Immunity to tetanus, diphtheria and poliomyelitis in the adult population of Sweden in 1991

Margareta Böttiger, a Olle Gustavsson b and Åke Svensson c

**Background**

During 1990 and 1991 a survey of immunity was carried out in Sweden. The main purpose was to estimate the level of immunity to diphtheria, tetanus and polio in the adult population. In total, 4800 people, randomly selected according to a stratified, two-stage, sampling plan, were contacted and asked to contribute a blood sample. Of those selected, 70.6% gave a blood sample.

**Methods**

Estimates and confidence intervals of the proportion of the population with antibodies exceeding some titre was calculated. The population was divided according to sex, year of birth (five age groups) and residence (four regions).

**Results**

In age groups that were born after the introduction of childhood vaccination, >90% and 75–90% of people have demonstrable antibodies at a protective level against tetanus and diphtheria respectively. Those born earlier, especially women, are poorly protected with less than 50% having protective antibody levels for both tetanus and diphtheria. Differences between men and women were particularly seen in the age groups born between 1930 and 1950. Less than 5% of the Swedish population lacked the protective level antibodies against polio types 1, 2 and 3 respectively.

**Conclusions**

Vaccination against tetanus, which can be combined with vaccination against diphtheria, can be recommended especially to women born before 1950 and with no documented previous vaccination. The same recommendation can be given for men born before the 1930s. As regards poliomyelitis, general booster vaccination of the adult population does not appear to be necessary at present.

**Keywords**

Diphtheria, tetanus, poliomyelitis, serology, vaccination, immunity

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During 1990 and 1991, the National Bacteriological Laboratory in Sweden (SBL) (since then re-organized as the Swedish Institute for Infectious Disease Control) planned and carried out a new survey of immunity based on a random sample of the population. The main purpose was to estimate the level of immunity to diphtheria, tetanus and polio in the adult population. In this paper, the results and conclusions concerning particular infections are presented. The design, execution and the methods used to analyse the results of the survey are described in a separate article.1

The epidemiology of the three infections are different. All three infections are at present covered by the general childhood vaccination programme. However, only in the case of poliomyelitis has there been an effort to give the entire population protection by vaccination of adults. Swedish men have, since the 1940s, been given a tetanus vaccination during compulsory military service.

**Background**

**Tetanus in Sweden**

In contrast to the majority of diseases caused by microbes and against which vaccination affords protection, the possibility of eradicating the tetanus microbe is not practicable. The bacterium is ubiquitous, especially in the soil. Thus, we shall always have to depend upon vaccination to avoid tetanus.

The number of tetanus cases from 1920 to 1950 was estimated to be 50 to 100 per year.2 Thereafter the numbers declined gradually. From 1969 to 1985, on average, between three and four cases were reported per year. Analyses3,4 showed that the disease mainly affected older unvaccinated people. From 1986 to 1994, 12 cases were reported; eight of these in people born before 1920 and none had documented vaccination.
All tetanus vaccines used in Sweden were produced by the National Bacteriological Laboratory. The strength and composition have varied. Table 1 gives a survey of the D and T vaccine doses used.

Vaccinations were first performed in Sweden on military personnel during World War II. General vaccination of infants with a combined diphtheria-tetanus-pertussis vaccine (DTP) or only DT was introduced during the 1950s and was estimated to cover 97-99% of children by the end of the decade. All Swedish men have to do compulsory military service, with their first tour of duty at about the age of 20. Since the 1940s and until 1990, a tetanus vaccination (T or Td) has been given on this first tour. T-diphasic prophylaxis (T or Td) was a common routine after injuries up to the 1980s. Since 1990, such prophylaxis has been mainly recommended for the unvaccinated or the not fully vaccinated. Those who have received four doses are regarded as protected for 30 years.

