Mumps: A year of enhanced surveillance in Catalonia, Spain

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\textbf{A B S T R A C T}

Mumps is a vaccine-preventable disease candidate for elimination. Positive predictive value (PPV) of clinical case definition was assessed. During 2007, 410 suspected cases were reported in Catalonia: 348 fulfilled clinical case definition and 159 were laboratory confirmed. Incidence rate was 4.8 per 100,000 for cases that fulfilled the clinical definition, and 2.2 for laboratory confirmed cases. Global PPV was 44.5%; 38.5% in <15 years and 50% in \( \geq 15 \) years (\( p = 0.04 \)). Most laboratory confirmed cases (72.3%) received at least one MMR dose. With sustained high MMR coverage, laboratory confirmation is necessary to control the disease and assess vaccine failure.

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\textbf{1. Introduction}

Mumps is an acute infectious disease caused by a virus of the \textit{Paramyxoviridae} family. Although generally considered a benign childhood disease, complications are not uncommon in adolescents and adults \cite{1}. Mumps virus infection is asymptomatic in one-third of cases, mainly in children. The disease is characterised by enlargement of the parotid or other salivary glands, although orchitis, arthritis, pancreatitis, mastitis, oophoritis or meningitis can also occur. Humans are the only natural reservoir for the mumps virus and this, together with the availability of an effective vaccine, led the International Task Force for Disease Eradication to consider the disease potentially eradicable \cite{2}. Post-licensure studies showed that one dose of vaccine was effective in preventing clinical mumps, but outbreaks in schools with very high vaccine coverage of one dose of vaccine suggested this was not sufficient to prevent outbreaks. In Catalonia, a region in the northeast of Spain with more than 7 million inhabitants, one dose of the measles, mumps and rubella (MMR) vaccine at 12 months of age was introduced into the routine vaccination schedule in 1980. In 1987, the first dose shifted to 15 months of age and in 1988, a second dose of MMR was added at 11 years of age to replace the rubella vaccine administered to girls. In 1998, the second dose began to be administered at 4 years of age. This vaccination policy resulted in mumps incidence decreasing from 457 per 100,000 inhabitants in 1983 to 1.8 per 100,000 in 2006 (Fig. 1). This dramatic decrease encouraged the implementation of a program aimed at eliminating autochthonous mumps by the end of 2010, with enhanced disease surveillance by laboratory confirmation of clinically suspected cases being a key component of the program.

The objective of this study was to evaluate the results of the first year of enhanced surveillance of mumps in Catalonia and the sensitivity and positive predictive value (PPV) of the clinical case definition.

\textbf{2. Materials and methods}

Data were collected from the register of clinically suspected cases of mumps reported to the epidemiological surveillance units of the Department of Health of the Generalitat of Catalonia. The study period was 1 January to 31 December 2007. A clinical case was defined as acute onset of uni- or bilateral swelling of the parotid or other salivary glands for two or more days with no other apparent cause. The laboratory criteria for confirmation were detection of the viral genome by real time reverse transcription polymerase chain reaction (RT-PCR) in oral sample \cite{3}, positive serologic test for mumps immunoglobulin M (IgM) antibody or a significant rise between acute and convalescent phase titers in serum mumps immunoglobulin G (IgG) antibody level by enzyme immunoassay. A confirmed case was a case that was laboratory confirmed or a
case that met the clinical case definition and was epidemiologically linked to a laboratory confirmed or to a clinical case.

Reporting of mumps by physicians has been mandatory since 1982 in Catalonia, but reporting of full demographic and epidemiological data in all suspected cases is only mandatory since 1997. In the context of the Mumps Elimination Program, since 2007 all suspected cases must be reported to the Department of Health urgently (within 24 h of the suspicion) and support for laboratory confirmation was obtained.

Laboratory analyses were carried out by the microbiology laboratory of the Hospital Clinic of Barcelona.

The sensitivity of the clinical case definition was calculated as the proportion of confirmed cases (by laboratory or by epidemiological link) that met the clinical definition. Positive predictive value was calculated as the proportion of clinical compatible cases that were confirmed (by laboratory or by epidemiological link). For each case, an epidemiological form containing the following variables: age, clinical manifestations, complications, hospitalization and vaccination history, was completed.

Incidence rates were calculated using the estimated population of Catalonia for 2007. The 95% confidence intervals (CI) were calculated assuming a Poisson distribution. The CI of sensitivity and PPV were calculated by the exact binomial method. The $\chi^2$ and Fisher’s exact tests were used to determine statistically significant differences between proportions. The level of statistical significance was established at $\alpha = 0.05$.

### 3. Results

During the study period, 410 suspected cases of mumps were reported. Of these, 348 (84.9%) fulfilled the clinical case definition, 320 (78%) were laboratory tested, 159 (38.8%) were laboratory confirmed (74 by IgM detection, 70 by RT-PCR, 15 by RT-PCR and IgM), and 131 (32.9%) met the clinical case definition and were epidemiologically linked to another case. Complications were observed in 12 patients, including orchitis (11 cases) and meningitis (1 case), of which 10 cases of orchitis and the case of meningitis occurred in the <15 years age group. Four cases were hospitalized. No deaths occurred.

The global incidence rate was 4.8 per 100,000 (4.3–5.4) in the 348 cases that fulfilled the clinical case definition, 2.2 per 100,000 (1.9–2.6) in laboratory confirmed cases, and 4 per 100,000 (3.6–4.5) in any confirmed case (laboratory or epidemiological link). Highest incidence rates corresponded to 5–14 and 15–24 years for all categories of cases and the incidence of male was higher than the incidence of females (Table 1). A total of 72.3% of laboratory confirmed cases (91.7% in the 5–14 years age group) and 76.2% of all confirmed cases (95.5% in the 5–14 years age group) had received at least one MMR dose; 56% of laboratory confirmed cases and 55.5% of all confirmed cases, respectively, had received two doses.

