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Immunological and Epidemiological Effectiveness of Live Poliomyelitis Vaccine in the USSR *

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In 1959 a total of 1 700 000 children up to 14-18 years old in the Latvian, Byelorussian, Moldavian and Russian Republics of the USSR were given live poliovirus vaccine prepared from attenuated Sabin strains. The results show that the vaccine is highly effective and quite innocuous.

The mean reduction in poliomyelitis incidence in the different republics varied from sixfold to tenfold, and among very young children (the age-group at greatest risk) was as high as 15-fold. In regions where live vaccine was administered to the bulk of the susceptible population under 14 years of age, it was found that the usual seasonal rise in poliomyelitis incidence did not take place, although it did occur in the unvaccinated control regions. The number of cases of paralytic poliomyelitis was negligible among vaccinated children but relatively high among children in potential or actual contact with them. This suggests that "blind" immunization of contacts by spread of the attenuated vaccine virus is irregular and unreliable, and the authors therefore recommend vaccination of the susceptible population on the widest possible scale in order gradually to eliminate the reservoir of pathogenic wild strains of poliovirus.

The optimum immunization schedule appears to be a first inoculation with type-1 monovaccine, a second inoculation 4-6 weeks later with divaccine of types 2 and 3, and a third inoculation with trivaccine after a similar interval.

INTRODUCTION

The extensive use of the Salk inactivated vaccine for poliomyelitis control during the last few years has not eliminated the danger of paralytic forms of the disease developing in triply vaccinated children and has had no effect on the circulation of the virus among vaccinated children. The limited duration of post-vaccinal immunity has made re-immunization necessary after completion of the schedule of three vaccinations with the inactivated vaccine.

The fact that 1500 monkeys are needed in the production of every million doses of killed-virus vaccine has already created great difficulties in the supply of monkeys for the ever-expanding manufacture of this wasteful preparation.

Nowadays large-scale production of the complex, expensive and insufficiently effective Salk vaccine, which, in addition, involves scarring of children because of the repeated injections required, has been rendered unnecessary by the development of a more effective, completely harmless live vaccine for oral administration, which is easy to produce and to use and is prepared from the Sabin or Koprowski strains.

The live vaccine is free from the main defects of the Salk vaccine. It not only establishes a long-lasting humoral immunity which prevents the virus from invading the central nervous system, but also renders the intestinal tract highly insusceptible, thus making it difficult for the causative agent to develop in the susceptible organism. The live vaccine provides an opportunity of carrying out a most important epidemiological task—the extermination of the immense horde of highly pathogenic wild viruses threatening the child

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population on all sides. This is a task quite beyond the powers of the killed vaccine.

The large-scale trials carried out in the USSR in 1959 by the Institute of Experimental Medicine and the Institute of Poliomyelitis of the USSR Academy of Medical Sciences to assess the epidemiological effectiveness against poliomyelitis of the live vaccine prepared from the Sabin strains in about three million children inoculated in April-May, before the beginning of the seasonal rise in the incidence of the disease, was made possible by the research carried out by our laboratory in 1956-58. During those years we assumed the responsibility of testing the innocuity and immunogenicity of the Sabin vaccine strains on gradually increasing numbers of young children. This made it possible by the end of 1958 to give an affirmative reply to the basic question whether the live vaccine was harmless and effective on the basis of data obtained from laboratory and clinical examinations of 2500 healthy children of pre-school age inoculated with the live vaccine produced in Leningrad (Smorodintsev et al., 1958).

The results of this work, carried out in close co-operation with the Nervous Diseases Clinic of the Leningrad Medical Paediatric Institute (Director: E. F. Davidenkova) and the Infectious Diseases Clinic of the Leningrad Institute of Medical Sanitation and Hygiene (Director: V. V. Kosmachevski), showed that the live vaccine was quite innocuous, both for the children actually inoculated and for uninoculated susceptible children in close contact with them.

Observation of vaccinated and non-vaccinated children over a period of two years showed that the live vaccine caused no lesions of the central nervous system which reproduced even the slightest meningeal forms of poliomyelitis, and caused no damage to the intestinal canal, the respiratory tract or any other organs. Even feverish reactions were very rare in the children vaccinated with the live vaccine and were usually no more frequent than in establishments containing children of similar age in which the live vaccine had not been used at all (Davidenkova & Savelyeva-Vasilyeva, 1959; Kosmachevski et al., 1960; Vasilyev & Glinskaya, 1960).

The observations established that the live attenuated vaccine possesses a high degree of immunogenicity for susceptible children when administered in two doses in the form of monovalent vaccines. A single administration of two and three viruses of different types combined in a double or triple vaccine proved immunogenically somewhat less effective.

The immunization of susceptible children in three stages with monovalent preparations of live poliomyelitis vaccine of types 1, 2 and 3 produces similar rises in antibody level independently of the order in which the various vaccine serotypes are administered. A relatively lower level of antibodies to type 3 virus than to types 1 and 2 was noted in all cases (Kurnosova & Zhilova, 1960).

The proportion of susceptible children who responded to a single administration of monovalent vaccine by developing humoral immunity amounted to 90%-95% of the total for vaccines of types 1 and 2, and about 80%-90% for vaccine of type 3. The revaccination of triply vaccinated children with polyvalent vaccine of types 1, 2 and 3 eliminates the shortcomings of the first immunizing schedule and gives the majority of originally unresponsive children complete immunity against all three types.

The ready-for-use polyvalent vaccine, containing 100 000 tissue units of each type of vaccine, is the most convenient form of combined preparation for practical use.

A single administration of trivaccine results in a lower level of antibodies to all three types than three administrations of monovalent vaccine or divaccine, but three administrations of the trivaccine produce immunity in almost 100% of cases (Table 1).

A very convenient method in regard to speed and effectiveness is triple immunization on the following schedule: monovaccine of type 1, divaccine of types 2 and 3, and trivaccine of types 1, 2 and 3, given at intervals of a month (Table 1). This schedule produces the maximum immunogenic effect and requires the same amount of vaccine as three administrations of monovaccines followed by revaccination with trivaccine after one to three months. Its great advantage lies in the fact that the schedule is completed more quickly and medical personnel are not required to give a fourth revaccination.

The high immunogenicity of the live vaccine is due to the multiplication of the vaccine viruses in the intestinal canal of immunized children; this follows a regular cycle with maximum accumulation of the virus between the seventh and the twenty-first day, followed by a gradual dimi-

TABLE 1. IMMUNOLOGICAL ACTIVITY OF LIVE POLIOVIRUS VACCINE IN RELATION TO SCHEDULE OF IMMUNIZATION OF NEGATIVE CHILDREN

Vaccine used	Type of virus	Number of children tested		Fourfold and greater increase in antibody	
		Total	Negative	Total	%
Monovaccine (once)	1	227	148	143	97
	2	81	68	68	100
	3	89	68	65	96
Divaccine (once)	2	150	70	57	81
	3	150	55	44	80
Trivaccine (once)	1	189	102	70	69
	2	189	129	97	75
	3	189	144	66	46
Trivaccine (twice)	1	141	84	76	90
	2	141	82	81	99
	3	141	108	82	76
Trivaccine (3 times)	1	141	84	84	100
	2	141	82	82	100
	3	141	108	94	87
Monovaccine of type 1 + divaccine of types 2 & 3 [a]	1	860	360	283	79
	2	860	510	463	91
	3	860	432	312	72
Monovaccine of type 1 + divaccine of types 2 & 3 + trivaccine [a]	1	860	360	352	98
	2	860	510	507	99
	3	860	432	412	95

[a] Subjects selected at random.

nution in its concentration during the subsequent 15-20 days.

