Tetanus immunity among Italians born after the introduction of mandatory vaccination of children

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In Italy systematic mandatory tetanus immunization of children started in 1968. In a national sample of 241 young males born after 1968 the prevalence of non-immune subjects was 11.2% (5.5% in the North-Centre, 15.9% in the South-Islands; p < 0.02). Comparing these data with the corresponding figure obtained in a previous study of subjects born before 1968 a significant decrease (11.2% versus 32.6%; p < 0.01) is observed. The prevalence of non-immune subjects born after 1968 is significantly lower than that observed in subjects born before 1968 by geographical area as well as by area (urban/rural) of residence. These findings indicate that the introduction of compulsory tetanus vaccination for all newborns has favourably affected the immune status of younger Italian men. However, more efforts should still be addressed to decrease regional inequalities in the delivery of health care.

Keywords: Antitoxin; tetanus; seroepidemiology; vaccination

Vaccination of children with tetanus toxoid became mandatory in Italy in 1968. Before then regular immunization against tetanus applied only to military recruits (since 1940) and a few selected job categories with special occupational exposure such as farmers and livestock breeders (since 1963).

However, some regular immunization of children against tetanus already existed in Italy before 1968, as a consequence of individual general practitioners’ recommendations, and also because many children immunized against diphtheria, compulsory since 1940, were in fact vaccinated with a combined vaccine containing diphtheria and tetanus toxoids.

A seroepidemiological survey in a national sample of 4770 young males born between 1956 and 1963 has shown that about one-third of them were not protected. Prevalence of non-immune subjects was greater in the southern regions, in rural areas and among the older birth cohorts.

The aim of the present study was to evaluate immune status against tetanus in a national sample of young men, 18–22 years old, born after 1968 and to compare these results with those obtained in the previous study.

MATERIALS AND METHODS

Study population

The subjects, 241 young men, 18–22 years old, drafted into military service in January and February 1991, consecutively seen in an induction centre and coming from every geographical region of the country, were all included in the study. A standard precoded questionnaire was used to collect demographic information.

Sample size

In order to evidence a 15% reduction in the prevalence of non-immune subjects from the previous study, with χ = 0.05 and β = 0.90, a sample size of at least 200 subjects was required.

Laboratory test

Blood samples were drawn from all study subjects on the day they arrived at recruiting centre, before receiving repeated immunizations. Tetanus antitoxin was measured by an enzyme-linked immunosorbent assay and expressed as IU ml⁻¹ using as a reference a preparation of human tetanus immunoglobulin (HTIG) calibrated against the current International Standard for Tetanus antitoxin. Previous studies have shown that results obtained by this technique are well correlated with those found using the seroneutralization test in mice.
Statistical methods

Differences in proportions were estimated by the $\chi^2$ test. A value of $p < 0.05$ was considered to be significant.

RESULTS

The crude prevalence rates of antitoxin level by geographical region of residence are reported in Table 1. In total, 11.2% subjects did not show detectable antitoxin in their sera and therefore were considered to be non-immune. The prevalence of non-immune subjects was 5.5% in the North-Centre and 15.9% in the South-Islands ($p < 0.02$).

Comparing the results of the present study with the corresponding figure from the study of subjects born before 1968: a significant decrease in the prevalence of non-immune subjects is observed (11.2 versus 32.6%; $p < 0.01$). The proportion of subjects with a good protective level (0.10–4.99 IU ml$^{-1}$) increased remarkably (62.2 versus 35.2%; $p < 0.01$) (Table 2).

The proportion of non-immune subjects among those born after 1968 is significantly lower than that observed in subjects born before 1968 in all geographical regions (Table 3) as well as in area (urban/rural) of residence (Table 4).

**Table 1** Crude prevalence rates of immunological categories by region of residence

<table>
<thead>
<tr>
<th>Region of residence</th>
<th>Antitoxin levels (IU ml$^{-1}$)</th>
<th>No. tested</th>
<th>0</th>
<th>0.01-0.09</th>
<th>0.1-4.99</th>
<th>≥5</th>
</tr>
</thead>
<tbody>
<tr>
<td>North-Centre</td>
<td>109</td>
<td>n</td>
<td>6</td>
<td>5.5</td>
<td>67.0</td>
<td>24</td>
</tr>
<tr>
<td>South-Islands</td>
<td>132</td>
<td>21%</td>
<td>15.9</td>
<td>58.3</td>
<td>9.9</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>241</td>
<td>n</td>
<td>27</td>
<td>150</td>
<td>62.2</td>
<td>15.4</td>
</tr>
</tbody>
</table>

*By the $\chi^2$ test, $p < 0.02$

**Table 2** Crude prevalence rates of non-immune categories in subjects born after 1968 (present study) compared with those born before 1968 (Ref. 1)

<table>
<thead>
<tr>
<th>Antitoxin levels (IU ml$^{-1}$)</th>
<th>Subjects born after 1968 (total tested 241)</th>
<th>Subjects born before 1968 (total tested 4770)</th>
<th>n (%)</th>
<th>n (%)</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>27</td>
<td>158</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>0.01-0.09</td>
<td>27 (11.2)</td>
<td>1857 (32.6)</td>
<td>27</td>
<td>1189</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>0.10-4.99</td>
<td>150 (62.2)</td>
<td>1680 (35.2)</td>
<td>37</td>
<td>348</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>≥5</td>
<td>37 (15.4)</td>
<td>348 (7.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*By the $\chi^2$ test

**Table 3** Crude prevalence rates of non-immune subjects born after 1968 (present study) compared with those born before 1968 (Ref. 1) by region of residence

<table>
<thead>
<tr>
<th>Region of residence</th>
<th>Subjects born after 1968</th>
<th>Subjects born before 1968</th>
<th>n (%)</th>
<th>n (%)</th>
<th>$p^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>North-Centre</td>
<td>6/109 (5.5)</td>
<td>376/2137 (17.6)</td>
<td></td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>South-Islands</td>
<td>21/132 (15.9)</td>
<td>1177/2833 (44.7)</td>
<td></td>
<td>&lt;0.01</td>
<td></td>
</tr>
</tbody>
</table>

*By the $\chi^2$ test

In addition, while in the previous study the prevalence of non-immune subjects was higher in rural areas (46.0 versus 25.0%), in the present study differences are not observed (12.2 versus 11%) (Table 4).

DISCUSSION

These results refer to a cohort of men born after 1968 in whom vaccination coverage is as high as 90%. In this study just over 11% of sera contained no antibodies at all, while in the previous study of subjects born before 1968 about one-third of sera contained no antibodies.

The introduction of compulsory vaccination for all children in 1968 appears to have affected the immune status of the younger Italian generations. Moreover, although the transformation of Italian society from an agricultural to an industrial one after World War 2 contributed to a decrease of tetanus incidence, immunization has been the main tool for the decreasing morbidity observed over the last few decades in Italy.

Even so, prevalence of non-immune subjects amounts to 15.9% in the South-Islands and to 5.5% in the North-Centre ($p < 0.02$). These findings are in agreement with the results of a recent survey in the Naples area, where only 21.2% of the children attending a primary school had received a full course of tetanus vaccination. These data reflect differential North–South health-care delivery, as already shown in the previous study.

Despite reductions in inequality in the health sector in Italy over the last few decades, more efforts should still be addressed to decrease regional differences. This study concerns only male subjects who will be boosted at the time of military service. It should be stressed that the female population is more at risk and particular attention should be paid to it.

REFERENCES


