Some Results of the Work on Mass Immunization in the Soviet Union with Live Poliovirus Vaccine prepared from Sabin Strains*

M. P. CHUMAKOV, M. K. VOROSHILOVA, S. G. DROZDOV, S. G. DZAGUROV, V. A. LASHKEVICH, L. L. MIRONOVA, N. M. RALPH, A. V. GAGARINA, E. E. ASHMARINA, G. A. SHIRMAN, G. P. FLEER, E. A. TOLSKAYA, I. S. SOKOLOVA, L. B. ELBERT & K. M. SINYAK

> In the course of campaigns for the mass immunization of large segments of the population of the Soviet Union with live poliovirus vaccine prepared in the USSR from attenuated Sabin strains, some 15 200 000 persons received oral vaccine in 1959 and over 77 478 800 persons (mainly between 2 months and 20 years old) in 1960. Approximately 95 % of these were given the vaccine incorporated in dragées.

> The present paper gives data on the safety and immunological activity of the live vaccine, on virus carriage and transmission of the vaccine virus to contacts, and on virus interference.

> In a comparison between poliomyelitis incidence in 1960 in regions where mass live vaccine immunization had been carried out and the incidence in areas where inactivated Salk vaccine was used in 1958-60, it is shown that, while the Salk vaccine did not fundamentally influence the epidemic process, the Sabin live vaccine brought about a sharp reduction in incidence and prevented the usual summer-autumn rise in the number of poliomyelitis cases.

> It is concluded from the two years' experience in the mass use of live vaccine from Sabin strains that poliomyelitis epidemics can be prevented.

INTRODUCTION

The principal results of the work carried out in 1959, under the guidance of workers of the Institute for Poliomyelitis Research of the USSR Academy of Medical Sciences, on mass immunization of the population in the Soviet Union with live poliovirus vaccine from Sabin's strains (Sabin, 1957, 1959a, 1959b) have already been published in a special report in Russian and English (Chumakov et al., 1959b, 1960).

These results were discussed in detail on two occasions and approved by the Presidium of the USSR Academy of Medical Sciences. On the basis of recommendations of that Presidium and resolutions passed by the Board of the USSR Ministry of Public Health, an order was issued by the Minister of Health on 16 December 1959, providing for mass immunization of the population aged two months to 20 years with poliovirus vaccine during 1960, and mainly up to July of that year. This involved about 35% of the total population, or about 77 million persons. On this number about 74 250 000 persons were to be vaccinated with live poliovirus vaccine and 3 000 000 persons with inactivated vaccine (Salk) only.

For the first time in the USSR—and, indeed, in the world—the immense task was to be undertaken of immunizing tens of millions of persons in one year with the aim of eradicating epidemic manifestations of poliomyelitis throughout a vast area. Further developments in specific poliomyelitis prophylaxis in the country and in other countries depend to a considerable extent on the successful fulfilment of this task.

We are now in a position to communicate briefly some preliminary results achieved in 1959-60 in that part of a large programme of live poliovirus

^{*} From the Institute for Poliomyelitis Research, USSR Academy of Medical Sciences, Moscow, USSR.

vaccination with which the Institute for Poliomyelitis Research was concerned.

First, however, we should like to mention the outstanding part played by Professor Albert B. Sabin. He successfully selected three types of poliovirus vaccine strains, thoroughly tested and evaluated them and provided us with original seed material for the preparation in the USSR of live vaccine in the quantities necessary for mass immunization. On many occasions he gave us great help by sharing his vast knowledge of poliomyelitis problems and was very active in organizing fruitful international collaboration among virologists in matters concerning the investigation and large-scale use of live poliovirus vaccine.

Poliomyelitis is a severe but relatively rare disease. Nevertheless, it proved necessary to adopt extremely wide-ranging measures for creating artificial immunity against the disease in the total population of the country by immunization in a short period of time. This was so because poliomyelitis is an infection with a large number of completely asymptomatic torms which are difficult to diagnose; and therefore only with the most extensive measures ensuring rapid development of artificial immunity in the entire susceptible population is it possible to strike at the root of the problem and to avert the menace of poliomyelitis epidemics.

To achieve this, it is necessary to have an effective, readily available, completely harmless, non-reactogenic vaccine, which will give rise to no difficulties when put to the widest use.

Trials of live poliovirus vaccine carried out in a number of countries, and particularly in the USSR in 1959, furnished convincing proof that live vaccine is the most suitable for mass immunization.

A great advantage of the live vaccine over the killed Salk vaccine lies in the possibility it affords of creating in vaccinated persons more or less complete immunological resistance of tissue cells in the portals of entry of infection. This may be expected to bring about a sharp reduction in the circulation of wild epidemic strains of poliovirus among the population as a result of repeated immunization with attenuated viruses. In this way an important basis for inhibiting poliomyelitis epidemics is laid.

One of the most frequent objections raised against the use of live poliovirus vaccine is that the attenuated poliovirus strains may undergo reversion (recurrence or restoration) to pathogenic properties as a result of selection in the human intestinal tract

of virulent virus particles and of repeated passages through the susceptible population.

Much evidence is now available testifying to the fact that the Sabin attenuated strains are of sufficient genetic stability to persist unaltered for several passages through the human body. Theoretically and experimentally, however, it is not possible to exclude entirely the possibility of degeneration occurring in the vaccine strains under the influence of propagation in inappropriate conditions or owing to long-term selection of virulent virus particles and their multiplication on passage through susceptible human beings. We know that under certain conditions it is possible to separate from a vaccine strain more virulent virus particles than those in the original vaccine viruses. The only question is how long or how many passages in cultures or through the human body it will take to restore the neuropathogenicity of the vaccine poliovirus. Numerous data indicate that the process of reversion to or restoration of pathogenicity in adequately purified vaccine strains is considerably longer and less constant than the process of immunity development in the population following ingestion of those strains.