The multiplication of the virus follows an extremely regular course with no interference from other viruses and reaches its greatest intensity in children with a low level of immunity to poliomyelitis, growing gradually less intense in persons with specific antibodies in their blood (Ilyenko & Alekseyev, 1960).

The most important feature of the live vaccine has been the formation of intense long-lasting resistance in the intestinal canal to the subsequent administration of maximum doses of homologous virus, which do not multiply intensively and are quickly eliminated from the intestinal tract (Gorev, 1960).

In rare instances the virus administered later proves capable of multiplication but at a considerably lower rate than that shown by the initial quantitative multiplication curve in the same child.

Observations over a long period of the immunity of the intestinal canal in children who had been immunized with the live vaccine between four months and two years beforehand showed that their revaccination at the prescribed dates after the first administration of vaccine promotes the regular maintenance of intense and durable

immunity of the intestinal canal to subsequent infection with the vaccine strain.

The resistance of the intestinal tract in children to the primary administration of vaccine strains depends markedly on the state of their humoral immunity to homologous virus. The intestinal tract has been found to possess only weak defensive powers against infection by vaccine strains when the initial titres of virus-neutralizing antibodies are low (1:4-1:16), whereas at higher antibody titres the vaccine viruses do not multiply, or else develop at a low rate and for a short time.

In order to establish durable local resistance in the intestinal tract, it is important to ensure guaranteed vaccination with high-quality vaccine, in view of the unreliability of the results of immunization which develops after contact with inoculated children.

The results of vaccination depend in the main on the doses of the preparation administered and on the level of specific and non-specific immunity in the children to be inoculated.

Liquid vaccine containing 5.0 $\log_{10}$ TCD of virus is a guaranteed way of ensuring oral immunization against poliomyelitis and obtaining the greatest possible uniformity and standardization of dosage between different children.

The intensive excretion of vaccine strains from the intestines of inoculated children in the first month after immunization leads to the natural dissemination of vaccine viruses among susceptible persons in contact with those inoculated (Ilyenko et al., 1960).

This process of spread of the vaccine virus to contact groups is one of the most characteristic features of the live poliomyelitis vaccine, creating conditions in which population groups in contact with the inoculated persons may become immunized, while those already immunized may be re-immunized.

The real epidemiological importance of this blind immunization should not be exaggerated. Thus the data quoted below, obtained in 1959 in epidemiological surveys in the Byelorussian and Moldavian Republics, showed that uninoculated groups of children in potential contact with inoculated ones had a rather high incidence of paralytic poliomyelitis, varying but little from the incidence among persons not in such contact.

"Blind" infection with the vaccine virus reaches its highest intensity under primitive sanitary and hygienic conditions or where there is a low level of personal hygiene. This latter feature is particularly common among infants, for example, in crèches. As the age of the children increases, the intensity of contact infection falls quickly (among children of pre-school and school age) and reaches a minimum among susceptible adults.

We paid much attention to the cardinal problem of the possibility of the Sabin vaccine strains reverting to the initial pathogenic form after 12 passages through the intestinal canal of susceptible children (Smorodintsev et al., 1958, 1959a, 1959b).

A study of changes in the neurotropic activity for monkeys of the vaccine viruses after 12 artificial or four natural passages in susceptible children showed a periodic and comparatively slight increase in the neurotropic properties of the vaccine strains which did not lead, however, to a progressive intensification of their neurovirulence.

These data will go a long way towards ending the bitter arguments on the dangers of reversion in the group of vaccine strains we studied.

In November 1958 our preliminary data on the innocuity of live poliomyelitis vaccine enabled the Sera and Vaccines Commission and the Collegium of the USSR Ministry of Health to give permission to the Institute of Experimental Medicine to carry out large-scale epidemiological surveys to study the innocuity yet further. At this stage, the Poliomyelitis Research Institute of the USSR Academy of Medical Sciences joined in our activities (Director: M. P. Chumakov).

In April and May 1959 we used the reserves of vaccine produced in the Virus Department of the Institute of Experimental Medicine, amounting to about two million doses, for immunizing 1 700 000 children aged up to 14-18 years in the Byelorussian, Latvian and Moldavian Republics, and in June-July 1959 in the Pskov and Novgorod regions. The vaccination was carried in two stages. The first stage, in April 1959, consisted of administration of monovaccine of type 1, and the second stage, in May 1959, of the administration of a divaccine of types 2 and 3.

ORGANIZATION OF VACCINATION AND EVALUATION OF EPIDEMIOLOGICAL EFFECTIVENESS

The Ministries of the Union Republics responsible for carrying out the vaccination arranged in good time for the detailed briefing of senior physicians and epidemiologists from the rayon

(district) sanitational and epidemiological centres on the purpose and methods of vaccination, and drew up with them a detailed vaccination plan; staff was provided for vaccination teams on the basis of 300-500 vaccinations per day per team, a team consisting of a physician or feldscher and two nurses.

Similar work was carried out in every city or rural region, all medical workers taking part in the immunization campaign being summoned for instructions.

The establishments responsible for the carrying out of vaccination sent permanent representatives to each city or region who stayed there during the whole vaccination campaign and helped in carrying it out.

Before and during the vaccination campaign, extensive health education work was carried out to acquaint parents and the staff of children's establishments with the objectives and importance of vaccination.

In organized children's communities, vaccination was carried out on the spot; children not attending organized establishments were inoculated in children's polyclinics near their homes or in the course of domiciliary visits.

The names of all the children to be inoculated and children exempted from inoculation for various reasons were entered by the inoculation teams on a list or individual card index, drawn up separately for each children's establishment or centre of population in accordance with a standard procedure. The lists contained entries giving basic information concerning the child in question and recording any previous inoculations against poliomyelitis.

The district epidemiologist summarized the data concerning vaccinations carried out in individual establishments or centres of population in standard vaccination reports. Copies of these reports were sent to the regional sanitary and epidemiological centre or to the local institute of epidemiology and microbiology, which generalized the results of the work carried out on each vaccination.

To study the incidence of poliomyelitis in 1959 and the epidemiological effectiveness of vaccination against the disease, there was set up in each republic a scientific group, consisting of clinicians and epidemiologists and of a size determined by ministerial order, for expert investigation of each reported case of poliomyelitis in the regions where inoculations had been carried out, and to settle questions of diagnosis in doubtful or disputed cases.

To study the epidemiological effectiveness of immunization against poliomyelitis, two control groups were formed in each republic or region: the first consisted of children in direct or potential contact with those vaccinated on the territory covered by the live vaccine campaign (internal control); the second consisted of children and young people aged up to 14-18 years living in areas not covered by the campaign (external control).

In selecting the three groups, it was recommended that immunization with the live vaccine should be carried out in areas with a high incidence of poliomyelitis in previous years, leaving as external control areas with a lower morbidity. It was possible to carry out this recommendation in the Byelorussian and Latvian Republics but not in the Moldavian Republic, where the morbidity among children under 7 years old had been higher in the preceding years in the areas not included in the 1959 vaccination campaign.

In order to leave a sufficiently large internal control group, not more than 50% of the population under 7 years was vaccinated in the areas concerned.