**Diphtheria in Sweden**

During World War I, there were up to 40,000 cases of diphtheria in Sweden in a population of less than 6 million. In the 1920s and 1930s, the disease decreased drastically without any vaccination and at the end of 1930s only sporadic cases were seen. During World War II, the disease was introduced from Finland and led to the mass vaccination of children. In the following 30 years, diphtheria almost disappeared; a few imported cases were notified. In 1984–1986, smaller outbreaks occurred in Gothenburg on the west coast of Sweden and in Stockholm on the east coast. Since 1988, no cases of diphtheria have been reported in Sweden.

Only Swedish diphtheria toxoid vaccine prepared by the National Bacteriological Laboratory has been in use in Sweden. The vaccines have been composed as shown in Table 1. The first vaccine was prepared in the early 1940s and was given during the period 1943–1947 mainly to children under 15 years of age. About 60% were estimated to have participated with at least one injection. Between 1947 and 1952 there was no general vaccination programme. Diphtheria-tetanus toxoid (DT) and diphtheria-tetanus-pertussis vaccine (DTP) were successively introduced during the 1950s and from 1958 onwards it was estimated that all children were offered three doses of DTP or DT before the age of 12 months. The vaccination coverage was estimated to be up to 97–99%. From 1965 onwards an extra vaccine dose containing a minute dose of 0.5 Lf diphtheria toxoid (Td) was given to schoolchildren.

**Poliomyelitis in Sweden**

Poliomyelitis was formerly a severe disease in Sweden with the first outbreak reported in 1881. In the 1950s, before the vaccination era, morbidity was on the average, 17 per 100,000 inhabitants. The proportions of adults and children were equal. The natural immunity was lower than in any other country at that time. Between 1957 and 1962, up to two-thirds of the population were vaccinated. Since 1962, polio has been eliminated in Sweden. Only a few unvaccinated people have been afflicted. With one exception, all were infected abroad.

The circulation of polio in the population ceased simultaneously with the disease. Interest in immunity to poliomyelitis has again been activated by the World Health Organization's (WHO) declaration that it aims to eliminate the disease by the year 2000.

In 1957, inactivated poliovaccine (IPV) from Eli Lilly, USA, was distributed. From 1958 to 1988, IPV produced by the Swedish National Bacteriological Laboratory (NBL) was used. A long-term study of this vaccine was published in 1992. From 1988 to 1995, IPV imported from the Netherlands' national vaccine-producing institute (RIVM) was used. Since IPV confers immunity mainly by producing IgG-antibodies, i.e. humoral immunity, it is comparatively easy to carry out an evaluation of the immunity by sero-epidemiological studies. In contrast, the immunity evoked by live, attenuated, oral vaccine (OPV) depends partly on antibodies—which generally do not rise to very high levels—and partly on local, intestinal immunity. All experience shows that specific neutralizing antibodies in the blood protect against paralytic disease.

The population studied, with the exception of foreigners, has been vaccinated with IPV vaccine and almost all with the Swedish vaccine. Many foreigners—all children but also many adults—have received the vaccination or a booster in Sweden. The general vaccination schedule comprises three initial doses and one booster dose 4–5 years later. The age groups born between 1949 and 1959 that received the first and antigenically weak vaccine distributed in 1957–1959 have been offered a fifth dose since the 1970s.

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**Table 1 Antigen contents per dose of vaccines against tetanus and diphtheria in Sweden**

