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A Controlled Field Trial of the Typhoid Component of Polyvalent Enteric Vaccine (NIISI Polyvaccine)*

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At the request of the Ministry of Health of the USSR, a controlled field trial of a polyvaccine containing typhoid, paratyphoid and dysentery antigens and a purified tetanus toxoid was undertaken in 1958. The main object of this trial, which was carried out over a 10-month period simultaneously in four localities, was to determine the efficacy of the typhoid component of the polyvaccine.

The study population comprised over 90 000 individuals of 16-60 years of age. These were divided into two approximately equal groups, one of which received an injection of the polyvaccine under test and the other an injection of a preparation containing only the purified tetanus toxoid.

The difference between the incidence of typhoid fever in the test group and that in the control group during the study period was statistically significant, and it was therefore concluded that a single injection of the polyvaccine afforded some protection against typhoid.

The polyvalent enteric vaccine "NIISI", developed in 1941 (Gefen, 1943; Alexandrov & Gefen, 1957) and subsequently widely used in the Soviet Union for the vaccination of the adult population, has been considerably improved at the Metchnikov Institute of Vaccines and Sera, Moscow. NIISI polyvaccine contains the complete antigens of *Salmonella typhi abdominalis*, *Salm. paratyphi* A, *Salm. paratyphi* B, *Shigella flexneri*, *Sh. sonnei* and *Vibrio cholerae*, as well as a purified tetanus toxoid. The antigens are extracted from broth cultures grown under conditions of deep aeration according to the method of Raistrick & Topley (1934), as modified by Kossova & Nechaeva (1956). Both the antigens and the tetanus toxoid are adsorbed on calcium phosphate.[4] The preparation is administered subcutaneously, in one dose.

Field investigations on the protective value of the polyvaccine against typhoid fever and dysentery carried out at various times by different workers, and experience with the mass application of the vaccine over the years (including during the Second World War), have suggested that one injection of this adsorbed preparation is quite effective (Jablokov, 1956; Julaev, 1947; Karpov, 1955; Kheifets et al., 1958; Slavin, 1956; Sorinson, 1947). However, many of the field trials were not organized in an entirely satisfactory manner, the chief shortcoming being that they were not strictly controlled. While conducting a field trial in 1956, the present writers came to the conclusion that it would be quite impossible to find a non-vaccinated control group which would completely match the vaccinated group and that it would therefore be better to use as controls a group of individuals taken from the same population as the test group and subjected to a single injection of a preparation not containing the bacterial antigens (Kheifets et al., 1958).

The data presented in this paper relate to a controlled field trial of the typhoid component of the polyvaccine carried out simultaneously in four localities in the USSR in 1958.

MATERIALS AND METHODS

The procedure adopted in the 1958 field trial was devised in the light of the local conditions and of the latest available data on the advantages of controlled field trials (Cockburn, 1956; Cvjetanović, 1957; Hill, 1951; Poliomyelitis Vaccine Evaluation Center, 1957). The basic features of this new procedure are: (*a*) injection of the control group with a preparation not containing bacterial antigens; (*b*) use of code letters for the test and control preparations; (*c*) random allocation of individuals to the test and control subgroups, made possible by the adoption of a

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[4] Since 1960, aluminium hydroxide has been used for adsorption.

TABLE 1

DISTRIBUTION OF STUDY POPULATION IN TEST AND CONTROL GROUPS, ACCORDING TO AGE, SEX, ENVIRONMENTAL CONDITIONS, PREVIOUS ENTERIC INFECTIONS AND PREVIOUS TYPHOID VACCINATION