Although strictly voluntary, the vaccination proved extremely popular with parents, with the result that 80% of the children under school age who were not attending an institution were brought to the children's polyclinics to be vaccinated. This gave the vaccination teams a chance to select for vaccination only those children who had been completely healthy for the previous two months and were free of any commitments in regard to other vaccinations for three months ahead, and to leave 50% or more of the crèche-age children unvaccinated. In the institutions for children under school age (crèches, kindergartens etc.), the medical staff vaccinated 50% of the children present, keeping the rest for internal control. This gave two groups of maximum comparability in regard to age, conditions of life and state of health.

Of the school-age children, 75% were vaccinated, about 25% being kept for internal control. The latter group included all children who had been absent at the time of the first immunization, or for whom there were medical

contra-indications. Selective serological examination of the children in the internal control group and of those who had been vaccinated, performed on sera taken before the vaccination was begun, established complete comparability of the immunological indices for each age-group of vaccinated and internal control children. On these grounds we considered it possible to make use of the effectiveness indices of the live vaccine not only for comparison with the geographically determined external control group (territories not covered by the vaccination) but also, and particularly, for comparison with the more comparable and representative internal control group.

In order to provide a correct basis for the evaluation of the epidemiological effectiveness of the live vaccine, we tried to ensure that the following main conditions were met.

1. The first condition was the receipt of full information concerning morbidity in all three groups mentioned, vaccinated and unvaccinated. The following special measures were taken to ensure complete reporting of all cases of paralytic and non-paralytic poliomyelitis:

(*a*) From the beginning of the vaccination campaign, by decree of the Ministry of the Union Republic concerned, a system was introduced for the urgent reporting of every case diagnosed as poliomyelitis throughout the whole republic or oblast. The report, with brief information concerning the patient, was given by telephone or telegram to the nearest republic sanitary-epidemiological centre or institute of epidemiology and microbiology.

(*b*) A member of one of the groups of neuropathologists which were established was sent as quickly as possible to the place where each case occurred to check the diagnosis and to obtain basic material for virological laboratory examination (the patient's faeces and the first blood from a vein; a second portion of blood was taken 3-4 weeks after the beginning of the illness).

(*c*) Persons who contracted poliomyelitis were sent to the central oblast or republic hospitals immediately after the beginning of the disease, or, in cases where this was impossible, after the acute stage had passed. Experienced neuropathologists ensured accurate diagnosis of each case or checked the correctness of the primary clinical diagnosis, taking into account the results of the laboratory examination.

(*d*) For the analysis of the epidemiological effectiveness of the vaccine, figures for paralytic and non-paralytic cases of poliomyelitis were used separately. The group of patients with paralytic poliomyelitis included those with the more certainly diagnosable forms of spinal and bulbo-spinal poliomyelitis with residual effects. The pontine forms, among which illnesses of a non-poliomyelitic nature predominated, were placed in the non-paralytic group.

(*e*) The analysis of epidemiological effectiveness was based on morbidity figures taken for the period of the whole epidemic rise in poliomyelitis and covered not less than six months of observation. The material on the effectiveness of vaccination in 1959 was processed on the basis of the period June-December 1959 and January-February 1960, which began three to four weeks after completion of the second immunization in the middle of May 1959.

2. A proof of the high quality of the work done in assessing the epidemiological effectiveness of vaccination was the completeness of the laboratory examination of notified cases, with full virological examination of the faeces of the majority of patients who had been diagnosed as having poliomyelitis. It was recommended that a faecal specimen be taken within ten days of the beginning of the disease, that a further specimen should be taken in the first days of illness, and that the two specimens should be examined separately or after combination.

In addition to virological examinations of faeces, which showed that 50% of the patients investigated were excreting poliovirus of type 1 and 15% poliovirus of types 2 and 3, we also carried out a serological examination of the patients by serum titration during the period of convalescence.

In cases where the clinical diagnosis was doubtful, positive laboratory findings made it possible to place the patients concerned in the poliomyelitis group. Where the clinical diagnosis was positive but the laboratory findings were negative, the case was considered to be one of poliomyelitis.

3. An important condition for carrying out epidemiological analysis of the effectiveness of vaccination was the obtaining of accurate information concerning the numerical composition by age-group of the children and young people vaccinated with the live vaccine or forming part of the internal and external control groups (Table 2).

TABLE 2

NUMBERS OF PERSONS VACCINATED AND NUMBERS IN CONTROL GROUPS IN 1959 POLIOMYELITIS VACCINATION CAMPAIGN IN USSR

Region	Age-group (years)	Vaccinated group	Internal control group	External control group
Byelorussian SSR	¾-2	74 868	77 612	344 076
	3-6	119 897	152 353	614 350
	7-14	347 754	85 371	977 375
	Total	542 519	315 336	1 935 801
Moldavian SSR	¾-2	72 274	63 755	87 375
	3-6	80 551	30 543	79 301
	7-14	201 782	24 139	164 857
	15-18	52 905		
	Salk vaccine:			
	¾-14		25 373	49 601
	Total	407 512	143 810	381 134
Latvian SSR	¾-2	27 840	56 065	32 103
	3-6	55 349	32 752	35 744
	7-14	159 751	18 055	73 488
	15-30	177 604		
	Total	420 544	106 872	141 335
Pskov oblast	¾-2	49 292	7 133	—
	3-6	45 679	6 526	—
	7-14	102 843	21 594	—
	Total	197 814	35 253	—
Novgorod oblast	¾-2	41 438	6 979	—
	3-6	39 990	3 970	—
	7-14	80 341	13 875	—
	Total	161 769	24 824	—
Grand total		1 730 158	626 095	2 458 270

For all the groups concerned we received from the local statistical offices information on the composition of the population by age in the areas covered and the areas not covered by the vaccination campaign.

In carrying out the vaccinations the accurate registration of vaccinated children was ensured by means of the data from card indexes and lists and by undertaking primary analysis of the age composition of those vaccinated in the rayon sanitary and epidemiological centres.

This information, put together in accordance with a standard procedure, was summarized by each centre or by the Epidemiology Department of the Institute of Epidemiology and Microbiology.

Where the republic or oblast contained a sufficiently large group of children who had been given triple vaccination with the killed Salk vaccine, we did not administer the live vaccine to them but kept them under observation as a separate group, thus providing an opportunity of settling the question of the comparative effectiveness of live and killed vaccine under comparable epidemiological conditions.

VACCINATION GROUPS AND CONTROL GROUPS

In the Byelorussian Republic 542 519 city children up to 14 years of age were immunized. This was 63% of the total number of children in the cities. The remaining 37% (315 336) formed the internal control group. The children in the rural areas, who were two-and-a-half times as numerous as the urban child population of the same age, were not given the live vaccine; they constituted the external control group. In previous years the absolute number of poliomyelitis cases had been much the same among the rural and urban groups of children, which explains the lower percentage indices for poliomyelitis in rural localities in those years (Kardash et al., 1960).

In the Moldavian SSR the vaccination campaign covered 13 central rayons of the Republic and the four large cities, which account for more than half the population of the Republic and in which, in the previous years, about 50% of the annual number of poliomyelitis cases in the Republic had been recorded. Altogether 407 512 children and young people aged between 9 months and 18 years were vaccinated; 143 810 formed the internal control (contact) group. Groups consisting of 381 134 persons of the same age constituted the external control group (Bulychev et al., 1960).

In the Latvian SSR 420 544 children and adults up to 30 years of age were vaccinated (in Riga and a number of rayons in the Republic); 106 872 persons were left unvaccinated in contact groups in the regions where the live vaccine was employed. A total of 141 335 persons between 9 months and 14 years of age were located in rayons where live vaccine had not been administered.