<table>
<thead>
<tr>
<th>Years</th>
<th>Diphtheria (Lf)</th>
<th>Tetanus (Lf)</th>
<th>Pertussis</th>
<th>Aluminum-phosphate</th>
<th>No. of doses</th>
<th>Age (year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basic</td>
<td>1943–1947</td>
<td>40–50</td>
<td>12–19</td>
<td>Y</td>
<td>1</td>
<td>1–15</td>
</tr>
<tr>
<td></td>
<td>1952–1962</td>
<td>12–15</td>
<td>5–10</td>
<td>Y</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>1962–1979</td>
<td>30</td>
<td>5–10</td>
<td>Y</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td></td>
<td>1979–1990</td>
<td>12.5–15</td>
<td>3.75</td>
<td>N</td>
<td>3</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Boosters</td>
<td>1965–1973</td>
<td>12.5</td>
<td>7.5</td>
<td>Y</td>
<td>1</td>
<td>7–8</td>
</tr>
<tr>
<td></td>
<td>1973–1986</td>
<td>0.5</td>
<td>3.75</td>
<td>Y</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>1987–1990</td>
<td>7.5</td>
<td>1.9</td>
<td>Y</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>Adults</td>
<td>1940–1942</td>
<td>3–11</td>
<td></td>
<td>Y</td>
<td>1</td>
<td>recruits</td>
</tr>
<tr>
<td></td>
<td>1942–1944</td>
<td>13–56</td>
<td></td>
<td>Y</td>
<td>1</td>
<td>recruits</td>
</tr>
<tr>
<td></td>
<td>1950–1956</td>
<td>10–15</td>
<td></td>
<td>Y</td>
<td>1</td>
<td>adults</td>
</tr>
<tr>
<td></td>
<td>1957–1961</td>
<td>0.5</td>
<td>7.5–1.0</td>
<td>Y</td>
<td>1</td>
<td>adults</td>
</tr>
<tr>
<td></td>
<td>1962–1990</td>
<td>0–0.5</td>
<td>3.75–7.5</td>
<td>Y</td>
<td>1</td>
<td>adults</td>
</tr>
</tbody>
</table>
As vaccination in Sweden makes us mainly dependent on serum antibodies, it is most important to check the antibody status at regular intervals. As the only nationwide study was undertaken over 20 years ago in 1968,\textsuperscript{19} it was high time to carry out a new one in the 1990s.

Material and Methods

Population studied

The reference population was people born before 1973 and entered in a parish register. In Sweden, all permanent residents are entered in a parish register, regardless of citizenship. The total number eligible for the survey was about 6 million.

Sampling plan

In total, 4800 people, randomly selected according to a stratified, two-stage, sampling plan, were contacted and asked to contribute a blood sample. In the first stage of the sample, a number of parishes were selected. In the second stage, a sample of 48 people was taken from each of the selected parishes. The sample is stratified in such a way that four people of each sex born before 1930, between 1931 and 1945 and between 1946 and 1955 and six born between 1956 and 1965 and between 1966 and 1972 were selected.

The survey was planned to give results regarding the proportion of the population that had antibodies exceeding some titre with a precision about ± 5%, when divided according to sex and year of birth (five age groups) or divided according to sex and geographical areas (four regions). The four geographical areas are referred to as Southern (S), Western (W), Central (C) and Northern (N) Sweden.

Statistical methods

In total, 3390 (70.6%) of the 4800 people selected gave a blood sample. The response rate differs considerably between ages and geographical areas. In analysing the results of the survey, we have treated non-participation as uninformative, i.e. we have postulated that non-response is due to chance and is not related to the presence or absence of antibodies in the blood. A comprehensive description of how the survey was planned and analysed is given in a special report.\textsuperscript{1}

Comparisons between immunity in different regions or between the sexes are made by comparing the estimates pair-wise with regard to their estimated precision. The results of these comparisons are represented by a division of the regions into homogeneous groups that consist of regions which cannot be shown to differ significantly. Homogeneity of the titre distributions for different age cohorts is tested by a $\chi^2$-test. Unless otherwise stated statistical significance is implied by a $P$-value $<$0.05.