	Number of persons in:						
	Both groups	Test group (A+G)	Control group (B+E)	Test subgroup		Control subgroup	
				A	G	B	E
Locality:							
T.	16 054	8 124	7 930	4 158	3 966	3 828	4 102
A.	29 124	14 389	14 735	7 212	7 177	7 231	7 504
Am.	20 882	10 421	10 461	5 335	5 086	5 192	5 269
S.	26 921	13 331	13 590	6 754	6 577	6 865	6 725
Total	92 981	46 265	46 716	23 459	22 806	23 116	23 600
Sex:							
Male	43 130	21 494	21 636	10 789	10 705	10 751	10 885
Female	47 739	23 684	24 055	12 112	11 572	11 935	12 120
Not stated	2 112	1 087	1 025	558	529	430	595
Age (years):							
16	4 560	2 309	2 251	1 223	1 086	1 118	1 133
17-19	21 645	10 759	10 886	5 386	5 373	5 348	5 538
20-39	54 259	27 198	27 061	13 942	13 256	13 345	13 716
40-49	9 002	4 257	4 745	4 032	2 225	2 405	2 340
50-60	3 515	1 742	1 773	876	866	900	873
Housing situation:							
Apartment	56 065	28 125	27 940	14 244	13 881	14 057	13 883
Room	12 172	6 122	6 050	3 207	2 915	3 118	2 932
Hostel	14 046	6 929	7 117	3 423	3 506	3 523	3 594
Barrack	3 562	1 713	1 849	830	883	887	962
Unknown	7 136	3 376	3 760	1 755	1 621	1 531	2 229
Water supply:							
Piped water	30 767	15 121	15 646	7 605	7 516	7 693	7 953
Water pump	51 817	25 923	25 894	13 230	12 693	12 982	12 912
Well	3 080	1 589	1 491	750	839	739	752
River or irrigation canal	657	332	325	193	139	167	158
Unknown	6 660	3 300	3 360	1 681	1 619	1 535	1 825
History of typhoid vaccination in past two years:							
Not vaccinated	44 370	22 235	22 135	11 392	10 843	10 802	11 333
Vaccinated in 1956-57	41 925	20 611	21 314	10 392	10 219	10 778	10 536
Unknown	6 686	3 419	3 267	1 675	1 744	1 536	1 731
History of previous enteric infections:							
Typhoid (1914-26)	2 783	1 400	1 383	707	693	666	717
Dysentery/diarrhoea (1956-57)	3 121	1 538	1 583	749	789	793	790

special system of registration. A detailed description of the procedure has been published elsewhere (Kheifets & Khasanov, 1959a, 1959b).

The main object of the trial was to study the effectiveness of the typhoid component of the polyvaccine and to examine the reactions caused by this preparation.

The batch of polyvaccine used in the trial was submitted to extensive laboratory tests. Since the preparation in question did not contain the cholera antigen, it was expected to give rise to fewer reactions than the usual type of polyvaccine. One dose (1.5 ml) of the test preparation contained 1.15 mg of bacterial antigens (including 0.1 mg of typhoid antigen) and 100 international units of tetanus toxoid; one dose of the control preparation contained simply 100 international units of tetanus toxoid. Ampoules containing one dose of either the test or the control preparation were labelled with the code letters A or G for the former and B or E for the latter, each preparation thus being under two designations.

The field trial was carried out in four localities where in 1956-57 the typhoid fever morbidity rate was still rather high. It was thought unlikely that by 1958 this rate would have fallen to such an extent that it would be impossible to draw reliable conclusions as to the effectiveness of the vaccine. From 10% to 30% of the population in the selected localities were included in the trial, which involved a total of 92 981 persons of 16-60 years of age. Table 1 shows the distribution of the persons in the test and control groups according to age, sex, environmental conditions, previous history of enteric infections, and previous typhoid vaccination. It can be seen that the main test and control groups were quite similar in all these respects, as were the subgroups resulting from the random allocation of individuals to the labelled preparations. In Table 1 the data on age, sex, etc. are summarized for the four localities together, but a detailed analysis (not presented here) of these data for the separate localities (and for different districts within each locality) also showed that the control and test groups and subgroups were satisfactorily comparable. The similarity of the groups in respect of environmental and epidemiological conditions is of great importance because it indicates that a difference in morbidity rate between the groups cannot be attributed to different levels of exposure to infection in the groups in question.

Table 2 shows the incidence in the test and control groups of infectious diseases other than the enteric infections under study and of non-infectious diseases during the study period. It can be seen that the various groups were comparable in respect of these diseases. In general, therefore, the test and control groups were equally exposed to infection.

The data on the incidence of disease among the study population were obtained in two ways:

(*a*) All the local health centres daily sent a duplicate notification of any case of infectious disease to a given registration centre, and confirmation of the diagnosis and information on the course of the disease were provided by the hospital to which the case was referred.