Somewhat later, in June and July, children in the cities and settlements of the Novgorod and Pskov oblasts were immunized. Here 359 603 children up to 14 years of age were vaccinated and 60 077 persons left unvaccinated. Thus the unvaccinated persons constituted 14.3% of the population of that age.

In all republics the vaccine was administered in two stages at an interval of one month. The first dose—type 1 vaccine—was given in April, and the second—divaccine of types 2 and 3—in May 1959. On 1 June 1959, i.e., two weeks after completion of the second immunization and one-and-a-half months after completion of the first, our study of the epidemiological effectiveness of the vaccination began.

STUDY OF THE IMMUNOLOGICAL STRUCTURE OF THE POPULATION BEFORE AND AFTER VACCINATION

The great importance of humoral indices in the blood of children and adults for the epidemiological prognosis of poliomyelitis and a properly based evaluation of the results of immunization is well known.

When we began immunization with the live vaccine we determined the percentage of persons susceptible to poliomyelitis in the various age-groups to be immunized in relation to the different virus serotypes. For this purpose, the sera of the groups of population to be investigated, taken before vaccination, were subjected to the colour test in a dilution of 1:4 in the presence of 100 minimum doses of virus and monkey kidney cells (Kurnosova & Zhilova, 1960).

More than 1500 serum tests showed the existence in various geographical areas of the USSR of quite a high percentage of susceptible children. This percentage was at its maximum among children up to 2-4 years of age (60% and over) and gradually fell towards the age of 10-12 (Table 3).

TABLE 3

PERCENTAGE OF SERA IN CHILD AGE-GROUPS NEGATIVE TO POLIOVIRUS IN LENINGRAD, NOVGOROD OBLAST, LATVIAN SSR, MOLDAVIAN SSR AND BYELORUSSIAN SSR

Age-group (years)	Percentage negative to type 1					Percentage negative to type 2					Percentage negative to type 3					Percentage triply negative				
	Leningrad	Novgorod oblast	Latvian SSR	Moldavian SSR	Byelorussian SSR	Leningrad	Novgorod oblast	Latvian SSR	Moldavian SSR	Byelorussian SSR	Leningrad	Novgorod oblast	Latvian SSR	Moldavian SSR	Byelorussian SSR	Leningrad	Novgorod oblast	Latvian SSR	Moldavian SSR	Byelorussian SSR
0-2	77	63	64	64	60	72	87	78	79	65	64	82	66	64	65	48	48	41	34	36
3-4	41	31	42	28	45	41	60	50	38	54	48	47	35	39	50	23	15	20	9	22
2-6	28	18	25	20	40	38	46	41	25	53	37	35	23	29	26	18	6	6	5	0
7-9	29	18	25	20	31	26	42	39	21	37	29	33	29	26	38	14	6	4	4	13
10-12	26	11	19	15	35	26	33	34	19	50	37	30	27	22	27	7	4	0	3	20

TABLE 4

PROBABLE NUMBER OF PERSONS SUSCEPTIBLE TO POLIOMYELITIS AMONG THE POPULATION IMMUNIZED WITH LIVE VACCINE ON THE BASIS OF THE PERCENTAGE OF SERA SEROLOGICALLY NEGATIVE TO POLIOVIRUS TYPES 1, 2 AND 3 (MOLDAVIAN SSR)

Age-group (years)	No. in group vaccinated	Persons susceptible on basis of results of colour test with serum diluted 1:4									Probable number of susceptible persons without antibodies to the types indicated			
		No. investigated	Type-1 negative		Type-2 negative		Type-3 negative		Triply negative		1	2	3	Triply negative
			No.	%	No.	%	No.	%	No.	%				
¾-2	72 274	138	79	57.2	99	71.7	81	58.7	39	28.3	41 300	51 800	42 400	20 500
3-6	80 551	107	24	22.4	30	28.0	34	31.8	7	6.5	18 000	22 600	25 600	5 200
7-9	120 872	81	16	19.8	19	23.5	20	24.7	4	4.9	23 900	28 400	29 900	5 900
10-14	80 910	95	15	15.8	18	18.9	21	22.1	3	3.2	12 800	15 300	17 900	2 600
15-18	52 905[1]	84	8	9.5	13	15.5	14	16.7	2	2.4	5 000	8 200	8 800	1 300
Total	407 512	505	142		179		170		55		101 000	126 300	124 600	35 500

TABLE 5. SUSCEPTIBILITY TO POLIOMYELITIS OF CHILD POPULATION IN BYELORUSSIAN SSR BEFORE VACCINATION AND SIX MONTHS AFTER DOUBLE IMMUNIZATION WITH LIVE VACCINE

Age-group (years)	Before vaccination					After vaccination				
	No. examined	Percentage without antibody to poliovirus type:				No. examined	Percentage without antibody to poliovirus type:			
		1	2	3	All		1	2	3	All
0- 2	55	60	65	65	36	60	20	13	20	0
3- 4	22	45	54	50	22	11	10	0	9	9
5- 6	15	40	53	26	0	30	0	0	6	0
7- 9	45	31	37	38	13	27	4	15	22	4
10-12	48	35	50	27	20	43	12	14	16	0
13-15	35	28	31	17	0	29	10	3	3	0
Total	220					200				

TABLE 6. SUSCEPTIBILITY TO POLIOMYELITIS OF CHILD POPULATION IN LATVIAN SSR BEFORE VACCINATION AND SIX MONTHS AFTER DOUBLE IMMUNIZATION WITH LIVE VACCINE

Age-group (years)	Before vaccination					After vaccination				
	No. examined	Percentage without antibody to poliovirus type:				No. examined	Percentage without antibody to poliovirus type:			
		1	2	3	All		1	2	3	All
0- 2	67	64	78	66	41	33	0	10	3	0
3- 4	45	42	50	35	20	30	10	13	13	0
5- 6	44	25	41	23	6	41	10	5	22	0
7- 9	72	25	39	29	4	67	2	1	12	0
10-12	43	19	34	27	0	84	2	5	14	0
13-15	25	16	22	4	0	78	1	1	5	0
16-20	22	18	18	10	0	56	10	6	16	0
Total	318					389				

TABLE 7. SUSCEPTIBILITY TO POLIOMYELITIS OF CHILD POPULATION IN MOLDAVIAN SSR BEFORE VACCINATION AND SIX MONTHS AFTER DOUBLE IMMUNIZATION WITH LIVE VACCINE

Age-group (years)	Before vaccination					After vaccination				
	No. examined	Percentage without antibody to poliovirus type:				No. examined	Percentage without antibody to poliovirus type:			
		1	2	3	All		1	2	3	All
¾- 2	138	57	72	59	28	91	14	18	33	0
3- 6	107	22	28	32	7	104	5	4	14	1
7- 9	81	20	23	25	5	148	3	1	3	0
10-14	95	16	19	22	3	121	1	0	0	0
15-18	84	10	15	17	2	80	6	4	3	0
Total	505					544				

Parallel examinations of all negative sera by testing neutralization of the cytopathogenic action of the virus in monolayer tissue cultures showed that the proportion given by the colour test was 5%-10% too high. Taking into account the fact that a similar correction is necessary for sera examined by the colour test after completion of vaccination, we took the percentage of negative sera as a relative index of actual susceptibility.

Re-estimation of the susceptible population based on the computed percentages of negative sera shows that more than 25% of the population in the regions surveyed was succeptible to one of the poliovirus serotypes, and 10%-15% belonged to the most highly susceptible group (triply negative). Table 4 gives an example of this calculation for the vaccinated population in the Moldavian SSR.