In connexion with this, the principle was put forward (by M. P. Chumakov) in 1958-59 of mass and simultaneous immunization with live poliovirus vaccine throughout an entire district, city or region, so as to ensure the maximum coverage by immunization within the shortest possible time and to minimize the possibility of the long-term circulation of any poliovirus strains among the susceptible population and of any increase in their neurovirulence during serial passages in children.

The process of rapidly spreading immunization should effectively counteract that of reversion, thus eliminating conditions suited to repeated passages. In conducting the mass immunization programmes during 1959 and 1960 we adhered closely to this principle in the organization of live virus vaccine administration.

PROCEDURE

During 1959 mass immunization of the population with live poliovirus vaccine from Sabin strains was conducted on an ever-increasing scale in 14 republics of the Soviet Union. By the end of the year the total number of persons vaccinated throughout the country exceeded 15 200 000. Of these, about 1 670 000 subjects were immunized under the supervision of Professor A. A. Smorodintsev and his

co-workers with vaccine prepared at the Institute of Experimental Medicine in Leningrad, and over 13 500 000 persons under the supervision of our Institute with the vaccine prepared in Moscow.

The total population in the areas where vaccination was done in 1959 numbered about 65 000 000, or approximately one-third of the entire population of the country. Over 2 500 000 persons in 1959 received live vaccine incorporated in dragées (in Azerbaijan, Armenia, Georgia, the Khabarovsk region, and partly in the Moscow region). The remaining eligible persons were each given two drops of liquid vaccine diluted 1: 10, measured with an eye-dropper. The use of live vaccine incorporated in dragées proved to be an important element in facilitating mass poliomyelitis immunization. With the unusually large scope of the programme and the narrow time-limits set for oral immunization, it would have been extremely difficult to ensure the dilution of thawed liquid vaccine and its distribution in drop form by the local medical staff throughout the country.

The Institute for Poliomyelitis Research, in cooperation with the Research Institute of the Confectionery Industry, developed a new presentation of the live vaccine, incorporated first in paste candies and later in dragées. This was done on the basis of data showing that satisfactory preservation of vaccine strains could be achieved in strong solutions of invert sugars and in the sweetmeat mass at sub-zero temperatures for at least three months, at 4°C for about a month and at room temperature for three to five days. Tests to establish whether live vaccine was properly incorporated in dragées and to determine its immunogenicity in that form carried out in 1959 in the town of Klin, Moscow region (Fleer, 1961), and in 1960 in Moscow (Ashmarina, 1961) showed quite satisfactory results which could be favourably compared with those obtained in immunization with liquid vaccine. The investigations of Dobrova (1961) and of Voroshilova et al. (1961) also revealed a quite satisfactory development of immunity in children vaccinated with candied vaccine. Dzagurov & Shmeleva (1961) and Lashkevich et al. (1961) have presented extensive proof of the good preservation of dragée-vaccine at -20° C, at 4° C, and for three to five days at room temperature. The distribution of the virus in individual pieces of dragées was quite satisfactory (variation of titres from 0.1 to 0.25 log₁₀).

The technique of immunization with the vaccine in candy turned out to be extremely convenient and attractive in many respects. All this contributed to

wider use of dragées incorporating live poliovirus vaccine. Production of three to five tons of dragée-vaccine was set up in the Moscow "Marat" confectionery factory.

In 1960 the vast majority of poliomyelitis vaccinations (about 95%) were performed with live vaccine incorporated in dragées, and only 5% with liquid vaccine dispensed in drop form, chiefly for infants unable to suck candies.

Separate papers by members of the Institute for Poliomyelitis Research present information on the conditions of production and control of live vaccine from Sabin strains, preservation at different temperatures of live vaccine incorporated in dragées, standards of inoculation doses, variations of vaccine virus content in individual candies, as well as virological and serological data obtained in investigations of persons given dragée-vaccines (Chumakov et al., 1961; Fleer, 1961; Lashkevich et al., 1961).

In accordance with an order of the Minister of Public Health of the USSR on mass poliomyelitis vaccinations, the Institute for Poliomyelitis Research was entrusted in 1960 with the task of supplying live vaccine and exercising methodological guidance over vaccinations throughout the entire country. In conformity with this, the Institute drew up and the Ministry approved "Methodological instructions for organization of live vaccine immunization" and "Directions for use of dragées with live vaccine for oral immunization against poliomyelitis".

During the twelve months of 1960 the Institute for Poliomyelitis Research distributed throughout the country 263 282 800 doses of live vaccine, prepared in Moscow from Sabin strains (this figure includes monovaccines of types 1, 2 and 3 and trivalent vaccine) (Table 1).

It should be said that since a great deal of work connected with immunization of the population with live poliovirus vaccine had already been done in many republics in 1959, in these republics (Estonia, Lithuania, Georgia, Azerbaijan, Moldavia, Uzbek, Tadzhik, Kirgiz, and Turkmenia) only two feedings (as vaccinations and revaccinations) were given in 1960, first with type 1 monovaccine, and then with trivalent mixture (types 1, 2 and 3). These covered the total population from 2 months to 20 years of age, and in some republics (Uzbekistan, Estonia, Lithuania) up to 35-55 years of age.