(*b*) Every individual in the test and control groups was visited at 3-monthly intervals and the occur-

TABLE 2

NUMBER OF CASES OF DISEASES OTHER THAN ENTERIC INFECTIONS AMONG TEST AND CONTROL GROUPS DURING THE STUDY PERIOD

Disease	Test group			Control group			Total
	Subgroup A	Subgroup G	Total	Subgroup B	Subgroup E	Total	
Infectious hepatitis	12	14	26	16	10	26	52
Diphtheria	8	6	14	12	10	22	36
Poliomyelitis	1	1	2	1	3	4	6
Influenza	778	837	1 615	843	767	1 610	3 225
Sore throat	360	333	693	388	378	766	1 459
Non-infectious diseases	472	399	871	445	427	872	1 743
Total . . .	1 631	1 590	3 221	1 705	1 595	3 300	6 521

rence of any disease during the preceding 3-month period was recorded. The data obtained from these visits were compared with those received at the registration centre, so that the two sources of information checked and supplemented each other.

In each locality the work of vaccinating, visiting and card-indexing was undertaken by special groups of workers (vaccination teams, health visitors and local authorities). These groups carried out their functions in conformity with the detailed specifications of the field trial.

To ensure uniformity in the methods used in the trial, representatives of the Metchnikov Institute of Vaccines and Sera periodically visited the localities under observation to co-ordinate the activities of the local authorities, vaccination teams and health visitors.

The vaccination campaign was carried out over a period of 45 days in March-May 1958 and the follow-up study was continued for 10 months.

RESULTS

Reactions to vaccination

A considerable proportion of the study population (more than 1000 persons from each of the main test and control groups) was examined for reactions to the vaccination. The general condition of each of these persons immediately after the vaccination was noted and the temperature, the local reaction and, again, the general condition were recorded 24-48 hours afterwards and, in some cases, also 10 hours afterwards. Slight malaise, becoming manifest in 5-6 hours and reaching a maximum in 10-12 hours, was reported in a considerable proportion of the vaccinated subjects, some of whom complained of weakness, headache, sickness, pains in limbs, etc. After 24 hours the majority of the vaccinated individuals did not complain of ill-effects and, as a rule, after 48 hours all the people were quite well. The highest degree of fever occurred after 10-12 hours. Since temperature is the most objective criterion it was taken as the main basis for the evaluation of the reactions to vaccination. Table 3 presents data on the temperature reactions of a small group of persons who were vaccinated before the start of the field trial. It can be seen that the sum of the moderate (37.6-38.5°C) and the severe (38.6°C or higher) reactions was 20.5%±2.8% 10 hours after vaccination and 6.5%±1.5% 24 hours after. Since the temperature of all persons in the group was normal 48 hours after vaccination, the observations after 48 hours are not included in the table.

In the field trial, no significant differences were observed in the data from the four localities. The reactions to injections recorded after 24 hours by the vaccination teams (each team observed approximately 200 persons) are summarized in Table 4. From the data presented it can be seen that the percentage of marked reactions to the polyvaccine was not high, being only a little greater than the percentage of marked reactions to the control preparation containing tetanus toxoid alone, which was considered to be non-toxic. The average sum of the moderate and severe temperature reactions to the polyvaccine (6%) was considerably lower than that observed with the usual type of polyvaccine containing cholera antigen (Kheifets et al., 1958).

Omission of the cholera antigen from the polyvaccine, the epidemiological situation permitting, is one way of reducing the number of toxic reactions to the vaccine. Another way is to include novocaine in the preparation. In one of the test localities, a small group of persons was vaccinated with a preparation containing 2% novocaine and the reactions compared with those of a similar group vaccinated with the ordinary test preparation (the two groups were formed by random selection). As is evident from

TABLE 3

TEMPERATURE REACTIONS OBSERVED AMONG SMALL GROUP OF PERSONS 10 AND 24 HOURS AFTER ADMINISTRATION OF POLYVACCINE WITHOUT CHOLERA ANTIGEN

Time after vaccination (hours)	No. of persons observed	Temperature reactions (%)					Sum of moderate and severe reactions (%)	Double error of the index (%)
		37.0°C or less	37.1-37.5°C	37.6-38.0°C	38.1-38.5°C	38.6-39.0°C		
10	886	59.4	19.8	11.3	4.6	4.6	20.5	±2.8
18-24	1 264	77.6	15.9	5.1	1.0	0.4	6.5	±1.5