With 25% of susceptible children among the 1 700 000 persons we vaccinated, we had no fewer than 400 000 persons susceptible to type 1, 2 or 3 and more than 100 000 triply negative children. If a poliomyelitis virus capable of reverting to one of the existing pathogenic strains had been administered to this number of children, about 2000 cases of paralytic poliomyelitis could have been expected among them, caused by the slightly virulent, moderately virulent and highly virulent strains of type 1, and about 400 cases of poliomyelitis caused by types 2 and 3 similar to the naturally encountered viruses. In actual fact, despite the administration to hundreds of thousands of children of a highly active vaccine virus which began to circulate intensively among the healthy contacts, not only was no increase in the number of cases of poliomyelitis recorded in the months immediately following immunization in the areas covered by the campaign, but, on the contrary, a marked diminution in poliomyelitis morbidity was observed compared with what had been expected on the basis of the incidence among the external control group, among whom the live vaccine had not been used.

The twofold immunization carried out in April-May 1959 brought about essential changes in the immunological structure of the population by decreasing between fourfold and eightfold the percentage of susceptible children and young people (Tables 5, 6 and 7).

The third immunization, completed in a number of places by means of the trivaccine containing 100 000 cytopathogenic doses of each type, caused a further and very sharp change in the quantitative antibody level, reducing the percentage of susceptible children among the most severely threatened groups (4 years old and under) to between 2% and 5% (Table 8).

TABLE 8

IMMUNOLOGICAL ACTIVITY OF LIVE POLIOVIRUS VACCINE IN RELATION TO SCHEDULE OF IMMUNIZATION AND AGE-GROUP (BASED ON RANDOM OBSERVATION OF 4006 CHILDREN)

Poliovirus type	Vaccination group [a]	Percentage [b] without antibody to poliovirus tested in indicated age-group					
		¾-2 years	3-4 years	5-6 years	7-9 years	10-12 years	13-14 years
1	A	69	33	21	23	18	20
	B	19	5	4	2	3	2
	C	1	1	0	0	0	0
2	A	70	50	35	40	37	20
	B	10	6	1	2	3	2
	C	0	0.9	0	0	0	0
3	A	70	42	31	30	26	15
	B	31	13	5	7	7	3
	C	4	2	0	0	0	0
1+2+3	A	41	13	5	6	6	3
	B	1	0.7	0	0.3	0	0
	C	0	0.6	0	0	0	0

[a] Group A: no vaccination.
Group B: vaccinated twice (monovaccine of type 1 + divaccine of types 2 and 3).
Group C: vaccinated 3 times (monovaccine of type 1 + divaccine of types 2 and 3 + trivaccine of types 1, 2 and 3).

[b] The percentage value was estimated on 200-300 samples of sera examined in each of the 18 groups tested.

These results demonstrate the high degree of immunogenicity of the live vaccine administered in three stages—a monovaccine of type 1, a divaccine of types 2 and 3, and a trivaccine of types 1, 2 and 3—which almost completely eliminated susceptibility among the population, giving them protection against all three serotypes of the virus.

EFFECT OF VACCINATION ON SEASONAL INCIDENCE

The changes in the incidence of paralytic cases of poliomyelitis in the Byelorussian, Latvian and Moldavian Republics and also in the Novgorod

TABLE 9

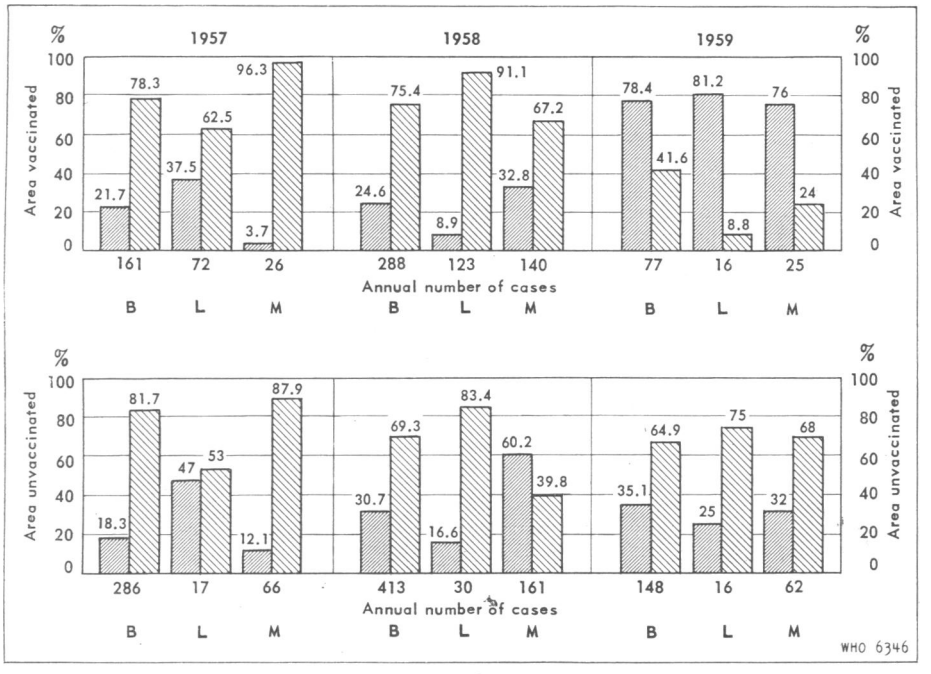
SEASONAL DYNAMICS OF PARALYTIC POLIOMYELITIS IN BYELORUSSIA, LATVIA AND MOLDAVIA IN 1957-59 IN REGIONS COVERED AND NOT COVERED BY 1959 VACCINATION CAMPAIGN

Republic	Year	1959 vaccination region [a]	Number of cases of paralytic poliomyelitis													Annual rate per 100 000 persons under 7 years
			Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total	
Byelorussia	1957	+	5	5	3	4	4	14	20	30	29	23	6	18	161	38.3
		—	6	8	5	5	6	21	59	58	43	33	18	24	283	29.7
	1958	+	11	6	12	6	15	21	62	48	47	35	16	9	288	67.7
		—	20	10	26	13	13	45	49	53	82	51	31	20	413	43.1
	1959	+	9	5	5	5	12	9	5	8	6	6	6	1	77	18.1
		—	8	12	3	12	17	12	20	20	19	11	11	7	152	15.8
Latvia	1957	+	11	5	4	2	3	2	6	9	12	13	3	2	72	41.8
		—	2	0	1	2	0	3	1	4	2	0	0	2	17	25.0
	1958	+	0	3	1	2	2	3	17	28	18	22	17	10	123	71.5
		—	2	1	0	0	0	2	3	6	6	1	6	3	30	44.2
	1959	+	4	2	5	1	0	1	0	2	0	1	0	0	16	9.3
		—	0	1	0	0	0	3	6	3	1	2	0	0	16	23.6
Moldavia	1957	+	0	0	0	1	0	0	0	0	3	7	8	7	26	10.4
		—	0	3	0	2	2	1	2	16	25	11	2	2	66	30.4
	1958	+	1	5	3	3	7	21	30	16	28	12	5	3	134	49.6
		—	7	17	33	14	3	23	19	22	17	4	0	2	161	74.3
	1959	+	4	5	2	3	1	4	1	2	0	1	1	1	25	10.0
		—	5	1	7	1	1	5	3	12	10	13	3	1	62	28.6

[a] + = Region covered by vaccination in 1959. — = Region not covered by vaccination in 1959.

