95% VC [4], so as to avoid undesired effects, such as new cohorts of susceptible individuals, an increase in the mean age of acquisition of the infection, and the broadening of the inter-epidemic period. The commitment made by Italy to eliminate measles and congenital rubella (<1 case/100,000 newborns) by 2010 [29] will also allow Italy to reach the targets established for mumps for the WHO European Region, which have been endorsed in the 2003–2005 National Health Plan and the 2005–2007 National Vaccine Plan [15,30,31].

In Italy, mumps incidence remained almost unchanged until 2001 (range: 25.9–125.1/100,000 inhabitants) and outbreaks were reported every 2–4 years. Since 2002, notifications have rapidly decreased, and in 2004 the lowest number of cases (2,604) was reported every 2–4 years. Since 2002, notifications have rapidly decreased, and in 2004 the lowest number of cases (2,604) was reported every 2–4 years. Since 2002, notifications have rapidly decreased. Nonetheless, recent epidemiological data show a decrease in mumps cases yet not an increase in the mean age of acquisition of infection, as already reported in other countries [32–35].

Comparison of seroprevalence data from 1996 and 2004 showed a statistically significant increase in seroprevalence only in the age class 2–4 years (41.2% vs. 64.4% in 1996 and 2004, respectively) [21]. This seems to be the result of the latest immunization campaigns; the efforts recently sustained in order to address the national plan for the elimination of measles and congenital rubella through vaccination have had a significant impact on seroprevalence data.

Of note is the finding that in this age class, as well as in the 5–9- and 10–14-year age classes, more than 20% of children were seronegative, and more than 10% of individuals 15–39 years of age were susceptible. These results demonstrate that VC in Italy is still sub-optimal and that there exists a risk of outbreaks. The lack of adequate vaccine data processing management in some Regions and the high rate of parents (18%) who intend to vaccinate their children at an undue age [17] could explain these observations and represent a critical point in planning further priority activities.

In conclusion, this research highlights that vaccination strategies and programmes should be further strengthened if the targets for primary vaccine failure and waning vaccine-induced immunity. J Infect Dis 2005;192:1078–82.

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