TABLE 4
REACTIONS OBSERVED BY VACCINATION TEAMS 24 HOURS AFTER VACCINATION

Locality	Preparation[a]	No. of persons observed	Temperature reactions (%)							Local reactions (%)				
			37.0°C or less	37.1-37.5°C	37.6-38.0°C	38.1-38.5°C	38.6-39.0°C	39.1°C or higher	Sum of moderate and severe reactions	Double error of the index	None	Mild	Moderate	Severe	Sum of moderate and severe reactions	Double error of the index
A.	A	2 823	82.6	12.0	3.3	1.3	0.6	0.2	5.4	±0.8	48.2	38.0	11.2	2.6	13.8	±1.3
	K	2 867	90.6	7.5	1.2	0.6	0.1	0.03	1.9	±0.5	56.5	35.4	7.2	0.9	8.1	±1.1
T.	A	3 929	84.7	8.4	3.6	1.9	1.0	0.4	6.9	±0.8	56.3	24.9	15.4	3.4	18.8	±1.3
	K	3 546	91.4	5.3	1.8	1.1	0.4	—	3.3	±0.6	62.9	22.1	13.7	1.3	15.0	±1.2
Am.	A	1 244	81.3	15.1	2.8	0.6	0.2	—	3.6	±1.2	36.2	43.3	17.5	3.0	20.5	±2.5
	K	1 109	97.6	8.3	1.8	0.6	—	—	2.4	±1.0	42.3	45.8	11.0	0.9	11.9	±2.0
S.	A	1 149	83.8	9.1	5.5	1.0	0.4	0.2	7.1	±1.6	38.8	43.6	15.5	2.1	17.6	±2.4
	K	1 107	92.6	5.3	1.8	0.2	0.1	—	2.1	±0.9	43.8	42.0	13.5	0.7	14.2	±2.3
Total	A	9 145	83.5	10.5	3.6	1.4	0.7	0.3	6.0	±0.5	49.1	33.7	14.3	2.9	17.2	±0.8
	K	8 629	91.1	6.4	1.6	0.7	0.2	0.01	2.5	±0.3	55.0	32.7	11.2	1.1	12.3	±0.7

[a] A = test preparation (polyvaccine without cholera antigen); K = control preparation (tetanus toxoid alone).

Table 5, the former group gave significantly fewer temperature reactions (over 37.5°C) than the latter group and also showed a lower percentage of persons who were incapacitated 24 hours after vaccination. An important consideration is that with the novocaine vaccine there was no painfulness after the injection—a fact that would make it practicable to carry out a large-scale vaccination campaign.

Epidemiological effectiveness

During the 10-month period of observation, 53 cases of typhoid and paratyphoid, confirmed by blood culture, occurred among the study population.[1] Of these, 51 were recorded during the first six months of the observation period. The distribution of the 51 cases in the four localities and in the various test and control groups and subgroups is shown in Table 6. It can be seen that the incidence of typhoid and paratyphoid in the test groups and subgroups was consistently lower than that in the corresponding control groups. In this connexion it is of interest that, in locality S., there were nearly as many cases in the dysentery vaccine control group [1] as in the tetanus toxoid control group, and that, in the other three localities, the number of cases in any control subgroup was higher than that in any test subgroup. It should be noted here that, for the data in Table 6, the level of significance was determined not only on the basis of the χ^2 test, but also on that of the binomial distribution (United States Army Ordnance Corps, 1952)—a procedure adopted in the statistical analysis of the data obtained in the 1954 field trial of poliomyelitis vaccine in the USA (Poliomyelitis Vaccine Evaluation Center, 1957). The lower confidence limit at the 5% level of significance (L) was also computed for the effectiveness of the polyvaccine.

In Table 7 the data on the 45 cases of typhoid and paratyphoid in the main test and control groups are presented separately. The table shows that the number of typhoid cases in the test group was significantly lower than the number in the control group, thus indicating that one injection of the polyvaccine affords some protection against typhoid.

[1] In the case of locality S., the study population included an additional control group (13 429 persons) which was inoculated with a dysentery vaccine instead of with the tetanus toxoid preparation. The protection afforded by this vaccine against dysentery is discussed in an article by the same authors on the effectiveness of the dysentery component of the polyvaccine, to be published shortly in *Žurnal mikrobiologii, epidemiologii i immunobiologii (Moskva)*.