FIG. 1

DISTRIBUTION OF PARALYTIC POLIOMYELITIS[a] IN BYELORUSSIA (B), LATVIA (L) AND MOLDAVIA (M) IN FIRST AND SECOND HALF-YEARS OF 1957-59 IN THE AREAS IN WHICH LIVE VACCINE WAS AND WAS NOT ADMINISTERED IN 1959



Percentage of cases in first six months.

Percentage of cases in second six months.

[a] Expressed as the percentage of all cases for the year.

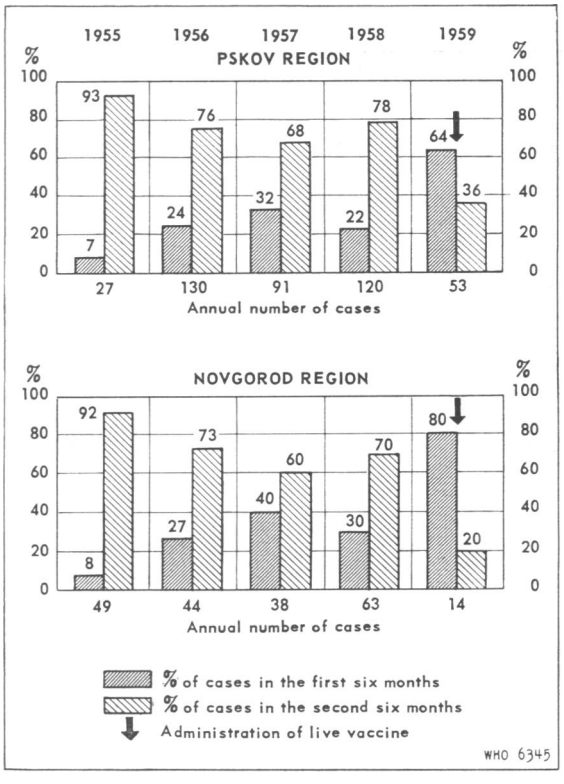
and Pskov oblasts of the RSFSR, where, among the population covered by the mass immunization campaign, there was for the first time in recent years a complete absence of the seasonal rise which usually takes place in the period from June to October, are very significant. The same phenomenon was also found among the whole population in the area under vaccination including both vaccinated and unvaccinated children (internal control), among whom cases were very sharply reduced as a result of the vaccination of a considerable proportion of the child population. These radical breakdowns in the usual seasonal rise in poliomyelitis in these areas in the first and second half-years constitute a convincing illustration of the effectiveness of the live vaccine (Table 9; Fig. 1 and 2).

The same thing is demonstrated even more clearly by data on distribution of the paralytic cases of poliomyelitis recorded in the period after completion of vaccination—i.e., in June-December 1959 and January-February 1960—among children of various ages inoculated and not inoculated with the live vaccine in the various republics (Table 10).

We obtained particularly clear-cut results showing the effectiveness of the live vaccine in June-December 1959 and in January-February 1960 in the Byelorussian SSR. Among the 74 868 children of up to 3 years of age to whom the live vaccine was administered, two cases of paralytic poliomyelitis were recorded in the period of observation. At the same time, among the 77 612 uninoculated children of the same age in potential contact with them, 31 paralytic cases were reported. This indicates a 15-fold reduction in the incidence of the disease among the vaccinated compared with the incidence which could have been expected

FIG. 2

DISTRIBUTION OF PARALYTIC POLIOMYELITIS [a] IN PSKOV AND NOVGOROD REGIONS IN FIRST AND SECOND HALF-YEARS OF 1955-59



[a] Expressed as the percentage of all cases for the year.

otherwise and an eightfold reduction compared with the actual incidence among the external control groups.

The effectiveness of the live vaccine among the older groups of pre-school and school-age children is expressed by the achievement of a moderate reduction. This is due to the lower incidence of poliomyelitis in the corresponding control groups aged 3-7 and 7-14 years. The total annual morbidity index was 1.5 per 100 000 for the whole of the vaccinated group, 17.8 for the internal control, and 7.4 for the external control group (Table 11).

The higher incidence of poliomyelitis among the internal control group in the Byelorussian SSR (urban children in contact with those inoculated) as compared with the external control (rural children not in contact with the inoculated) may be ascribed to the higher incidence of poliomyelitis among children in the towns which had been observed in all the previous years (Fig. 3). By calculating the number of cases anticipated among persons vaccinated with the live vaccine on the basis of the number of cases among the unvaccinated in the internal (contact) control group, we would have expected 45 cases of paralytic poliomyelitis among them instead of the six which actually occurred.

In the Moldavian SSR, among the 354 607 children up to 14 years of age who were vaccinated, two paralytic cases of poliomyelitis were recorded. Among the same age-group serving as internal control (118 437 persons, equivalent to about one-third of the vaccinated group), there were nine cases of paralytic poliomyelitis—a significant reduction in morbidity. Compared with the unvaccinated groups forming the external control, where there were 41 cases out of 331 533 children or 21.2 per 100 000 *per annum*, the probable reduction in the incidence of the disease was still greater (Table 12).

In the Latvian SSR in 1959, 242 940 children up to 14 years of age were vaccinated. Among these, in June-December 1959 there was one case of paralytic poliomyelitis as against the 17 cases which could have been expected on the basis of morbidity in the control groups where live vaccine was not administered (Table 13).

In all the previous years the number of poliomyelitis cases in the regions used for external

FIG. 3

SEASONAL DYNAMICS OF PARALYTIC POLIOMYELITIS IN BYELORUSSIA OVER THE PERIOD 1957-60 IN THE AREAS IN WHICH LIVE VACCINE WAS AND WAS NOT ADMINISTERED IN 1959

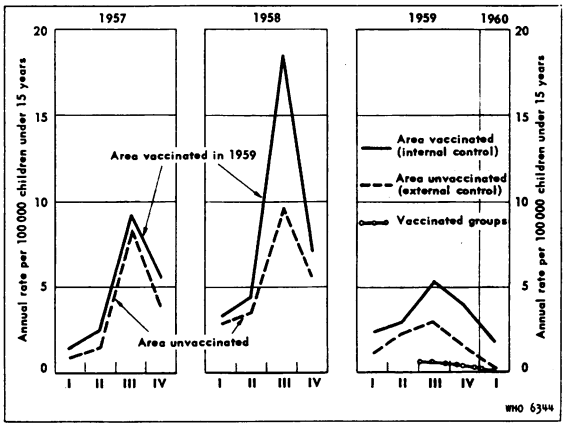


TABLE 10

NUMBER OF CASES OF PARALYTIC POLIOMYELITIS OCCURRING IN THE 1959 EPIDEMIC SEASON IN AREAS OF BYELORUSSIA, LATVIA AND MOLDAVIA COVERED AND NOT COVERED BY IMMUNIZATION