In the RSFSR, Byelorussia, Latvia and Armenia monovaccines were given three times in 1960 and subsequently trivalent vaccine was given for revaccination. In some regions of the Ukraine trivalent

	•	TABLE 1		
DISTRIBUTION US		POLIOVIRUS 31 DECEMBI	 IN	THE

Republic	Doses of live vaccine distributed ^a	Estimated number of persons vaccinated b
RSFSR	166 590 800	42 604 150
Ukraine	47 752 300	14 152 778
Kazakh	6 438 700	3 385 184
Uzbek	8 030 000	3 872 000
Byelorussia	12 495 600	2 888 000
Georgia	3 199 200	1 320 000
Azerbaijan	2 991 000	1 261 920
Moldavia	1 545 000	1 007 600
Lithuania	2 750 000	1 760 000
Latvia	2 608 000	880 000
Kirghiz	1 902 000	968 000
Tadzhjik	1 852 200	968 000
Armenia	1 702 000	792 000
Turkmenia	1 478 000	792 000
Estonia	1 948 000	827 240
Total	263 282 800	77 478 872

 $^{^\}alpha$ Including vaccine intended for primary vaccinations and vaccine for revaccination (monovaccines of types 1, 2 and 3, and polyvalent vaccines of types 1 + 3 and 1 + 2 + 3).

vaccine was administered twice, and in the remaining regions of the Ukraine monovaccines were administered separately and trivalent mixture was given later for revaccination.

There are no precise figures available at present showing the actual numbers of those immunized with live vaccine in 1960. But taking into account average losses incidental to the distribution of vaccine during immunization, found in selective checks to be 12%, it may be estimated that up to 31 December 1960 about 77 479 000 persons in the Soviet Union had received all three types of live poliovirus vaccine. Of this number about 5 200 000 persons were over 20 years old, the remaining 72 000 000 being under that age and constituting approximately 92% of the population most susceptible to poliomyelitis. Over 15 000 000 persons immunized with live vaccine in 1959 were revaccinated in 1960. Most

vaccinations were completed by the end of June 1960, the subsequent months being largely devoted to administration of the live vaccine to infants 1-8 months of age. In September 1960 mass immunization with live vaccine began in the Primorsk and Krasnodar regions where previously only killed Salk vaccine had been given, these being the so-called control regions in which no live vaccine had been used.

In addition to the production of supplies necessary to ensure the fulfilment of internal programmes of mass immunization with live poliovirus vaccine, the Soviet Union also furnished over 42 000 000 doses of live vaccine prepared from Sabin strains to a number of other countries (see Table 2).

It goes without saying that poliomyelitis vaccinations of such a scope and at such a pace would have been absolutely impossible with Salk killed vaccine. Only by oral immunization with live poliovirus vaccine incorporated in dragées is it possible to perform mass vaccination of all the susceptible population within a short time. And this guarantees radical prevention of poliomyelitis epidemics.

TABLE 2

DISTRIBUTION OF LIVE POLIOMYELITIS VACCINE FROM
THE USSR TO FOREIGN COUNTRIES

Country	Number of inocula- tion doses	Estimated number o persons vaccinated (in round numbers				
Hungary	7 700 000	2 400 000				
People's Republic of Viet-Nam	4 500 000	950 000				
Bulgaria	6 850 000	2 000 000				
Czechoslovakia	3 500 000 (types 2 and 3)	2 000 000				
German Demo- cratic Republic	18 100 000	5 000 000				
Korean People's Democratic Republic	1 250 000	350 000				
Albania	803 000	450 000				
Chinese People's Republic	9 000	3 000 ^a				
Japan	600	500				
Total	42 712 600	13 153 500				

 $[^]a$ In China, national production of live vaccine from Sabin strains has been started. Over 5 million children under 7 years of age have been immunized in China with this vaccine.

b Estimate based on the assumption that 88% of the vaccine intended for primary vaccinations was actually used. In addition about 5 % of the vaccine received for revaccination was used for primary vaccination.

Poliomyelitis vaccinations were conducted through the local medical establishments on a strictly voluntary basis, with the maximum public co-operation, achieved through mass sanitary propaganda involving the press, radio, television, newsreels, lectures, leaflets, etc.

Advisory teams, consisting of experienced physicians, were organized in a number of vaccination areas for detailed investigations of all cases of involvement of the central nervous system which were suggestive of poliomyelitis. In Estonia and Lithuania epidemiological groups were created for the detection and investigation of all poliomyelitis cases. In addition, special expedition teams were organized in Estonia, Lithuania, the Moscow region, Karaganda, the Krasnodar region, Stalingrad, Rostov and other regions. Over 5000 persons were examined serologically and virologically in vaccination areas.

Laboratory diagnosis in the vaccination areas was made use of on a considerably wider scale in the Baltic republics, Tashkent, Alma-Ata, Karaganda, the Moscow region and other areas. All this enabled us considerably to improve the organization of mass vaccinations and to organize thorough surveys of vaccinated persons, to broaden diagnostic findings with regard to poliomyelitis and to secure adequate and complete recording of all poliomyelitis cases during and after vaccination. In a number of places long-term control observations of the temperature and general condition of the vaccinated and their contacts were made in children's institutions.

RESULTS

From the research work and field trials carried out by our Institute in co-operation with sanitaryepidemiological stations and other scientific institutions, several conclusions may be drawn with regard to the major problems concerning live poliovirus vaccine.