TABLE 5

COMPARATIVE STUDY OF THE REACTIONS CAUSED BY POLYVACCINE WITH AND WITHOUT NOVOCAINE

Temperature after 24 hours						Temperature over 37.5°C (double error of the index)	Diameter of local reaction				Unable to work 24 hours after vaccination
37.0°C or less	37.1-37.5°C	37.6-38.0°C	38.1-38.5°C	38.6-39.0°C	39.1-39.5°C		0 cm	<2.5 cm	2.5-5 cm	>5 cm	
Vaccine with novocaine: 1965 persons vaccinated											
1 729 88.0 %	141 7.2 %	68 3.5 %	12 0.6 %	13 0.6 %	2 0.1 %	95 4.8% (±1.0%)	730 37.2 %	892 45.3 %	298 15.2 %	45 2.3 %	116 5.9 %
Vaccine without novocaine: 1940 persons vaccinated											
1 655 85.7 %	152 7.7 %	98 5.0 %	19 0.9 %	9 0.4 %	7 0.3 %	133 6.6% (±1.1%)	770 39.6 %	855 44.0 %	273 14.4 %	47 2.0 %	150 8.2 %
$\frac{6.6-4.8}{\sqrt{\frac{6.6(100-6.6)}{1940}+\frac{4.8(100-4.8)}{1965}}}=2.4$ $x^2 = 7.25;\ p<0.01$							$\frac{8.2-5.9}{\sqrt{\frac{8.2(100-8.2)}{1940}+\frac{5.9(100-5.9)}{1965}}}=2.9$ $x^2 = 5.14;\ 0.01<p<0.05$					

TABLE 6

DISTRIBUTION OF CONFIRMED TYPHOID AND PARATYPHOID CASES AMONG TEST AND CONTROL GROUPS DURING FIRST SIX MONTHS OF STUDY PERIOD

Locality	Test group (polyvaccine)				Control group 1 (tetanus toxoid)				Control group 2 (dysentery vaccine)	
	Number of cases			Rate per 10 000	Number of cases			Rate per 10 000	Number of cases	Rate per 10 000
	A	G	A + G		B	E	B + E			
T.	0	2	2	2.5	5	6	11	13.9		
A.	2	1	3	2.1	5	4	9	6.1		
Am.	1	1	2	1.9	5	3	8	7.6		
S.			3	2.3			7	5.2	6	4.9
Total			10	2.2			35	7.5	6	4.9

For test group and control group 1:

$$K = \frac{\text{morbidity rate in control group (b)}}{\text{morbidity rate in test group (a)}} = 3.4. \qquad E = \frac{100\,(b-a)}{b} = 71\,\%. \qquad x^2 = 13.8;\ 0.001>p>0.0001.$$

$$B = \sum_{k=0}^{n} \binom{n}{k} \left(\frac{N_1}{N_1+N_2}\right)^k \left(\frac{N_2}{N_1+N_2}\right)^{n-k};\ p = 0.0001235. \qquad \sum_{k=0}^{n_1} \binom{n}{n_1} p^k\,(1-p)^{n-k} = 0.05.$$

Lower confidence limit at the 5% level of significance (L) $= 100\left(1-\frac{N_2\,p}{N_1\,(1-p)}\right) = 46\,\%$.

TABLE 7
DISTRIBUTION OF CONFIRMED TYPHOID, PARATYPHOID A AND PARATYPHOID B CASES AMONG TEST AND CONTROL GROUPS DURING FIRST SIX MONTHS OF STUDY PERIOD

Locality	Typhoid		Paratyphoid A		Paratyphoid B	
	Test group	Control group	Test group	Control group	Test group	Control group
T.	2	10	—	—	—	1
A.	2	9	1	—	—	—
Am.	2	7	—	1	—	—
S.	3	6	—	1	—	—
Total	9	32	1	2	—	1

For typhoid: K = 3.5; E = 71 %; x^2 = 12.9; 0.001>p>0.0001.

The data obtained in our field trial are similar to those obtained in the 1953 field trial in Osijek, Yugoslavia (Cvjetanović, 1957; Yugoslav Typhoid Commission, 1957, 1962 [1]), where two doses of the heat-killed, phenol-preserved typhoid vaccine were administered. In each month after vaccination (Table 8) and in each age-group (Table 9) the number of cases in the control group was higher than that in the test one. The influence of previous vaccination with NIISI polyvaccine (in the past two years) on the incidence of typhoid during the study period is indicated in Table 10. It can be seen that, in the control group, the number of cases of typhoid fever was almost the same among the previously vaccinated persons as among the previously non-vaccinated (12 and 13 cases, respectively). It should be recalled here that the numbers of previously vaccinated and previously non-vaccinated persons in the study population were approximately equal (see Table 1). In the test group, the majority of the cases of typhoid (7 out of 10) occurred among the previously non-vaccinated persons.

If the differences shown in Table 10 were statistically significant, it would suggest that: (*a*) annual vaccination does not have a negative influence on immunity; (*b*) after a year or more vaccination has no longer any protective value; and (*c*) vaccination is most effective in persons who have been vaccinated previously. It should be borne in mind, however, that the data in Table 10 provide only a basis for the above suppositions; before final conclusions can be drawn a number of further investigations must be carried out.

