Immunogenicity of oral poliomyelitis vaccine (OPV) against variants of wild poliovirus type 3

B. Böthing,¹ L. Danes,² & S. Dittmann¹

Serological investigations of three groups of children from the German Democratic Republic (GDR) and from Czechoslovakia who had different immunization histories against poliomyelitis indicated that the immunity induced by oral poliovaccine (OPV) is effective against both the wild poliovirus Saukett strain and a new wild variant of poliovirus type 3 that was isolated during an outbreak of poliomyelitis in Finland in 1984. There is therefore no obvious risk that individuals in the GDR or Czechoslovakia, most of whom have been immunized with OPV, are threatened by new wild poliovirus variants. These findings are of importance, especially in connection with WHO's initiative for the global eradication of poliomyelitis by the year 2000.

Introduction

After 20 years' absence of poliomyelitis in Finland, an outbreak of the disease was reported in the country in 1984 (1, 2). In view of the high vaccination coverage—more than 90% of children had been immunized with inactivated poliomyelitis vaccine (IPV)—this outbreak, which was caused by poliovirus type 3, was surprising (3). Additional proof of the wide distribution of wild poliovirus type 3 throughout the country was established by isolating the virus from the wastewater of several towns (3).

Serological investigations showed that individuals under 19 years of age had lower antibody titres against the epidemic poliovirus strain compared with those against the Saukett reference strain of the virus, which is a component of IPV (3). Similar results were found by Magrath et al. (4), who examined sera from Finns, Norwegians, and Swedes who had been administered IPV. The geometric mean antibody titre of the Finnish sera against the Saukett strain was 1:25, but only 1:4 against the Finnish wild virus isolate (P3/Finland/23127/84).

Animal experiments revealed that the isolate of poliovirus type 3 from Finland exhibited strong antigenic variance; immune sera against the purified D antigen of this strain neutralized the homologous virus, but not the Saukett strain or the vaccine strain (Leon 12 a, b) of OPV. In contrast, an immune serum of the Sabin strain neutralized both the homologous virus and the Saukett strain, but only to a limited extent the P3/Finland/23127/84 isolate (4).

We therefore investigated whether the immunity induced by OPV provides adequate protection against the antigenically modified new Finnish wild poliovirus type 3 strain in the populations of the German Democratic Republic (GDR) and Czechoslovakia. In both countries oral poliovaccine (Sabin) strains are used. This vaccine is produced in bulk in the Institute of Poliomyelitis and Viral Encephalitis, Moscow, USSR. No poliomyelitis cases caused by wild virus strains and no circulation of wild polioviruses have been observed in the GDR or Czechoslovakia for more than 20 years.

Materials and methods

Serum samples

Group 1: sera from 155 children (GDR) aged 2–14 months who each received consecutively (at 4-week intervals) one dose of monovalent OPV (100,000 plaque-forming units (PFU) per dose) of type 1, type 2, and type 3.

Group 2: sera from 102 children (GDR) aged 9–16 years, who received the same dose of monovalent OPV (type 1, type 2, and type 3) as the children in group 1 plus two additional trivalent (3 x 100,000 PFU per dose) booster doses in their second and eighth years of life.

Group 3: sera from 76 Czechoslovakian children aged 12–23 months, who received OPV type 1, as monovalent vaccine, and type 2 and 3, as bivalent vaccine. One year later about 30% of these children were revaccinated with the same vaccines. Children aged less than 6 months received 500,000 PFU per dose of type 1 and type 2 vaccines and 1 million PFU per dose of type 3 vaccine; children aged greater than

¹ Central Institute for Hygiene, Microbiology and Epidemiology, Britzer Strasse 1–3, DDR-1190 Berlin (East), German Democratic Republic. Requests for reprints should be sent to Professor Dittmann at this address.

² Institute for Hygiene and Epidemiology, Prague 100 42, Czechoslovakia.
6 months received 100,000 PFU per dose of type 2 and type 3 and 200,000 PFU per dose of type 3 vaccine.

**Antibody determinations**

Antibody determinations were carried out in laboratories in Berlin (East) and Prague using the microneutralization test with 100 TCD<sub>50</sub> of the Leon 12a,b (Sabin), Saukett, and P3/Finland/23127/84 strains of poliovirus type 3 in both laboratories. In Berlin (East), RD cell cultures were used, and readings were taken on the fifth day; while in Prague, BGM cell cultures were used and readings were made on the third day.

**Results**

Table 1 shows the proportion of children who had antibody titres ≥ 1:4 against the Saukett, P3/Finland/23127/84, and Leon 12a,b strains of poliovirus type 3.

The proportion of children who were antibody-positive against the Leon 12a,b strain, i.e., against the homologous virus strain after oral vaccination, was a little greater than the proportion of children who had antibodies against the two wild virus strains. In contrast, there was no significant difference between the proportion of children with antibodies against the Saukett and P3/Finland/23127/84 wild viruses in all three groups.

Fig. 1 and 2 show the antibody titres against the Saukett and P3/Finland/23127/84 strains for groups 2 and 3, respectively. These plots indicate that the titres against these two wild virus variants were similar and that there was no tendency towards a lower immunity against one or other of these strains.

For all three groups the geometric mean titres against the Leon 12a,b strain also were slightly higher, but the difference between the titres for the two wild virus strains was not significant (Table 2).