Safety of live vaccine

It can now be taken for granted that the live vaccine from Sabin strains is completely safe and ar eactogenic provided it is prepared with due regard to certain conditions. Large-scale field trials of the vaccine have confirmed this. Safety tests during live vaccine production may still require some simplification and improvement, but even such as they are they ensure highly consistent and reproducible results.

The problem of reversion to pathogenic properties in live poliovirus vaccine strains proved to be practically non-existent under conditions of simultaneous mass immunization of the entire population in a given region. In the Soviet Union there were no poliomyelitis cases on record which could be attributed to the immunization with live vaccine from Sabin strains.

The reactogenicity of live poliovirus vaccine was studied by many physicians in vaccination areas on the basis of the recorded complaints made by vaccinated persons. Specialists hold that under conditions of mass immunization there may be instances when vaccinations coincide with all kinds of symptoms produced by other affections. It was impossible to establish unequivocally any relationship between various complaints and symptoms and the effect of the vaccine. The total number of the so-called reactions to the vaccine itself is quite insignificant (no more than 3 per 100 000). The question of reactogenicity of the live vaccine appears to require some further detailed study, but it is not now of any great practical importance.

Immunological activity of live poliovirus vaccine

Staff from the Institute for Poliomyelitis Research as well as from laboratories in Riga, Tashkent, and some other places have carried out very extensive serological investigations with several thousand paired blood specimens collected from persons immunized with live vaccine under different epidemiological conditions or in connexion with different vaccination schedules.

These investigations demonstrated that, as a rule, the immunological activity of Sabin attenuated strains compared quite favourably with the highest standards for Salk killed vaccine and was even superior with respect to the time and duration of seroconversion.

During 1960 the most frequently used immunization schedule in the Soviet Union was that with individual monovaccines (types 1, 3 and 2) followed by subsequent revaccination with the trivalent mixture.

The experience in 1959 had demonstrated that the optimal serological results were obtained with an immunization schedule involving administration of monovaccines of types 1, 3 and 2 in that order. In 1959 and 1960 vaccination schedules involving one or two feedings with trivalent mixtures were subjected to large-scale trials, and the serological data and epidemiological observations of 1959 show that these

schedules also gave fairly good results. It would evidently be best to be able to choose from among several immunization schedules according to the relevant epidemiological indications and local conditions. The results of serological investigations demonstrate that the immunological response of vaccinated persons increases with time; for instance, the results of antibody surveys three months after immunization with type 1 were definitely better than after one month.

In the course of observations on vaccine virus excretion during revaccination it was possible to establish that, in contrast to Salk killed vaccine, the live poliovirus vaccine produced not only serological but also to a certain extent local immunity, i.e., immunological resistance of cells of the alimentary tract. This may result in a progressive reduction of poliovirus circulation among the population.

However, the problems associated with the dynamics of the development of local immunological resistance to poliovirus demand further study and clearer definition.

Virus carriage and contact transmission

As evidenced by numerous observations, including those made at our Institute, oral immunization with live poliovirus vaccine is accompanied by more or less prolonged excretion of vaccine strains. The duration of virus excretion in children without antibodies is approximately twice that in those with antibodies. All persons susceptible to poliomyelitis in the environment of those who have been immunized pick up vaccine viruses within a very short time

and acquire a latent immunization. No untoward reactions could be noted in connexion with virus carriage or transmission of vaccine viruses by contact. On the contrary, it can be considered established that virus carriage and contact transmission during mass vaccinations are factors exceptionally conducive to general and more rapid immunization within families and communities.

Interference

In oral immunization with live poliovirus vaccine the phenomena of interference between non-poliomyelitis enteroviruses (ECHO and Coxsackie groups) and live vaccine strains and of interference between individual types of live vaccine acquire special importance.

As a result of extensive investigations it has been found that interference between vaccine strains and other enteroviruses occurs under various epidemiological conditions with different frequencies at different times of year. The winter months appear to be the most advantageous for vaccination. The data obtained enable us to draw the preliminary conclusion that most instances of oral immunization failure are due to the influence of interference upon the vaccination process. The interference may probably be overcome by particularly massive vaccinations (involving no less than 50% of the susceptible population) and by repeated vaccinations over at least three years.

Further, more complete study of patterns governing the interference between enteroviruses and vaccine strains of poliovirus is urgent.

TABLE 3
POLIOMYELITIS INCIDENCE IN THE USSR IN 1960 AS PERCENTAGE OF THAT IN 1959

Vaccine	Area	Form	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Total
	USSR	All forms Paralytic	94.2	132.2 151.3	142.3 161.0	97.9 105.6	78.8 89.9	65.7 72.1	33.9 34.6	29.9 32.4	32.8 32.0	34.1 37.7	28.9 32.3	41.0 45.7	53.1 57.3
Live vaccine	Ukraine	All forms	125.9 152.7	211.1 272.3	137.6 179.3	100.8 147.0	79.7 118.6	56.3 54.9	29.9 36.0	19.4 17.6	17.5 18.1	15.4 18.3	19.3	37.7	44.3
vacenie	RSFSR	All forms	95.7 108.0	123.1 126.9	162.4 180.3	101.5	80.0 86.0	68.8 76.4	32.9 34.4	29.3 30.8	31.5	28.5	30.3	32.7	52.3 53.7
		Faralytic	108.0	120.9	160.5	99.0	80.0	70.4	34.4	30.8	30.3	30.7	29.2	33.9	56.7
Killed vaccine	RSFSR (5 regions)	All forms Paralytic	162.8 183.9	174.4 260.9	160.5 195.4	139.4 154.5	114.0 130.3	150.9 147.3	143.2 133.0	145.8 164.6	146.8 137.0	263.9 194.0	104.3 93.4	82.0 89.0	145.0 153.5
(controls)	Krasnodar region	All forms Paralytic	150.0 175.0	225.0 425.0	325.0 300.0	131.0 150.0	121.0 132.0	256.0 342.0	278.0 281.0	363.0 383.0	384.6 377.0	277.4 353.6	126.3 115.1	134.8 152.6	227.0 234.9