Serological assays

Tetanus

As regards tetanus, for the first half of the samples, a combined, direct ELISA and a competitive inhibition ELISA were used, as described earlier.\textsuperscript{26,27} However, this method was very laborious. Thus, during the study a comparative evaluation was made between this ELISA method and the toxin-binding immune assay (ToBI).\textsuperscript{28} Comparisons and harmonization of both methods were successfully carried out and a change to the latter was made for the second half of the investigation. Both methods allowed a sensitivity level down to a concentration of 0.010–0.015 international units (IU)/ml which corresponds to the internationally accepted protection level. 0.01 IU/ml\textsuperscript{29}

Diphtheria

Diphtheria-antitoxin levels were determined by neutralization tests on Vero cell cultures in microplates.\textsuperscript{30–32} The challenge dose of the toxin was 100 cell-culture toxic doses. The titrations on microplates were carried out as follows: 75 µl of culture medium were added to each well followed by 25 µl of serum—each serum to two wells. Titrations were carried out in fourfold dilution steps from 1:4 in the first row up to 1:16 384. A serum standardized against the reference serum of the WHO was included in each test as a control. A dilution of the reference serum containing 0.01 IU/ml, i.e. the level which is considered to offer protection,\textsuperscript{33,34} corresponded in our test system to a neutralization of the toxin up to the dilution of 1:16. This level was used as the level affording protection.

Polio

For polio 25 µl of virus suspension (type 1 Mahoney, type 2 Mef 1 or type 3 Saukett) diluted to contain 10–50 CCH\textsubscript{50} was dropped into each well. Binding occurred at 37°C for 3 h. A cell suspension (100 µl) was added and the plates were incubated at 37°C. Virus controls were tested in tenfold dilutions, ten wells per dilution. Readings were carried out after 6 days by microscopic examination. The value of the 50% endpoint was used as the titre.\textsuperscript{19,25,35}

Results

Immunity to tetanus

The estimated proportions of men and women with acceptable immunity (0.01–0.015 IU) to tetanus are given in Table 2. In the

\begin{table}[h]
\centering
\caption{Immunity to tetanus by sex and year of birth. Estimates and 95\% confidence intervals (CI) and $P$-values for comparisons between men and women.}
\begin{tabular}{llll}
\hline
\textbf{Born during} & \textbf{Women} & \multicolumn{2}{c}{\textbf{Men}} \\
& Estimated & & \\
& proportion immune (%) & 95\% CI & Estimated & 95\% CI & $P$-value \\
& & & & & & \\
1966–1972 & 98.6 & (96.5–99.5) & 98.6 & (95.8–99.5) & ns \\
1956–1965 & 88.3 & (84.3–91.4) & 95.4 & (92.2–97.3) & 0.006 \\
1946–1955 & 51.5 & (47.5–59.4) & 89.9 & (84.9–93.4) & <0.001 \\
1931–1945 & 44.3 & (38.2–50.7) & 83.2 & (78.1–87.2) & <0.001 \\
\leq 1930 & 30.3 & (25.0–36.3) & 50.1 & (42.8–57.3) & <0.001 \\
All & 55.4 & (52.7–58.2) & 80.1 & (77.3–82.6) & <0.001 \\
\hline
\end{tabular}
\end{table}

\newpage
Table 3 Immunity to diphtheria by sex and year of birth. Estimates and 95% confidence intervals (CI) and P-values for comparisons between men and women

<table>
<thead>
<tr>
<th>Born during</th>
<th>Women</th>
<th>Men</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Estimated proportion immune (%)</td>
<td>95% CI</td>
</tr>
<tr>
<td>1966-1972</td>
<td>87.2 (82.5-90.7)</td>
<td></td>
</tr>
<tr>
<td>1956-1965</td>
<td>77.6 (73.0-81.7)</td>
<td></td>
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<tr>
<td>1946-1955</td>
<td>40.4 (34.9-46.1)</td>
<td></td>
</tr>
<tr>
<td>1931-1945</td>
<td>45.4 (39.4-51.6)</td>
<td></td>
</tr>
<tr>
<td>≤1930</td>
<td>25.8 (20.4-32.1)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>48.8 (45.9-51.7)</td>
<td></td>
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</tbody>
</table>

Age groups born after the introduction of general childhood vaccinations, which covered the whole country by the end of the 1950s, more than 85% of both men and women are protected. For those born earlier men are better protected than women. The proportion of protected women declines rapidly to under 50% among those born before 1945. Concerning the men, levels of over 80% were found in the age groups born between 1931 and 1936. Among the elderly both men and women are poorly protected. The main trends were similar in all parts of Sweden. The only significant difference found was that women in Western Sweden seem to have a higher percentage of protection than women in Central and Southern Sweden. No significant differences between regions were found for men.