Republic	Period of observation	Age-group (years)	Unvaccinated (external control)			Unvaccinated (internal control)			Vaccinated with live vaccine			No. of poliomyelitis cases anticipated
			No. of persons	No. of cases		No. of persons	No. of cases		No. of persons	No. of cases		
				Total	Annual rate per 100 000		Total	Annual rate per 100 000		Total	Annual rate per 100 000	
Byelo-russia	June-Dec. 1959 + Jan.-Feb. 1960	¾-2	344 076	73	28.2	77 612	31	53.3	74 868	2	3.6	30 [a]
		3-6	614 350	21	4.6	152 353	9	7.8	119 897	3	3.3	7 [a]
		7-14	977 375	13	1.8	85 371	2	3.1	347 754	1	0.4	8 [a]
		Total	1 935 801	107	7.4	315 336	42	17.8	542 519	6	1.5	45
Moldavia	June-Dec. 1959	¾-2	87 375	36	70.6	63 755	9	24.2	72 274	2	4.7	10 [a]
		3-6	79 301	4	8.6	30 543	0	0	80 551	0	0	4 [b]
		7-14	164 857	1	1.0	24 139	0	0	201 782	0	0	1 [b]
		Salk vaccine:										
		¾-14	49 601	6	20.7	25 373	1	6.8				
		Total	381 134	47	21.1	143 810	10	11.9	354 607	2	1.0	15
Latvia	June-Dec. 1959	¾-2	32 103	1	5.3	56 065	2	6.1	27 840	0	0	1 [b]
		3-6	35 744	3	14.4	32 752	0	0	55 349	0	0	5 [b]
		7-14	73 488	5	11.7	18 055	0	0	159 751	1	1.0	11 [b]
		Total	141 335	9	10.9	106 872	2	3.2	242 940	1	0.7	17

[a] Based on morbidity in the internal control group.
[b] Based on morbidity in the external control group.

TABLE 11

ANALYSIS OF THE INCIDENCE OF POLIOMYELITIS IN BYELORUSSIA IN NINE MONTHS OF 1959-60

Group	Age-group (years)	Population in group		No. of poliomyelitis cases in month indicated									Total cases for 9-month period	Annual rate per 100 000	No. of cases anticipated among persons vaccinated [a]
				1959							1960				
		No.	%	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Jan.	Feb.			
Vaccinated with live vaccine	5/12-2	74 868	13.8	—	—	1	—	—	—	—	—	1	2	3.6	30
	3-6	119 897	22.1	—	—	—	1	2	—	—	—	—	3	3.3	7
	7-14	347 754	64.1	—	—	—	1	—	—	—	—	—	1	0.4	8
	Total	542 519	100	—	—	1	2	2	—	—	—	1	6	1.5	45
Unvaccinated (internal control)	5/12-2	77 612	24.6	4	3	6	4	4	3	2	4	1	31	53.3	
	3-6	152 353	48.3	5	2	1	—	—	1	—	—	—	9	7.9	
	7-14	85 371	27.1	—	—	—	—	—	2	—	—	—	2	3.1	
	Total	315 336	100	9	5	7	4	4	6	2	4	1	42	17.8	
Unvaccinated (external control)	5/12-2	344 076	17.8	8	17	14	14	7	4	5	4	—	73	28.3	
	3-6	614 350	31.7	3	3	4	4	2	2	2	1	—	21	4.6	
	7-14	977 375	50.5	1	—	2	1	2	5	—	2	—	13	1.8	
	Total	1 935 801	100	12	20	20	19	11	11	7	7	—	107	7.4	

[a] Computed from unvaccinated (internal control) group.

TABLE 12

DISTRIBUTION OF PARALYTIC POLIOMYELITIS CASES IN JUNE-DECEMBER 1959 IN AREAS COVERED AND NOT COVERED BY IMMUNIZATION IN MOLDAVIAN SSR

Group	Vaccine administration	Age-group (years)	Population in group		No. of paralytic poliomyelitis cases in months indicated								Annual rate per 100 000	No. of cases anticipated
			No.	%	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total		
I Vaccinated	Live vaccine [a]	¾- 2	72 274	20.4	—	—	2	—	—	—	—	2	4.7	10 [b]
		3- 6	80 551	22.7	—	—	—	—	—	—	—	—	0	4 [c]
		7-14	201 782	56.9	—	—	—	—	—	—	—	—	0	1 [c]
		Total	354 607	100	—	—	2	—	—	—	—	2	1.0	15
II Internal control	Salk vaccine, 3 times	¾- 2	10 848	7.5	1	—	—	—	—	—	—	1	15.8	
		3- 6	11 938	8.3	—	—	—	—	—	—	—	—	0	
		7-14	2 587	1.8	—	—	—	—	—	—	—	—	0	
		Total	25 373	17.6	1	—	—	—	—	—	—	1	6.8	
III Internal control	Unvaccinated	¾- 2	63 755	44.3	3	1	2	—	1	1	1	9	24.2	
		3- 6	30 543	21.2	—	—	—	—	—	—	—	—	0	
		7-14	24 139	16.8	—	—	—	—	—	—	—	—	0	
		Total	118 437	82.4	3	1	2	—	1	1	1	9	13.0	
II + III. Grand total internal controls			143 810	100	4	1	2	—	1	1	1	10	11.9	
IV External control	Unvaccinated	¾- 2	87 375	22.9	4	2	9	9	10	1	1	36	70.6	
		3- 6	79 301	20.8	1	—	1	1	1	—	—	4	8.6	
		7-14	164 857	43.3	—	—	—	—	—	1	1	1	1.0	
		Total	331 533	87.0	5	2	10	10	11	2	1	41	21.2	
V External control	Salk vaccine, 3 times	¾- 2	19 902	5.2	—	—	1	—	2	—	—	3	25.8	
		3- 6	29 699	7.8	—	1	1	—	—	1	—	3	17.3	
		7-14	0	0	—	—	—	—	—	—	—	—	—	
		Total	49 601	13.0	—	1	2	—	2	1	—	6	20.7	
IV + V. Grand total external controls			381 134	100	5	3	12	10	13	3	1	47	21.1	

[a] 52 905 persons in the age-group 15-18 years were also immunized with live vaccine but are excluded from this table since none of the control groups includes this age-group.

[b] Calculated on the basis of unvaccinated group III (internal control). [c] Calculated on the basis of unvaccinated group IV (external control).

TABLE 13

ANALYSIS OF THE INCIDENCE OF POLIOMYELITIS IN LATVIA IN SEVEN MONTHS OF 1959

Group	Age-group (years)	Population in group		No. of poliomyelitis cases in month indicated							Total for 7-month period	Annual rate per 100 000	No. of cases anticipated among persons vaccinated[a]
		No.	%	June	July	Aug.	Sept.	Oct.	Nov	Dec.			
Vaccinated with live vaccine[b]	¾- 2	27 840	11.5	—	—	—	—	—	—	—	0	0	1
	3- 6	55 349	22.8	—	—	—	—	—	—	—	0	0	5
	7-14	159 751	65.8	—	—	1	—	–	—	—	1	1.0	11
	Total	242 940	100	—	—	1	—	—	—	—	1	0.7	17
Unvaccinated (internal control)	¾- 2	56 065	52.5	1	—	—	—	1	—	—	2	6.1	
	3- 6	32 752	30.6	—	—	—	—	—	—	—	0	0	
	7-14	18 055	16.9	—	—	—	—	—	—	—	0	0	
	Total	106 872	100	1	—	—	—	1	—	—	2	3.2	
Unvaccinated (external control)	¾- 2	32 103	22.7	—	1	—	—	—	—	—	1	5.3	
	3- 6	35 744	25.3	—	1	2	—	—	—	—	3	14.4	
	7-14	73 488	52.0	1	1	2	1	—	—	—	5	11.7	
	Total	141 335	100	1	3	4	1	—	—	—	9	10.9	

[a] Computed from unvaccinated (external control) group.

[b] Persons in the age-group 15-30 years who were also immunized with live vaccine are excluded from this table since neither control group includes this age-group.

control had not exceeded 20% of the number recorded in the areas in which vaccination was carried out in 1959. In the year under consideration, in seven months nine poliomyelitis cases were recorded among 141 335 unvaccinated children up to 14 years of age, i.e., 10.9 per 100 000 *per annum*, as against 0.7 per 100 000 among the children in the vaccinated group and 3.2 per 100 000 among the 106 872 children of the internal control group.