														Total for :	
Year	Jan.	Feb.	March	April	May	June	July	ly Aug.	Sept.	Oct.	Nov.	Dec.	Year	3rd quarter	4th quarter
					R	SFSR (1 96 0 po	pulatio	n : 119 6	603 000)					
1957	0.21	0.23	0.22	0.24	0.43	0.64	0.96	1.29	1.06	0.61	0.34	0.38	6.61	3.31	1.57
1958	0.33	0.28	0.30	0.36	0.55	0.78	1.32	1.53	1.32	0.72	0.43	0.33	8.25	4.17	1.48
1959	0.26	0.19	0.18	0.27	0.44	0.54	0.66	0.70	0.67	0.49	0.38	0.38	5.16	2.03	1.25
1960 ^a	0.30	0.26	0.32	0.29	0.40	0.46	0.32	0.34	0.27	0.24	0.15	0.16	3.51	0.93	0.55
1960 ^b	0.27	0.24	0.32	0.24	0.34	0.39	0.21	0.20	0.20	0.15	0.10	0.12	2.79	0.61	0.37
					Ui	raine (1	960 po	pulation	1 : 42 60	6 000)					
1957	0.13	0.13	0.17	0.13	0.23	0.42	0.65	0.94	0.82	0.46	0.23	0.23	4.54	2.41	0.90
1958	0.19	0.24	0.22	0.17	0.28	0.42	0.69	0.98	0.86	0.60	0.30	0.27	5.23	2.53	1.17
1959	0.18	0.11	0.14	0.16	0.20	0.34	0.56	0.65	0.61	0.52	0.50	0.31	4.28	1.82	1.35
1960	0.26	0.30	0.24	0.23	0.24	0.18	0.20	0.11	0.11	0.09	0.09	0.13	2.20	0.42	0.31
					13 othe	r repub	lics ^c (1	1 960 po	oulation	: 50 29	4 000)				
1958	0.33	0.19	0.32	0.16	0.34	0.66	0.80	0.84	0.90	0.58	0.34	0.27	5.73	2.54	1.19
1959	0.19	0.13	0.15	0.17	0.23	0.32	0.90	0.90	0.65	0.34	0.23	0.13	4.34	2.45	0.70
1960	0.10	0.13	0.13	0.10	0.12	0.09	0.07	0.09	0.12	0.07	0.07	0.07	1.17	0.28	0.21

TABLE 4
PARALYTIC POLIOMYELITIS INCIDENCE RATES IN THE USSR PER 100 000 PERSONS

Epidemiological effectiveness of mass immunization with live poliovirus vaccine

From the 1959 data it was already evident that mass immunization with live vaccine performed prior to the summer-autumn season (in Estonia, Lithuania, Latvia, Kazakhstan and other areas) led to a sharp reduction in incidence in the vaccination areas during the second half of the year. But even where live virus vaccination was conducted in the summer (Moscow region, Karaganda) a considerable reduction in the number of cases among the vaccinated was noted compared with that among the unvaccinated. Of special interest was the simultaneous mass immunization of 320 000 children under 15 years of age in Tashkent in July 1959 during a large poliomyelitis outbreak (Chumakov, 1959b, 1960, 1961).

It was possible in Tashkent with the aid of trivalent live vaccine to bring about mass interference with the wild type 1 poliovirus that was circulating and to break the chain of transmission, thus causing a rapid decline in incidence and terminating the outbreak.

In 1960, after mass oral vaccinations were completed (mainly before 1 July) all over the country, a sharp reduction in the number of poliomyelitis cases was observed during the usual poliomyelitis season.

Data are presented here showing the effect of live virus vaccinations on poliomyelitis incidence in 1960. Table 3 shows that in areas where mass live virus immunization was carried out in 1960, a threefold to fivefold reduction in incidence was observed in July, August, September and October compared with the corresponding months of 1959.

In contrast to this, in the "control" areas, where only killed vaccine was used, poliomyelitis incidence in 1960 was higher than that in 1959.

Table 4 presents data on paralytic poliomyelitis incidence (including cases with isolated facial palsy which were not fully confirmed) in the RSFSR,

^a The entire territory of the RSFSR, including regions where live vaccine was not used.

^b Without five regions where live vaccine was not used or was used with delay (Krasnodar, Primorsk, Leningrad, Sverdlovsk, and Novosibirsk regions).

^c Excluding the RSFSR and Ukraine.

