

Serologic Response of School Children to Delayed Second Inoculation of Poliomyelitis Vaccine.* (23428)

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In the spring of 1955 scheduled inoculations of poliomyelitis vaccine were greatly deranged by unanticipated shortages of vaccine. Furthermore, many children, having received the first injection in the spring at clinics held in schools, went away for summer vacations and it was not possible or practical even when vaccine was later available to continue mass inoculations until school opened again in the fall. This circumstance necessitated a delay of approximately 5 months between injections and many physicians were concerned about resuming immunization after such a delay. A question frequently encountered was whether or not the entire inoculation series should be started over again. The present paper attempts to answer this question by presenting evidence of the serologic status of children before and after such a delayed second inoculation and comparing the results with those obtained following 2 doses of vaccine administered at an interval of only one month.

Methods. Groups of children in 3 Ann Arbor schools were studied. All were in the 1st, 2nd or 3rd grades of school and none had received vaccine during the field trial of 1954. They had been injected with 1 ml of commercial vaccine in April, 1955, but since a shortage was not anticipated, no blood specimens, unfortunately, had been obtained at that time. Shortly after the opening of school in the fall, clinics were set up in each school to administer second doses of the vaccine 5 months after the first. At this time samples of blood were taken from a total of 221 subjects in 3 schools on the day of the second inoculation and again 2 weeks later. In addition, a small number of children who had not been inoculated in the spring but were receiv-

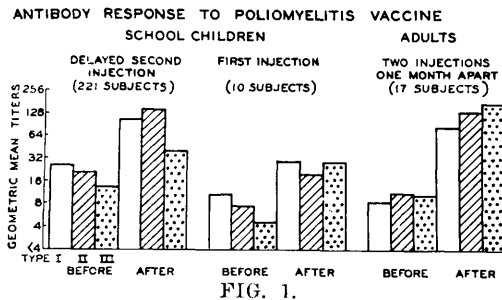
ing vaccine for the first time were studied as controls. Serum specimens were diluted 1/4, 1/8, 1/16, 1/64, 1/256 and 1/1024 and antibody titers against the 3 immunologic types of poliomyelitis virus were determined by neutralization tests against 100 tissue culture doses of virus in stationary tube cultures of HeLa cells.

Results. Table I presents the antibody status of the 221 subjects before and after the delayed second inoculation. It should be noted that these results represent the presence of antibody at any demonstrable titer starting with the lowest dilution tested ($1/4$). It is of considerable interest that so little antibody was demonstrated approximately 5 months following the first inoculation. This may be due in part to a temporal decrease in titer but more likely reflects the inadequacy of the single stimulus. Thirteen percent of the children had no demonstrable antibody to any type of virus prior to the secondary stimulus but none was left without some antibody to at least one type following the second injection. Percentages of children without antibodies to specific types of virus were also drastically reduced following the second stimulus. The most effective antigen had been that of the type II component which left only 23% (13% lacking in all 3 types plus 10% without type II) of the children deficient before the second injection. Only one child (0.4%) however, was without these antibodies after the additional stimulus of the second injection. Although a total of 33% of the children lacked type I antibodies before the second inoculation, only 4% were still deficient afterwards. The type III component of the vaccine was the least effective, leaving altogether 53% without antibodies prior to the second stimulus after which, however, only 12% failed to respond. On the positive side the percentage of subjects having antibodies to all 3 types was increased

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TABLE I. Antibody Pattern of School Children before and after Delayed Second Inoculation of Poliomyelitis Vaccine.

	221 subjects: Delayed 2nd inoculation				10 subjects: 1st inoculation	
	Before		After		Before	After
	No.	(%)	No.	(%)		
No antibody to any type	30	(13)	0	(0)	2	1
No antibody to:						
Type I only	20					
I or II	6					
I or III	19	45 (20)	10	(4)	4	2
II only	4					
II or III	13					
II or I	6	23 (10)	1	(0.4)	5	2
III only	56					
III or I	19					
III or II	13	88 (40)	27	(12)	6	5
Antibody to all three types	73	(33)	189	(85)	3	5



from 33 to 85% following the delayed second stimulus. In contrast to these results the antibody pattern of the 10 children receiving their first inoculation at the same time changed very little.

