Booster effect of Sabin poliomyelitis vaccine*

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Studies were carried out on 86 children aged 1–14 years who had titres of antibodies against poliovirus type 3 lower than 1 : 32 and against type 2 higher than 1 : 4. After a booster dose of poliomyelitis vaccine type 2+3, seroconversion took place in 44 (90%) of 49 children whose original titre was lower than 1 : 4 and the geometrical mean titre increased to 1 : 244. Of 37 children with low original titres of antibodies against type 3, i.e., 1 : 4, 1 : 8, or 1 : 16, the titre increased fourfold or more in 31 (84%) and the geometrical mean titre rose to 1 : 175. In 11 children (13%), no significant increase in titre took place.

Czechoslovakia was one of the first countries in the world to introduce compulsory vaccination with live attenuated poliomyelitis vaccine. Vaccination started in 1960 (*5*) and since that time it has been carried out each spring. Every child is vaccinated in the first year of life with two doses of poliomyelitis vaccine, first with type 1 and within 6 weeks with types 2+3. In the second year, the child is revaccinated to produce a booster effect, since 5–10% of children vaccinated in the first year of life do not develop sufficient antibodies (*3*).

The results of vaccination have been regularly reviewed by immunological surveys and remain satisfactory as regards seroconversion. In 1974, for example, antibody titres of at least 1 : 4 were found in 95% (type 1), 94% (type 2), and 75% (type 3) of vaccinees after the first vaccination, and in almost 100% (all three types) after revaccination in the second year. A titre of 1 : 4 was regarded as the lowest positive value (*4*).

When, however, immunological surveys are analysed in detail, individuals are always found who, although they have received the full course of vaccination, have no antibodies at all, usually against poliovirus type 3, or have low titres only. In the present study, an attempt was made to determine the possibility of stimulating antibody production in these individuals by means of a third course of vaccination with live poliomyelitis vaccine. The study was carried out in 1975 when there were few wild polioviruses circulating in Czechoslovakia and therefor little possibility of natural reinfection.

There have been several studies on the booster effect in immunization against poliomyelitis and such effects have recently been demonstrated, both with inactivated (*1*) and oral poliomyelitis vaccine (*2*), in persons previously vaccinated with an inactivated vaccine.

MATERIALS AND METHODS

Of 2013 persons aged 1–39 years examined, only those who had previously been vaccinated exclusively with the live attenuated vaccine were selected; this group consisted of 1829 persons aged 1–14 years. Attention was focused on poliovirus type 3, which provoked a lower antibody response. From this population, negative individuals and those with low positive titres of 1 : 4, 1 : 8, and 1 : 16 were selected; to ensure that only vaccinated persons were studied, those with a negative titre of antibodies against type 2, i.e., a titre lower than 1 : 4, were excluded. Thus, a group of 245 persons was obtained; however, only 86 children of that group came forward to give blood. All these children, half of whom came from Prague, were revaccinated with live poliomyelitis vaccine during nationwide vaccination in the spring of 1975 and blood samples were taken 5–6 weeks later. The 86 sera were examined for the presence of antibodies against poliomyelitis by means of the routine seroneutralization pH test, with fourfold serum dilutions from 1 : 4 to 1 : 1024. The sera were mixed with virus and incubated for 6 h at 37°C and for 12 h at 4°C. Monkey kidney cells were then added and the test was read after 5 days.

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Table 1. Number of children in Group A by age distribution and number in Group B by age distribution and lapse of time from the end of the first course of vaccination

Year of birth	Group A	Group B															Total
		Time from first course of vaccination (years)															
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	
1973	22		4														4
1972	1			6													6
1971					3												3
1970		1			1	3											5
1969			1			1	7										9
1968						1	1	1									3
1967									2								2
1966	1							1	1	1							3
1965									2		1						3
1964	1											2					2
1963	1												2				2
1962												2		2			4
1961													1	1	2		4
1960														3		1	4
1959						1									1	4	6
		1	5	6	4	6	8	2	5	1	1	4	3	6	3	5	
Total	26	12			18			16						14			60

The population was divided into two groups according to vaccination history: Group A consisted of 26 persons vaccinated " incompletely ", i.e., once only with type 1 and a mixture of types 2 and 3; Group B comprised 60 persons vaccinated " completely ", i.e., with type 1 and the mixture of types 2 and 3 in 2 successive years.

RESULTS

The age distribution of the selected children and the time that had elapsed from the end of the first course of vaccination against poliomyelitis are shown in Table 1. It can be seen that most children in Group A had been born in 1973 and therefore could not have received the complete course of vaccination. In Group B, the first vaccination had been performed in the first 2–3 years of life; only three children were older than this when the first vaccination was carried out.

More detailed information is given in Table 2, which shows the distribution of antibodies against type 3 within 6 weeks after the application of a booster dose. It may be seen that in all groups under examination (Group B was divided into four subgroups according to the lapse of time from the first vaccination), the antibody titre increased considerably in 83–100% of those vaccinated. The mean titre caused by the booster dose in Group A was 1 : 320 and that in Group B was 1 : 133; these two values are significantly different at the 5% level of significance.