TABLE, 5

PARALYTIC POLIOMYELITIS INCIDENCE RATES PER 100 000 PERSONS IN THE REGIONS OF THE RSFSR WHERE ONLY

SALK VACCINE WAS USED IN 1960

													Tota	al for:
Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Year	3rd quarter
					Krasnod	ar region	(1960 pc	pulation	: 3 828 0	00)				
1958	0.32	0.24	0.32	0.41	1.00	1.24	1.32	1.19	1.54	0.95	0.65	0.60	9.79	4.05
1959	0.21	0.11	0.05	0.42	0.58	0.32	0.82	0.64	0.35	0.74	0.88	0.50	5.63	1.81
1960	0.37	0.44	0.16	0.63	0.76	1.07	2.27	2.40	1.31	1.85	0.99	0.76	13.01	5.98
					Primors	k region	(1960 po	pulation	: 1 405 00	0)				
1958	0.30	0.37	0.30	0.44	0.66	2.21	4.35	4.72	2.73	1.33	0.52	0.30	18.20	11.80
1959	0.22	0.29	0.29	0.43	0.14	0.58	0.58	0.58	0.43	0.14	0.43	0.51	4.63	1.59
1960	0.21	0.64	0.43	0.71	0.57	1.07	0.71	0.64	0.57	1.00	0.71	0.71	7.97	1.92
					Leningra	ad region	(1 96 0 pc	opulation	: 1 267 0	00)				
1958	0.65	0.82	0.57	0.90	1.47	1.39	3.10	3.35	2.70	1.14	1.14	0.82	18.05	9.15
1959	0.64	0.48	0.16	0.64	0.80	0.80	1.28	0.96	1.12	0.32	0.32	0.56	8.11	3.36
1960	0.24	0.24	0.16	0.24	1.03	0.40	0.71	0.95	0.47	0.08	0.08	_	4.58	2.13

the Ukraine and 13 other republics of the Soviet Union by months, in rates per 100 000 persons. These data clearly demonstrate the extent of the reduction in incidence in the third quarter of 1960 compared with the corresponding period in previous years.

In Table 5 rates per 100 000 persons are presented for three separate regions of the RSFSR, where during nine months of 1960 no live poliovirus vaccine was used. As the table shows, in 1960 poliomyelitis incidence in these regions (at least, in two of the three) was rather high and the summer

TABLE 6

MONTHLY NUMBER OF POLIOMYELITIS CASES IN THE ESTONIAN SSR (POPULATION: 1 200 000) a

													Tota	d for :
Year	Jan.	Feb.	March	April	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	Year	3rd quarter
1955	4	2	_	3	4	3	7	16	58	56	27	13	193	81
1956	13	5	1	3	2	10	15	39	45	64	28	11	236	99
1957	5	13	5	9	5	7	17	20	27	15	5	11	139	64
1958	8	2	6	8	4	5	20	151	407	266	90	24	991	578
1959	31	7	5	6	2	2	2	2	2	_	_	_	59	6
1960	-	2		_	1	_	1	l –	1	1	_	_	6	2
											l	1		

^a Mass immunization with live poliovirus vaccine in the Estonian SSR was first done before 10-20 June 1959, and repeated in the second quarter of 1960.

		Feb.			May	June	July						Tota	d for :
Year	Jan.		March	April				Aug.	Sept.	Oct.	Nov.	Dec.	Year	3rd quarter
1955	1	1	6	3	5	20	46	116	106	58	34	31	427	268
1956	18	17	12	19	32	46	64	51	33	32	11	10	345	148
1957	12	9	12	9	6	19	37	23	21	8	4	12	172	81
1958	5	3	10	1	3	21	39	66	55	35	23	25	286	160
1959	10	12	6	4	3	3	7	2	1	2	1	1	52	10
1960	_	2	1	_	_	1	1	_	2	1	_	1	9	3
						ŀ				Į				

TABLE 7
MONTHLY NUMBER OF POLIOMYELITIS CASES IN THE LITHUANIAN SSR (POPULATION: 2 700 000) a

^a Mass immunization with live poliovirus vaccine in the Lithuanian SSR was first performed before 10-20 June 1959, and repeated in the second quarter of 1960.

seasonal prevalence (the third quarter) of poliomyelitis was clearly marked.

During the period 1958-60 over 1 500 000 children aged 6 months to 15 years in these three regions had received Salk vaccine (two or three injections). Investigation of the effectiveness of these vaccinations revealed a fourfold reduction in the number of paralytic cases among the vaccinated as compared with the unvaccinated; and yet on the whole the summer seasonal rise of poliomyelitis incidence in these regions could not be prevented.

Tables are also presented showing the absolute numbers of poliomyelitis cases in Estonia (Table 6) and Lithuania (Table 7) by months for the years 1955-60. In these republics mass immunization of the population with live vaccine was not begun before May-June of 1959. Since that time, only sporadic poliomyelitis cases have been recorded; most of these have given negative results in virological tests and were also clinically doubtful. For instance, of nine cases recorded in Lithuania in 1960 six were of isolated facial palsy which were not confirmed virologically (five patients were examined) and only three cases had clinical features of the spinal form of poliomyelitis. Of eight cases examined seven gave negative serological and virological results.

Thorough clinical and laboratory investigations of cases diagnosed and officially recorded as being paralytic poliomyelitis in Moscow city and the Moscow region regularly demonstrate that many such cases are in fact not poliomyelitis. They are mainly cases of facial monoparesis.

The accompanying graphs show poliomyelitis incidence rates in individual republics or in groups of regions of the USSR for various years.

FIG. 1
MONTHLY INCIDENCE RATES OF POLIOMYELITIS
(ALL FORMS) IN THE USSR SINCE 1953

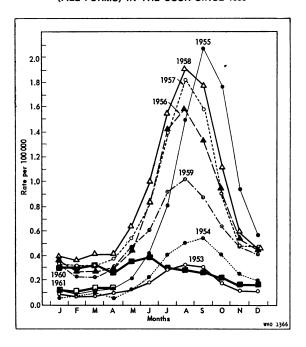


Fig. 1 shows the seasonal dynamics of poliomyelitis in the Soviet Union for the years 1953-60

and part of 1961. It is evident that even during the years of minimal incidence (1953 and 1954) there was a marked summer-autumn seasonal prevalence. The only exception was in 1960, when mass vaccination with live vaccine had been carried out.