Since the above data were based on the presence or absence of detectable antibody at the lowest dilution tested ($\frac{1}{4}$), the mean increase in actual antibody titer is a better measure of the serologic response of these subjects. Fig. 1 compares the geometric mean titers of children receiving the delayed second injection with those being inoculated for the first time and with a small group of adults which were vaccinated twice at an interval of one month with the same vaccine. The delay did not inhibit a satisfactory response. A better measure of the effectiveness of vaccination is usually seen when only those having no demonstrable antibodies prior to injection are considered. Fig. 2 presents, therefore, the mean titers attained by persons without antibody to any type and by those

who had been negative to specific types prior to the second injection. The response was quite satisfactory when compared with that of a small group of adults who were negative to type prior to the first of 2 injections of the same vaccine.

Fig. 3 is a further effort to compare the present results with other groups of individuals receiving only 2 injections of vaccine at an interval of one month. Unfortunately, no data are available in this laboratory on school age children receiving 2 injections 4 weeks apart. However, several groups of infants, pre-school children and adults have been observed as part of other studies(1,2) and are therefore included for comparison. From these data it is apparent that the mean antibody titers to types I and II poliomyelitis are higher in school children following the delayed second inoculation than in any of the

POLIOMYELITIS SEROLOGY AFTER TWO DOSES OF VACCINE IN SUBJECTS WITH NO PREVIOUSLY DEMONSTRABLE ANTIBODIES

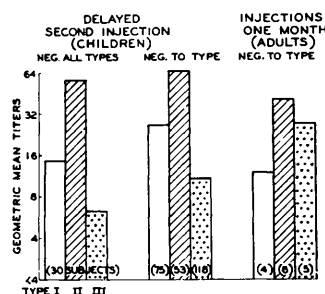


FIG. 2.

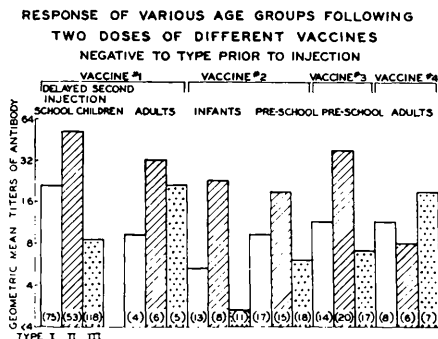


FIG. 3.

other groups which received 2 inoculations 4 weeks apart. Furthermore, only 2 groups, both adults, had higher type III responses than were found in the present study.

Discussion. The data presented are not intended in any way to imply that a deliberate lengthening of the time interval between the first and second inoculation of poliomyelitis vaccine should be practiced, nor are they presented as a substitute for the recommended schedules of inoculation. Salk(3) has recently discussed thoroughly the effect of variations in dosage schedules and has noted that response to multiple injections is enhanced with the increase in time between inoculations. He has pointed out, however, that such an interval would be undesirable if the incompletely vaccinated person by virtue of season or community would be undergoing a greater risk of infection. The present study was made because of the fact that such unforeseen deviations from recommended schedules do occur and raise doubt in the minds of the physicians and of the subjects themselves as to the degree of response under these circumstances.

It is no surprise that a second inoculation delayed 5 months seems to act exactly as a booster injection, the effects of which have been adequately documented for poliomyelitis vaccine(4,5,6). Perhaps the most unex-

pected finding is the extent of this response when preceded by only a single primary stimulus. Serologically at least the individuals are better conditioned than those receiving 2 inoculations one month apart and not followed up with a third or booster injection.

Summary. The serologic response of school children receiving the second inoculation of poliomyelitis vaccine 5 months after the first injection was studied. Thirteen percent had no demonstrable antibodies to any of the 3 types of virus prior to the second stimulus and many others were lacking in antibodies to one or two types. Only 33% had antibodies to all 3 types. Two weeks following the delayed second injection none was without antibodies to any type, and 85% had antibodies to all 3 types. The antibody levels attained by these children were at least as good if not better than those of other age groups following 2 injections at an interval of one month. The conclusion is made that a delay of 5 months between the first and second injections of poliomyelitis vaccine, although not normally recommended, actually proves advantageous in terms of serologic response.

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