The probable reduction of morbidity in the Latvian SSR among the children vaccinated with the live vaccine is not so evident as it was in Byelorussia and Moldavia when account is taken of the negligible number of cases in the internal control group and the very untypical age distribution of poliomyelitis cases in the external control group.

According to preliminary figures collected in the Pskov oblast, the incidence among those inoculated with the live vaccine also decreased very significantly.

CONCLUSIONS

The study of live poliomyelitis vaccine carried out in 1959 under our guidance in the Latvian, Byelorussian, Moldavian and Russian Republics in 1 700 000 inoculated persons has established the innocuity of the product used, which was made from attenuated Sabin strains, and proved its high degree of epidemiological effectiveness.

In all republics and oblasts where live vaccine was administered to the bulk of the susceptible child population under 14 years of age, radical changes took place in the seasonal dynamics of poliomyelitis morbidity. In areas of mass immunization the seasonal rise in the incidence of poliomyelitis did not occur at all, while it was observed in the same months among unvaccinated children in areas where live vaccine was not given.

The number of paralytic cases of poliomyelitis among children to whom the live vaccine had been administered proved quite negligible compared with the number among the uninoculated groups of children of the same age. The indices of the effectiveness of the live vaccine were highest (15-fold) in the very young children, among whom most cases occurred in the control groups, and fell in the older age-groups parallel with the fall in incidence in the control groups. The mean minimum index of effectiveness varied in the different republics from sixfold to tenfold.

The live vaccine proved considerably more effective than three injections of the Salk inactivated vaccine when both preparations were studied in the most highly comparable conditions.

The fairly high incidence of paralytic poliomyelitis among children in the internal control groups in 1959, i.e., among children in potential contact with those to whom the live vaccine had been administered, demonstrates the unreliability and irregular nature of "blind" immunization by means of the circulating vaccine virus. This underlines the need for universal and obligatory immunization of all children with the live vaccine, a procedure which will produce the best immunological effect and will lead to the maximum displacement of the "wild" pathogenic viruses.

We may summarize as follows the conclusions to be drawn from these studies and the plans for future action that flow from them:

1. The live poliomyelitis vaccine made from attenuated Sabin strains which we studied is completely harmless and carries no threat of the vaccine strains reverting to a more virulent state.

2. Mass immunization by this method is extremely convenient and simple and ensures the widest possible coverage of the population within a very short period—two or three weeks in each cycle of vaccination.

3. The absence in the vaccinated children of any general or local reactions which differ in frequency from similar symptoms in the uninoculated external control groups provides an adequate basis for sharply reducing the list of contraindications to the use of live vaccine when other inoculations are being carried out.

4. The high degree of epidemiological effectiveness of the live vaccine shown by our observations in 1959 in four Republics fully justifies the proposal to cease further use of the less effective Salk vaccine and to go over completely from 1960 onwards to immunization with the live vaccine.

Only the live vaccine is capable of meeting quickly in practice the demands of many countries for an effective vaccine, by virtue of its cheapness and the fact that it can be produced on a very large scale.

5. The relatively high incidence of poliomyelitis among unvaccinated child contacts indicates the need to carry out universal administration of the live vaccine, as in the case of smallpox or diphtheria immunization. Only such widespread immu-

nization, carried out under strict State control, will make it possible gradually to eliminate the reservoir of wild pathogenic strains, and to suppress their circulation, thus leading inevitably to the eradication of poliomyelitis as a dangerous, large-scale infection of children.

6. For the forthcoming mass immunization, it will be advisable to administer the live vaccine three times, in accordance with the following optimum schedule: the first inoculation with a monovaccine of type 1, the second with a divaccine of types 2 and 3, the third with a trivaccine of types 1, 2 and 3, administered at intervals of four to six weeks. This schedule ensures two administrations of each virus serotype in the course of the triple immunization; it is convenient in practice; and, to judge from immunological findings, it is more effective than the administration of monovalent vaccines unless such administration is followed by a fourth revaccination with trivaccine.

7. In 1960 the age-groups to be immunized in the USSR can be restricted to those up to 16-20 years, whose need for immunization is greatest. The comparatively rare cases of illness among older people in the USSR are caused by infection with viruses circulating among children and young people.

8. The elimination of the main reservoir of the virus—i.e., that among children and young people up to 20 years of age—will inevitably greatly assist in eliminating the virus among the older population in the Soviet Union, who may be included in the immunization campaign at a later stage with a view to reducing as completely as possible the circulation of pathogenic wild viruses.

RÉSUMÉ

En 1959, 1,7 million d'enfants et d'adolescents ont été vaccinés contre la poliomyélite dans les Républiques de Lettonie, de Byélorussie, de Moldavie et de Russie, au moyen du vaccin vivant préparé en URSS à partir des souches de Sabin. Les auteurs décrivent l'organisation des campagnes et leurs résultats. Ils concluent que là où le vaccin a été administré à l'ensemble des enfants réceptifs, âgés de moins de 14 ans, la courbe saisonnière de morbidité a changé d'allure. Dans les régions où l'on a procédé à une vaccination de masse, le clocher annuel ne se forma pas, alors qu'il se produisit dans les populations d'enfants non vaccinés. Dans le premier groupe, le nombre des cas paralytiques peut être considéré comme négligeable par rapport à celui du groupe non vacciné. L'indice d'efficacité le plus élevé a été observé chez les jeunes enfants — ceux aussi qui furent le plus touchés, dans le groupe témoin. L'indice minimum moyen a présenté de larges variations d'une République à l'autre.

La fréquence relativement élevée de la forme paralytique dans le groupe non vacciné, mais resté en contact étroit avec les vaccinés, indique qu'il ne faut pas trop compter sur les avantages de l'immunisation secondaire, par ricochet, qu'assurerait la circulation d'un virus-vaccin dans la collectivité. Ces résultats parlent au contraire en faveur de l'immunisation directe, systématique et obligatoire, de tous les enfants, ce qui aura pour conséquence à longue échéance l'élimination des virus « sauvages ».

L'absence de réactions fâcheuses spécifiques du vaccin — par comparaison avec les groupes non vaccinés — semble permettre de réduire la liste des contre-indications, au cas où des injections d'autres vaccins devraient être pratiquées. Les résultats obtenus dans les quatre Républiques mentionnées justifient la proposition de renoncer à l'immunisation par vaccin tué pour n'appliquer que la vaccination par virus vivant. Cette vaccination devrait être aussi généralisée que la vaccination antivariolique ou antidiphtérique. Seule une prévention massive, strictement surveillée et contrôlée, peut aboutir à l'élimination graduelle des virus sauvages dans la collectivité.

L'administration du vaccin se fera avantageusement en trois fois: vaccin monovalent (type 1), vaccin bivalent (types 2 et 3), vaccin trivalent (1, 2, 3), à intervalles de 4-6 semaines. Ce schéma semble plus efficace que celui qui comporte des vaccins monovalents seulement, à moins que ces derniers ne soient suivis de l'administration d'une quatrième dose, de vaccin trivalent.

Il semble qu'en 1960, on puisse limiter la vaccination, en URSS, aux sujets jusqu'à 16 ou 20 ans, car les rares cas survenus chez des individus plus âgés avaient pour origine des infections d'enfants ou d'adolescents.

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