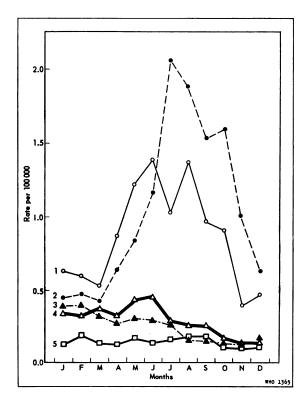
Fig. 2 shows poliomyelitis incidence rates in the RSFSR for regions where mass immunization with live vaccine was carried out, regions where only Salk vaccine was used, and areas where first killed vaccine and later live vaccine were used. Rates are also shown for the Ukraine and for 13 other

FIG. 2

MONTHLY INCIDENCE RATES OF POLIOMYELITIS

(ALL FORMS) IN 1960 IN THE RSFSR, UKRAINE AND 13

OTHER REPUBLICS IN USSR



^{1 =} Areas of the RSFSR where killed vaccine was used first and live vaccine was used from May 1960 onwards (Sverdlovsk and Novosibirsk oblasts; 6 458 000 inhabitants).

republics where live vaccine was used in 1959 and in 1960.

This figure clearly shows that the live vaccine sharply reduces poliomyelitis incidence and prevents the seasonal increase.

Fig. 3 shows paralytic poliomyelitis rates per 100 000 in 68 regions of the RSFSR where live vaccine was used, and in five regions where killed vaccine was used in 1960.

FIG. 3
PARALYTIC POLIOMYELITIS INCIDENCE RATES IN
REGIONS OF THE RSFSR WHERE LIVE OR KILLED
VACCINE WAS USED IN 1960

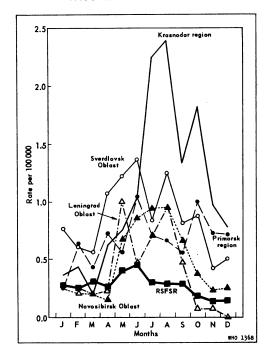


Fig. 4-7 show poliomyelitis incidence rates per 100 000 by months for three- or four-year periods in the Ukraine (Fig. 4), Byelorussia (Fig. 5), the Kazakh republic (Fig. 6) and for 13 republics of the Soviet Union, excluding the RSFSR and the Ukraine (Fig. 7).

All these curves reflect with general regularity the reduction in poliomyelitis incidence after a complete course of live vaccine administration and the absence of any trend to a seasonal rise in incidence in the third quarter of the year.

^{2 =} Areas of the RSFSR where only killed vaccine was used (Krasnodar and Primorsk regions and Leningrad oblast; 6505 000 inhabitants).

^{3 =} Ukrainian SSR.

^{4 =} Areas of the RSFSR where mass immunization with live vaccine was carried out (106 639 000 inhabitants).

^{5 = 13} republics where live vaccine was used in 1959.

FIG. 4
MONTHLY INCIDENCE RATES OF POLIOMYELITIS
(ALL FORMS)
IN THE UKRAINIAN SSR

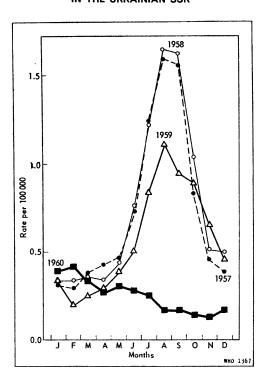


FIG. 6
MONTHLY INCIDENCE RATES OF POLIOMYELITIS
(ALL FORMS) IN THE KAZAKH SSR

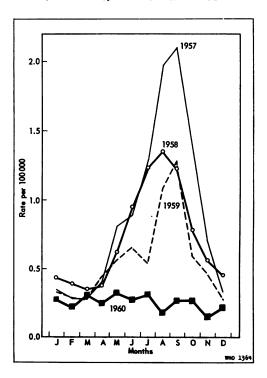


FIG. 5
MONTHLY INCIDENCE RATES OF POLIOMYELITIS
(ALL FORMS) IN THE BYELORUSSIAN SSR

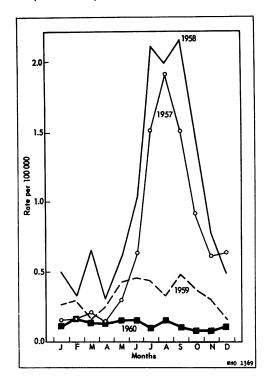
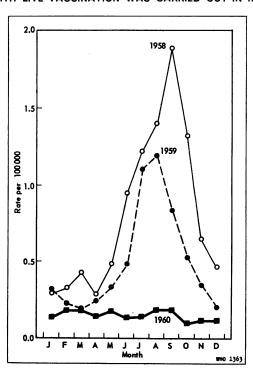


FIG. 7

MONTHLY INCIDENCE RATES OF POLIOMYELITIS (ALL FORMS) IN 13 REPUBLICS OF THE USSR (EXCLUDING RSFSR AND UKRAINE) WHERE MASS IMMUNIZATION WITH LIVE VACCINATION WAS CARRIED OUT IN 1959



CONCLUSION

It has consequently been proved that mass use of live poliovirus vaccine from Sabin strains incorporated in candy exerts a significant influence upon the epidemic process and leads to elimination of poliomyelitis epidemics.