Immunity to diphtheria

The estimated proportions of men and women in different age cohorts with an antibody level (i.e. >0.01 IU/ml, i.e. titre 1:16) are shown in Table 3. It is estimated that over 75% of those born after 1956 have satisfactory protection, irrespective of sex. However, for those born before 1955, the situation is different. For women born between 1931 and 1955, the percentage is about 40%, and for men, about 60%. In the oldest age cohorts, only about 25% of both men and women have satisfactory protection. The proportions protected of those who were not included in the child vaccination programme are significantly different between men and women for all but the oldest age group.

A closer examination shows that grouping according to year of birth as used in the planning of the study and in Table 3 hides some interesting patterns. It turns out that about 56% of the women born between 1932 and 1941 have satisfactory protection but only 33% of those born between 1942 and 1945. A similar but much smaller difference is observed for men. This is obviously due to the vaccinations given between 1943 and 1947 mentioned above.

Women in Western Sweden are protected to a greater extent than women in other regions. There also seem to be regional differences for men. A further division of the data which also takes age into account means dividing the sample into 48 distinct groups. The number of people in each group is small and the statistical variation becomes large. However, some significant differences are observed. Among the middle-aged and older population, those living in Western Sweden had comparatively better protection than those living in other parts. The population in the North had the lowest levels in this age group.

The proportions of men and women with titres exceeding different levels are shown in Figure 1. The threshold level for...
satisfactory protection used by us corresponds to the titre 1:16 (corresponding to the WHO protection level of 0.01 IU/ml). Interpolation between the titre levels 1:64 and 1:256 indicates that about 40% of men and 30% of women possess good protection according to the WHO standard (0.1 IU/ml, corresponding to the titre 1:160).

In Figures 2a and 2b, the distribution of titre levels for those having a measurable antibody level are given for men and women divided according to year of birth. There is a significant difference between the age groups both for men and women ($P < 0.001$).

**Immunity to poliomyelitis**

The percentages of men and women with demonstrable antibodies (i.e. titre $>1:4$) against the three types of polio, respectively, in different age groups are illustrated in Table 4. It is clear that the immunity to polio is high. In total, antibodies against the three types were present at the dilution $>1:4$ in over 95%
Table 4 Immunity to poliomyelitis by sex and year of birth. Estimates and 95% confidence intervals (CI) and P-values for comparisons between men and women