[1] See article on page 357 of this issue.

CONCLUSIONS

1. The data presented in this paper confirm the importance of studying the effectiveness of typhoid vaccination only in strictly controlled trials, where equal exposure of the test and control groups to the infection—an indispensable condition for obtaining reliable results—can be guaranteed.

2. One injection of a polyvaccine containing, instead of bacterial cells, complete typhoid antigen adsorbed on calcium phosphate gives satisfactory protection against typhoid fever.

3. Omission of the cholera antigen component from NIISI polyvaccine reduces the number of reactions to vaccination—a consideration which, together with the fact that only one injection of the vaccine is necessary to give protection, suggests that the modified polyvaccine could be used for the mass vaccination of the population.

TABLE 8
NUMBER OF CONFIRMED CASES OF TYPHOID AND PARATYPHOID OBSERVED IN TEST AND CONTROL GROUPS EACH MONTH AFTER VACCINATION

Diagnosis	Group	Month after vaccination										Total
		1	2	3	4	5	6	7	8	9	10	
Typhoid	Test	1	2	2	3	—	1	—	—	1	—	10
	Control	4	5	9	7	4	3	—	—	—	—	32
Paratyphoid A	Test	—	—	1	—	—	—	—	—	—	—	1
	Control	—	2	—	—	—	—	—	1	—	—	3
Paratyphoid B	Test	—	—	—	—	—	—	—	—	—	—	—
	Control	—	—	1	—	—	—	—	—	—	—	1
Total	Test	1	2	3	3	—	1	—	—	1	—	11
	Control	4	7	10	7	4	3	—	1	—	—	36

TABLE 9

AGE DISTRIBUTION OF CONFIRMED CASES OF TYPHOID AND PARATYPHOID IN TEST AND CONTROL GROUPS

Age (years)	Total number of cases		Number of typhoid cases	
	Test group	Control group	Test group	Control group
16	—	—	—	—
17-19	4	9	4	9
20-39	6	24	5	20
40-49	1	3	1	3
50-60	—	—	—	—
Total	11	36	10	32

TABLE 10

HISTORY OF TYPHOID VACCINATION IN THE PAST TWO YEARS AMONG PERSONS AFFECTED WITH TYPHOID AND PARATYPHOID DURING THE STUDY PERIOD

Previous history of vaccination	Total number of cases		Number of typhoid cases	
	Test group	Control group	Test group	Control group
Vaccinated in 1956-57	2	15	2	12
Not vaccinated	8	13	7	13
Unknown	1	8	1	7
Total	11	36	10	32

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RÉSUMÉ

Un polyvaccin, contenant les antigènes complets de *Salmonella typhi abdominalis*, *Salm. paratyphi* A, *Salm. paratyphi* B, *Shigella flexneri*, *Sh. sonnei*, de *Vibrio cholerae*, et une anatoxine tétanique purifiée, est utilisée depuis de nombreuses années en URSS, pour la vaccination des adultes.

A la demande du Ministère de la Santé, une épreuve pratique de ce vaccin, strictement contrôlée, a été entreprise en 1958, sur une population de plus de 90 000 personnes de 16-60 ans, dans 4 localités où les fièvres typhoïde et paratyphoïdes étaient encore des causes importantes de morbidité. Il s'agissait surtout d'évaluer l'efficacité des composants typhoïdiques du vaccin. La moitié environ des personnes participant à l'essai reçurent le vaccin complet (moins l'antigène cholérique), l'autre moitié un vaccin privé des antigènes bactériens et ne contenant que l'anatoxine purifiée. Les antigènes bactériens, comme l'anatoxine, étaient adsorbés sur phosphate de calcium.

Pendant les 10 mois d'observation, 53 cas de typhoïde et paratyphoïdes survinrent dans les divers groupes, la fréquence des cas étant significativement inférieure dans les groupes vaccinés par les antigènes typhoïdiques. On peut déduire de l'analyse statistique des chiffres de fréquence, qu'une seule injection de polyvaccin contenant les antigènes adsorbés sur phosphate de calcium assure une protection efficace.

La suppression de l'antigène cholérique du polyvaccin réduit le nombre des réactions à la vaccination, avantage qui, venant s'ajouter au fait qu'une seule injection est suffisante, permet d'envisager l'emploi de ce vaccin pour l'immunisation massive de la population.

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