The next stage in poliomyelitis control in the USSR is the eradication of sporadic poliomyelitis cases. A prerequisite for this is that the population must be completely freed of virulent poliovirus carriage. For this it will be necessary for a number of years to provide 100% coverage with live poliovirus vaccine of all children, including the newborn, infants and pre-school children, and also, possibly, to repeat mass revaccination of the entire population of the country.

In conclusion, mention must be made of the fruitful international co-operation in matters of live poliovirus vaccination which has been achieved between American, Soviet Union, Czechoslovak, Hungarian, German, Chinese, Bulgarian and other scientists, and which has taken the form of a broad exchange of scientific information, personal contacts, the mutual exchange of results obtained, and friendly support.

All that has been done so far is, undoubtedly, only a promising start towards regular future international co-operation among medical scientists with a view to the speediest possible eradication of poliomyelitis and certain other infectious diseases or, at least, a sharp reduction in their prevalence.

RÉSUMÉ

La production en série, sur une large échelle, du vaccin poliomyélitique vivant — souche atténuée de Sabin — a été entreprise en URSS pour la vaccination de masse par voie orale. Celle-ci a été effectuée à partir de 1959, année au cours de laquelle 15,2 millions de personnes ont été vaccinées. Ce chiffre s'est élevé à 77,478 millions en 1960, les sujets vaccinés ayant de 2 mois à 20 ans (55 ans dans certaines régions).

Près de 95% des vaccinations ont été effectuées au moyen de vaccin de Sabin incorporé à des dragées. Ce vaccin a été utilisé également en Albanie, Bulgarie, Hongrie, Viet-Nam, République démocratique allemande, Chine, Corée et Tchécoslovaquie, pays dans lesquels 13,15 millions d'enfants de moins de 15 ans ont été vaccinés.

Les auteurs apportent des données relatives à l'innocuité du vaccin, au pouvoir immunisant du vaccin vivant, aux porteurs de virus, à la transmission par contact et à l'interférence. On trouve aussi dans cet article la comparaison de la fréquence des nouveaux cas de poliomyélite en 1960 dans la région où se sont déroulées les vaccinations par le vaccin vivant, et dans certaines régions où seul le vaccin Salk inactivé a été utilisé en 1958-60.

Le vaccin Salk n'a eu aucune influence décisive sur le processus épidémique, dans les régions où il a été appliqué, tandis que là où l'on a administré le vaccin vivant de Sabin, le clocher estivo-automnal de la courbe de fréquence des nouveaux cas n'a pas été observé.

Les résultats de deux années d'expérience sur l'emploi systématique du vaccin poliomyélitique de Sabin en URSS, démontrent la possibilité d'empêcher l'apparition d'épidémies de poliomyélite. Cependant les efforts doivent se poursuivre en vue d'interrompre la circulation des virus sauvages dans la collectivité, qui est la condition de l'éradication de la poliomyélite.

REFERENCES

Ashmarina, E. E. (1961) Study of implication of type 1 vaccine poliovirus strain in persons of different age-groups in mass immunization, In: Oral poliomyelitis vaccine, Moscow (in press)

Boiko, V. M. et al. (1961) The experience of mass administration of live poliovirus vaccine during a poliomyelitis outbreak. In: Oral poliomyelitis vaccine, Moscow (in press)

Chumakov, M. P. et al. (1959a) Characteristics of live poliovirus vaccine produced in the Institute for Poliomyelitis Research, Academy of Medical Sciences of the USSR, and comparison to Sabin's original vaccine from attenuated poliovirus strains]. In: [First International Conference on Live Poliovirus Vaccines........... 1959], Washington, D.C., Pan American Sanitary Bureau, p. 140

- Chumakov, M. P. et al. (1959b) Vopr. Virusol., 4, 520
- Chumakov, M. P. et al. (1960) [On mass oral immunization of the population in the Soviet Union against poliomyelitis with live vaccine from A. B. Sabin attenuated strains. Report No. 2 as of December 31, 1959], Moscow (Publication of the Institute for Poliomyelitis Research of the USSR Academy of Medical Sciences)
- Chumakov, M. P. et al. (1961) Experimental tests of candied live poliovirus vaccine in tissue culture. In: Oral poliomyelitis vaccine, Moscow (in press)
- Dobrova, I. N. (1961) Survey of the presence of poliomyelitis antibody in the population of different regions of the Soviet Union. In: Oral poliomyelitis vaccine, Moscow (in press)
- Dzagurov, S. G. & Shmeleva, G. A. (1961) The thermal marker method in the control of live vaccine. In: Oral poliomyelitis vaccine, Moscow (in press)
- Fleer, G. P. (1961) Experimental verification of adaptability and immunogenicity of live poliovirus vaccine

- incorporated in pasty candies. In: Oral poliomyelitis vaccine, Moscow (in press)
- Lashkevich, V. A. et al. (1961) Concentration, even distribution and preservation of vaccine incorporated in dragée-candy under different conditions of storage. In: Oral poliomyelitis vaccine, Moscow (in press)
- Sabin, A. B. (1957) J. Amer. med. Ass., 164, 1216 Sabin, A. B. (1959a) Brit. med. J., 1, 663
- Sabin, A. B. (1959b) Recent studies and field tests with a live attenuated poliovirus vaccine. In: First International Conference on Live Poliovirus Vaccines . . . 1959, Washington, D.C., Pan American Sanitary Bureau, p. 14
- Smorodintsev, A. A. et al. (1960) In: [Live poliomyelitis vaccine], Leningrad
- Voroshilova, M. K. et al. (1961) Antibody response in children immunized with live trivalent vaccine from A. B. Sabin strains. In: Oral poliomyelitis vaccine, Moscow (in press)