<table>
<thead>
<tr>
<th>Born during</th>
<th>Women</th>
<th>Estimated proportion immune (%)</th>
<th>95% CI</th>
<th>Men</th>
<th>Estimated proportion immune (%)</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
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<td>Type 1</td>
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<tr>
<td>1966–1972</td>
<td>99.6</td>
<td>(98.4–99.9)</td>
<td>98.8</td>
<td>(96.6–99.6)</td>
<td>n.s.</td>
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<tr>
<td>1956–1965</td>
<td>98.8</td>
<td>(97.0–99.5)</td>
<td>95.8</td>
<td>(92.7–97.6)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1946–1955</td>
<td>97.6</td>
<td>(95.0–98.9)</td>
<td>95.4</td>
<td>(92.2–97.4)</td>
<td>n.s.</td>
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<tr>
<td>1931–1945</td>
<td>99.1</td>
<td>(96.9–99.9)</td>
<td>95.9</td>
<td>(92.7–97.7)</td>
<td>0.03</td>
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<tr>
<td>&lt;1930</td>
<td>96.8</td>
<td>(94.2–98.2)</td>
<td>93.0</td>
<td>(89.0–95.6)</td>
<td>0.03</td>
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</tr>
<tr>
<td>All</td>
<td>98.1</td>
<td>(97.2–98.7)</td>
<td>95.4</td>
<td>(94.1–96.4)</td>
<td>&lt;0.001</td>
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<td>Type 2</td>
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<tr>
<td>1966–1972</td>
<td>99.7</td>
<td>(98.1–99.9)</td>
<td>99.7</td>
<td>(97.0–99.9)</td>
<td>n.s.</td>
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<tr>
<td>1956–1965</td>
<td>99.3</td>
<td>(98.1–99.7)</td>
<td>99.1</td>
<td>(97.5–99.7)</td>
<td>n.s.</td>
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<tr>
<td>1946–1955</td>
<td>99.6</td>
<td>(98.1–99.9)</td>
<td>99.6</td>
<td>(96.3–99.7)</td>
<td>n.s.</td>
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<td>1931–1945</td>
<td>99.7</td>
<td>(96.8–99.9)</td>
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<td>(92.5–97.6)</td>
<td>0.04</td>
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<tr>
<td>&lt;1930</td>
<td>96.5</td>
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<td>93.8</td>
<td>(89.6–96.4)</td>
<td>n.s.</td>
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<tr>
<td>All</td>
<td>98.5</td>
<td>(97.1–99.3)</td>
<td>97.1</td>
<td>(95.8–98.0)</td>
<td>n.s.</td>
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<tr>
<td>Type 3</td>
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<td>1966–1972</td>
<td>98.8</td>
<td>(97.0–99.5)</td>
<td>97.3</td>
<td>(94.2–98.8)</td>
<td>n.s.</td>
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<td>(94.9–98.8)</td>
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<td>1946–1955</td>
<td>95.5</td>
<td>(92.6–97.3)</td>
<td>89.7</td>
<td>(85.4–92.8)</td>
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<td>1931–1945</td>
<td>99.1</td>
<td>(97.0–99.7)</td>
<td>94.4</td>
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<td>0.01</td>
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<tr>
<td>&lt;1930</td>
<td>96.4</td>
<td>(93.7–98.1)</td>
<td>90.0</td>
<td>(84.1–93.9)</td>
<td>&lt;0.01</td>
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<tr>
<td>All</td>
<td>97.3</td>
<td>(96.2–98.1)</td>
<td>93.4</td>
<td>(91.6–94.7)</td>
<td>&lt;0.001</td>
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</tr>
</tbody>
</table>

of the samples. Women lacking immunity were 1.9% against type 1, 1.5% against type 2 and 2.7% against type 3. The corresponding proportions for men were 4.6%, 2.9%, and 6.6%, respectively. There are significant differences between men and women for types 1 and 2. As is seen in Table 4, these differences seem to relate to the oldest age cohorts.

The proportion of those immune is somewhat lower in the oldest age cohorts. However, it seems that people born between 1931 and 1945 are protected to a higher degree than those born between 1946 and 1955. The differences are in all cases relatively small, even though some of them are statistically significant. No differences could be found between people living in the four regions of Sweden.

The low titre sera were also tested in undiluted sera. The percentages totally lacking antibody activity were 1.6, 1.0 and 1.5%, respectively, for the three types of polio (both sexes).

The estimated proportion of women and men with a titre exceeding different levels are shown in Figures 3a and 3b. As has been experienced in most earlier studies, the type 2 antibody titres reach high levels and the type 1 titres in this study are also high, while the type 3 titres are slightly lower. The median values (i.e. the titre levels exceeded by 50% of the population) are approximately 1:256, 1:256 and 1:64, respectively.

A comparison between the age cohorts show that, among those with titres >1:4, there are significant differences (P < 0.001) for the three types of polio and for both sexes. Older people tend to have higher titre levels to different polio types when compared to the young.

Discussion

The immunity pattern to tetanus and diphtheria does not seem to be influenced by the variation in vaccine used.

Tetanus

Concerning the laboratory methods for determining immunity, it may be argued that one should not change method in the middle of a study. The old method turned out to be laborious and needed extensive counting. The problem of sera with low titres that had to be re-titrated and also controls not fitting in encouraged us to try the new, toxin-binding, inhibition test. This method turned out to be easier and as reliable, and therefore, after double checking of a number of samples at varying titre levels, we decided to use this method.