**Discussion**

Using monoclonal antibodies, Huovilainen et al. (5) established that the Finnish isolates of wild poliovirus type 3 exhibited clear antigenic differences compared with the strains used in IPV or OPV. The viruses isolated during the outbreak displayed considerable heterogeneity, indicating that antigenic evolution of type 3 had occurred under natural conditions.

Through the use of oligonucleotide mapping procedures and monoclonal antibodies, Magrath et al. (4) confirmed that the Finnish wild virus isolates

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**Table 1: Proportion of children with antibodies against the three strains of poliovirus type 3 tested in the study**

<table>
<thead>
<tr>
<th>Poliovaccines received</th>
<th>% with antibody titres ≥ 1:4 against:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Saukett</td>
</tr>
<tr>
<td>Group 1</td>
<td></td>
</tr>
<tr>
<td>(n=185)*</td>
<td>Monovalent type 3</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
</tr>
<tr>
<td>(n=102)*</td>
<td>Monovalent type 3 + two doses trivalent</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
</tr>
<tr>
<td>(n=76)*</td>
<td>Bivalent type 2 + type 3</td>
</tr>
</tbody>
</table>

* 2–14-month-olds from the German Democratic Republic.
† 9–16-year-olds from the German Democratic Republic.
‡ 12–23-month-olds from Czechoslovakia.
Immunogenicity of OPV against wild poliovirus type 3 variants

Fig. 2. Plots showing antibody titres against the Saukett and P3/Finland/23127/84 strains in children immunized once with bivalent type 2 and type 3 OPV (group 3).

Table 2: Geometric mean titres against the three strains of poliovirus type 3 tested in the study

<table>
<thead>
<tr>
<th></th>
<th>Saukett P3/Finland/23127/84</th>
<th>Leon 12a,b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (n=156)*</td>
<td>1:8</td>
<td>1:11</td>
</tr>
<tr>
<td>Group 2 (n=102)*</td>
<td>1:9</td>
<td>1:13</td>
</tr>
<tr>
<td>Group 3 (n=78)*</td>
<td>1:8</td>
<td>1:15</td>
</tr>
</tbody>
</table>

* 2-14-month-olds from the German Democratic Republic.
* 9-15-year-olds from the German Democratic Republic
* 12-23-month-olds from Czechoslovakia.

were not related to the vaccine virus strains and that they were antigenically unusual type-3 variants.

Sequence analyses of the nucleotides of the region coding for the VP1 and amino acid sequence analyses (4-6) revealed that 3 of the 12 amino acids of the VP1 region are exchanged in the Finnish strain (4-6)

Investigations with monoclonal antibodies also led Guo et al. (7) to conclude that the Finnish wild virus differs markedly from other strains of poliovirus type 3. These workers suggested that the protection effects of IPV and OPV also against such antigenic variants should be tested.

The results of our study of three groups of children from two countries with different immunization schedules and histories were intended to determine whether the immunity induced by OPV gives protection against antigenically modified wild type 3 polioviruses. The results obtained using the Saukett and P3/Finland/23127/84 wild poliovirus strains showed that the immunity induced by OPV is sufficient for effective prevention also of poliomyelitis caused by modified wild strains.

Our investigation of immunity against variants of poliovirus wild strains in children who had received OPV suggests that there is little cause for concern. This is particularly reassuring, since in May 1988 the 41st World Health Assembly committed WHO to the global eradication of poliomyelitis by the year 2000.

Acknowledgements

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Résumé

Immunogénicité du vaccin antipoliomyélitique buccal (VPO) à l’égard des virus sauvages de type 3

Grâce à l’analyse séquentielle des nucléotides et aux anticorps monoclonaux, différents chercheurs ont établi que la souche de poliovirus de type 3 isolée lors d’une épidémie de poliomyélite en Finlande en 1984 présentait des différences antigéniques avec les souches de type 3 utilisées pour préparer le vaccin inactif (VPI) et le vaccin buccal (VPO). Ils ont décrit la souche P3/Finland/23127/84 comme une variante du virus de type 3 présentant des caractéristiques antigéniques inhabituelles. Chez les enfants vaccinés avec le VPI, les analyses sérologiques ont montré que le titre des anticorps dirigés contre la souche responsable de l’épidémie était plus faible que celui des anticorps dirigés contre la souche Saukett de référence utilisée pour préparer le vaccin.

Nous avons donc entrepris en République démocratique allemande et en Tchécoslovaquie une étude collective sur des enfants vaccinés avec le VPO, afin de déterminer leurs titres en anticorps dirigés contre les souches de type 3 suivantes: la souche Leon 12 a,b, la souche Saukett et la nouvelle variante finlandaise.

L’étude a porté sur trois groupes d’enfants...
vaccinés selon des modalités différentes. Le premier groupe n’avait reçu qu’une dose de vaccin monovalent de type 1, 2 ou 3; les deux autres groupes avaient en outre reçu respectivement deux doses de rappel de vaccin trivalent et une dose de vaccin bivalent préparé à partir de souches de types 2 et 3.

Le titre d’anticorps circulants dirigés contre la souche virale utilisée pour la vaccination a été plus élevé dans les trois groupes, mais aucune différence significative n’a été notée en ce qui concerne l’immunité à l’égard des deux variantes sauvages. Les résultats de cette étude sérologique montrent qu’il n’y a manifestement aucun risque de voir de nouvelles variantes de virus venir à bout de la défense immunitaire induite par le VPO.

References