The effect of the original antibody titre on the increase in titre after the booster dose is shown in Table 3. The difference in mean titre between those whose original titre was lower than 1 : 4 and those with an original titre of 1 : 4–1 : 16 was statistically significant. There was no significant increase in antibody titre in 11 children, of whom five were originally negative and six had original titres of 1 : 4–1 : 16.

Table 2. Number of children by group and by titre of type 3 antibodies after a booster dose of type 2+3 vaccine

Group	Titre of type 3 antibodies												Positive titres		Geometric mean titre
	<4	4	8	16	32	64	128	256	512	1024	>1024	total	No.	%	
A	1			1	2	1	8		4	3	6	26	25	96	320
B															
1–3 years	2	1			1			2	3	3		12	10	83	256
4–6 years	1		2		3		2	1	8		1	18	17	94	170
7–12 years	1	1		3	3		4		2	1	1	16	15	94	84
13–15 years				2	5		3		2	1	1	14	14	100	100
total B	4	2	2	5	12		9	3	15	5	3	60	56	93	133
Total A + B	5	2	2	6	14	1	17	3	19	8	9	86	81	94	

Table 3. Effect of original titre on increase in titre after booster dose of type 2+3 vaccine

Original titre	No. of sera tested	Sera in which titre increased		Geometric mean titre
		No.	%	
<1:4	49	44	89.8	244
1:4–1:16	37	31	83.8	175
total	86	75	87.2	213

DISCUSSION

In the present paper we have tried to ascertain to what degree individuals vaccinated against poliomyelitis, especially those who possessed low antibody levels against serological type 3, would react to further doses of vaccine. The system in Czechoslovakia of repeating vaccination in the second year of life made it possible not only to detect individuals who for various reasons did not develop antibodies after the first vaccination, but also to reveal increases in the levels of antibodies already formed. It is generally recognized that antibody levels against type 3 poliovirus found in regularly examined populations are lower than those of types 1 and 2, apart from the lower antigenicity of the Sabin type 3 vaccine strain already mentioned. The results of our study confirmed the fact that the third dose of the combined type 2+3 poliomyelitis vaccine provoked significant increases in antibody levels in vaccinated individuals who had either low initial antibody levels or were negative. Although not every increase in specific antibodies may be taken as a booster effect, we presume that the dose applied to the individuals under observation did provoke a secondary immune response acting as a booster effect.

The excellent results of vaccination against poliomyelitis have greatly reduced the importance of the disease. Given this situation, one may ask why we are still devoting attention to these problems when, moreover, the results of regular immunological surveys have shown satisfactory levels of antibodies against all three types of poliovirus in all age groups (the level of seropositivity being 75–100%). The reason is that the circulation of wild polioviruses in our population has been low for more than 15 years and the favourable effect of repeated contact with infection in a considerable part of our population has been completely lost. At the same time, there is as yet no comparable immunological situation anywhere in the world. We have repeatedly observed that the percentage of unvaccinated children varies considerably in different districts. Further disregard of the problem might be, in future, a dangerous source of infection, especially in regions where contact with foreign visitors is more likely. Our material, though limited, clearly shows that the health services are able to deal with such situations most effectively by means of booster doses of oral poliomyelitis vaccine.

RÉSUMÉ

EFFET DE RAPPEL DU VACCIN ANTIPOLIOMYÉLITIQUE SABIN

L'objectif des études relatées dans le présent article était de vérifier dans quelle mesure il est possible de provoquer un effet de rappel par une nouvelle vaccination chez des personnes antérieurement vaccinées contre la poliomyélite. En Tchécoslovaquie, la vaccination antipoliomyélitique est pratiquée au cours de la première et de la deuxième année de la vie: au printemps (généralement au mois de mars), les enfants reçoivent du vaccin antipoliomyélitique de type 1 (buccal) et six semaines plus tard du vaccin des types 2 + 3. L'étude a été axée sur une population d'enfants de 1 à 14 ans vaccinés exclusivement avec du vaccin Sabin, et en particulier sur les sujets qui, après la vaccination, avaient des titres d'anticorps faibles ou non mesurables contre le type 3 de poliovirus.

Les études ont porté sur une population de 86 enfants âgés de 1 à 14 ans dont une enquête immunologique effectuée en 1974 avait révélé qu'ils possédaient des titres d'anticorps inférieurs à 1 : 32 à l'égard du type 3 et à 1 : 4 à l'égard du type 2. Après la dose de rappel, sur 49 enfants ayant un titre initial inférieur à 1 : 4, on a observé une séroconversion chez 90%, le titre moyen géométrique étant passé à 1 : 244. Parmi les enfants ayant de faibles titres d'anticorps (c'est-à-dire 1 : 4, 1 : 8 ou 1 : 16) contre le type 3, on a noté une augmentation de quatre fois ou plus chez 84%; le titre moyen géométrique étant de 1 : 175. Chez 11 enfants (13 %) il n'y a eu aucune augmentation notable du titre.

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