The young adults of both sexes who were born after the introduction of general childhood vaccinations, i.e. those born at the end of the 1950s and later, are well protected. The wide gap between the sexes in the oldest age groups can probably be explained by at least two factors. The majority of men were vaccinated during military service since the World War II and boys and men have been more exposed to injuries which have led to prophylactic vaccinations.

A number of studies confirm the dose association between vaccination coverage and immunity and poor immunity in the older population. However, people who have not had the recommended primary vaccination comprising three doses may still retain their immunological memory for long periods and react with a rapid booster response when challenged.
**Figure 3a** Immunity to poliomyelitis. Estimated proportion of women with titres exceeding different levels

**Figure 3b** Immunity to poliomyelitis. Estimated proportion of men with titres exceeding different levels

**Diphtheria**

Immunity at the 0.01 IU level in young adults up to 30 years of age, i.e. those born in 1960 and later, is 75% or higher. In those born in 1930 or earlier, this level was reached by less than 30%. Noticeable is the comparatively high immunity among those born between 1932 and 1941. These age groups were offered vaccination with one to three doses during World War II. The phenomenon was also observed in an earlier study. This finding and the high immunity in the vaccinated younger generation born after 1960 indicates a close correlation between vaccination and immunity. It also seems that those born before 1920 have protection to a somewhat greater extent than those born during the 1920s. Such a difference may be explained by natural immunity acquired by the oldest who were born at a time when diphtheria was prevalent.

A comparison between men and women shows a consistently better general immunity among men than among women. The majority of men had received an extra booster (Td) during military service, although this dose was very small (0.5 Lf). The difference between the sexes is most apparent in the age groups born in 1931–1955. One small exception is the oldest women in the western part of Sweden. A diphtheria outbreak
in Gothenburg in 1984 led to mass vaccination, in particular of many middle-aged and elderly women.

In spite of the low general immunity in the population born before general childhood vaccinations were introduced, diphtheria did not spread widely when it was introduced in the 1980s. It mainly hit the socially deprived with reduced immune defences. It is evident both from old and recent experiences that the combination of a lack of specific immunity and poor living standards is necessary for a widespread epidemic. However, a few, quite healthy, isolated cases such as hospital personnel exposed to a high dose of diphtheria, also contracted the disease during the 1985 epidemic.

This study was timely—it was carried out just before it became obvious, in 1993, that diphtheria had spread and become a great problem in the former Soviet Union, especially in the area of St Petersburg. Knowledge of actual immunity to the disease in the Swedish population has become of great value and formed a basis for our evaluations of the adult population at risk of contracting diphtheria in Sweden.

**Polioimmunity**

The last, nationwide, sero-epidemiological study of polio—but with a different kind of sampling—in 1968 showed that the population of Sweden had protective antibodies in close to 100%, except in those age groups born at the end of the 1940s up to the end of the 1950s. The 1968 study and a supplementary study indicated that over 25% of recruits born in the 1950s lacked antibodies to polio type 3 and 10% to type 1. The above-mentioned age groups were informed over a 10-year period about the situation and offered a free booster vaccination. The remaining, slightly lower, antibody prevalence among males born in the period 1946–1955, i.e. 10% lacked the stated immunity level to type 3, indicates that perhaps not all and particularly men were reached by the booster campaign.

On the whole, however, the immunity status of the population must be regarded as very satisfactory. The majority of those whose vaccination immunity is lower than the stated level of 1:4 may still possess immunological memory, as was shown in a previous special study. The antibody-titre levels showed a pattern similar to that in earlier studies. The median titres were highest against type 2 and lowest against type 3. In this survey, the type 1 and type 2 antibody distributions are remarkably similar, with a median titre around 1:256, while the type 3 median titre, as in earlier studies, is lower, i.e. almost 1:64. Apparently even this level of type 3 immunity has been protective in Sweden, as we were not affected by the outbreak in Finland in the 1980s, in spite of the close connections between the two countries. It is furthermore of Interest, in this context, to discuss the importance of different variants of poliovirus type 3. Experience tells us that the type 3 poliovirus is more mutagenic than the other types.