The sensitivity and PPV of the clinical case definition are shown in Table 2. The sensitivity of laboratory confirmed cases, epidemiological confirmed cases and all confirmed cases were calculated as described above. The positive predictive value of the clinical case definition was also calculated for laboratory confirmed and all confirmed cases.

### Table 1
Incidence rates (per 100,000 population) of mumps. Catalonia, 2007.

<table>
<thead>
<tr>
<th>Age</th>
<th>Laboratory confirmed cases</th>
<th>All confirmed cases</th>
<th>Clinically compatible cases</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rate 95% CI</td>
<td>Rate 95% CI</td>
<td>Rate 95% CI</td>
</tr>
<tr>
<td>0–4 years</td>
<td>3.4 (1.8–5.7)</td>
<td>11.1 (8.0–15.0)</td>
<td>12.9 (9.6–17.0)</td>
</tr>
<tr>
<td>5–14 years</td>
<td>7.3 (5.3–9.7)</td>
<td>13.3 (10.8–16.4)</td>
<td>16.1 (13.2–19.5)</td>
</tr>
<tr>
<td>15–24 years</td>
<td>7.7 (5.9–9.9)</td>
<td>13.5 (11.0–16.3)</td>
<td>15.3 (12.7–18.3)</td>
</tr>
<tr>
<td>25–34 years</td>
<td>2.0 (1.9–2.6)</td>
<td>2.9 (2.0–3.9)</td>
<td>3.9 (2.9–5.1)</td>
</tr>
<tr>
<td>≥35 years</td>
<td>0.3 (0.2–0.5)</td>
<td>0.3 (0.5–0.7)</td>
<td>0.3 (0.6–0.9)</td>
</tr>
<tr>
<td>All ages</td>
<td>2.2 (1.9–2.6)</td>
<td>4.0 (3.6–4.5)</td>
<td>4.8 (4.3–5.4)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2.7 (2.2–3.2)</td>
<td>5.2 (4.4–6.0)</td>
<td>6.0 (5.3–6.9)</td>
</tr>
<tr>
<td>Female$^c$</td>
<td>1.8 (1.3–2.3)</td>
<td>2.9 (2.3–3.4)</td>
<td>3.6 (3.0–4.2)</td>
</tr>
</tbody>
</table>

a $p = 0.013$.
b $p = 0.0001$.
c Reference category.

### Table 2
Sensitivity and positive predictive value of mumps clinical definition.

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>Sensitivity % (95% CI)</th>
<th>Positive predictive value % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Laboratory confirmation</td>
<td>Epidemiological confirmation</td>
</tr>
<tr>
<td>&lt;15 years$^a$</td>
<td>177</td>
<td>98.4 (91.2–100)</td>
<td>95.1 (88.8–100)</td>
</tr>
<tr>
<td>≥15 years$^a$</td>
<td>231</td>
<td>96.9 (91.3–100)</td>
<td>100 (98.8–100)</td>
</tr>
<tr>
<td>All ages</td>
<td>410</td>
<td>97.5 (93.7–100)</td>
<td>96.9 (92.3–100)</td>
</tr>
</tbody>
</table>

a $p = 0.04$.
b $p = 0.01$.
c Reference category.
ologically linked cases without laboratory confirmation and all confirmed cases was 97.5%, 96.9% and 97.2%, respectively, with no significant differences between age groups. The PPV for the same categories was 44.5%, 36.5% and 81.0%, respectively, with significant differences between age being observed. The PPV increased with age in laboratory confirmed cases ($p = 0.04$), but was higher in children in epidemiologically linked cases without laboratory confirmation ($p = 0.01$).

4. Discussion

The incidence of reported cases fulfilling the clinical case definition (4.8 per 100,000 in 2007 vs. 1.8 in 2006) increased in the first year of enhanced mumps surveillance of mumps Catalonia. However, it is unclear if this increase is explained by changes in the surveillance system or if we are in an epidemic cycle. The incidence rate in laboratory confirmed cases was 2.2 per 100,000, similar to the reported rate in the United States in 2006 [4], but the incidence rate in all reported clinically compatible cases was more than twice as high. The incidence rate in all confirmed cases includes some cases epidemiologically related to other clinically compatible cases without laboratory confirmation and it is probable that some false cases are included. This reinforces the idea that, when the incidence of a disease is low, it is essential to use laboratory means to confirm cases. This recommendation is based on the fact that, when the incidence of a disease is low, it is essential to confirm the accuracy of the diagnosis. The PPV of confirmed cases was 97.5%, slightly higher than that reported by Guy et al. [14] and similar to that obtained by Vandermeulen et al. [12]. However, the PPV of 44.5% in the same laboratory confirmed cases was clearly higher than the 10% obtained in the study by Guy et al. [14].

In conclusion, our results show the importance of laboratory confirmation of suspected cases of mumps because, when a disease has a low incidence, as is the case of some vaccine-preventable diseases in countries with high vaccine coverages, the PPV of clinical diagnoses decreases. The availability of RT-PCR techniques for oral samples has been very useful during this first year of enhanced surveillance in Catalonia. All confirmed cases should be laboratory confirmed or, at least, be linked to a laboratory confirmed case. Achieving elimination of mumps requires assessment of the number and nature of vaccine failures and adjustment of vaccination policies according to the new information obtained.

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References