The Saukett strain which is used as seed virus in the vaccine was isolated in the 1940s in the USA. Serum from Saukett-vaccinated children neutralized the epidemic type 3 strain isolated in Sweden in 1957 five times less efficiently than the Saukett strain. The type 3 strain that caused the Finnish outbreak was, in our tests, four times less efficient. We have thus also to take into consideration these antigenic variations in evaluating the immunity.

In contrast to immunity to diphtheria and tetanus, no geographical differences were seen as far as polio immunity was concerned and only small differences were seen between age groups. The explanation of this may be that, in contrast to the two vaccinations against diphtheria and tetanus, the polio vaccination was offered to and also reached the majority of the population, and not only children. The adult population, the majority of whom were already naturally immune, thus to a large extent received an effective booster with this killed vaccine. In people already possessing some naturally induced immunity, a potent, killed vaccine gives rise to a better antibody response than administration of an oral, attenuated, vaccine virus, which does not multiply effectively in naturally immune people. Older people actually had slightly higher antibody titres than the young.

In this study immigrants now settled in Sweden appeared to be as well protected as Swedes. Many of them would have been offered vaccination on entering the country, but the majority of those coming from developing countries are likely to be naturally immune. As many return to visit their native countries it must be wise to be extra cautious and recommend at least one booster.

It should be pointed out here, too, that up to the end of the 1980s so-called enhanced poliovaccine was not used in Sweden. The results presented were achieved with an ordinary, unconcentrated vaccine containing originally, before formalin treatment, about 10 million (10^7) cell-culture infectious doses per millilitre. With the enhanced vaccine, the effect can be expected to be even better. A further improvement would be to give the fourth dose a little later than at the age of 6, as is the rule in Sweden. A booster at the age of 10 improved the immune response. A booster as late as possible, when one can still reach all children, would, from the immunological point of view, be the most effective for long-term protection.

**Conclusions**

People who were born after the general childhood vaccinations were introduced are satisfactorily protected against tetanus and diphtheria. Those born before this era—especially women—are less well protected; over 50% of older women lack protective antibody levels.

Older people who do not have a documented vaccination against tetanus should be encouraged to have themselves vaccinated. Documentation of vaccination should be promoted. Older people—especially those who come into contact with the soil, i.e. who work in agriculture, forestry and gardening—should be made aware of the risks.

The unvaccinated, healthy population runs a small risk of contracting diphtheria while staying in Sweden or visiting similar countries. However, it is advisable that everyone, irrespective of age and sex, should have a documented, valid vaccination, especially those running an increased risk, such as the socially deprived, those exposed professionally or people who travel to areas where the disease is endemic.

In Sweden, and very likely also in other countries with no epidemic diphtheria, the outcome of sero-epidemiological studies is directly correlated to the vaccination status of the population. Knowledge of the sero-epidemiology is therefore a useful tool for vaccination policy-makers.

The WHO is now in a very active phase in its endeavour to hit the target of eliminating poliomyelitis and the virus causing
it by the year 2000. In evaluating the feasibility of success, many factors have to be taken into consideration, such as the absence of disease and circulating virus. One of the background factors to be taken into consideration is the immunity, as measured by the prevalence of neutralizing antibodies in the population. It is thus important that such studies should be carried out elsewhere. As regards Europe, favourable results of immunity studies have recently been reported. Thus, in Germany the prevalence of immunity was over 90% to types 1 and 2 and 80% against type 3. In north-eastern Italy, the corresponding figures were over 98% to all three types. In the industrialized parts of Europe, the majority of the reports are favourable, with the exception of concern about type 3 immunity in some areas. The Americas have already declared that polio has been eliminated.

References


