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VIII. IMMUNOLOGICAL EFFECTIVENESS OF THE TWO DOSE SCHEDULE†

The immunological effectiveness of the Middletown oral poliovirus vaccination program was determined by testing pre- and post-vaccinal neutralizing antibody levels in blood specimens from a selected group of children, representing about five per cent of the school children and 10 per cent of the preschool vaccinees. The present paper is concerned with the results of these tests in terms of the antibody status of the study group before they received oral vaccine, the conversion rates in antibody-negative children, and antibody rises in those with low levels before oral vaccination.

MATERIALS AND METHODS

Selection of children for antibody survey and collection of specimens. The plan was to obtain blood specimens from approximately 600 children, 200 from each of three socio-economic classes. Actually, 682 were bled at the time the first dose of vaccine was given. Post-vaccinal specimens, collected approximately six weeks after the second dose, were obtained from 676 of this group. Satisfactory antibody tests were completed on 671 paired specimens, which form the basis for the analyses to be presented.

Most of the 671 children included came from the randomly selected families in the interview sample,[1] but it was necessary to enlarge the "upper" and "lower" socio-economic categories, both in school age and preschool groups. This was done with the aid of the city directory, school nurses, and the Board of Education's preschool census. Questionnaires were filled out for all children surveyed. The information obtained included the number of injections of Salk-type vaccine received and the dates on which they were given. Data on the vocation and educational level of the family head were recorded also, for the purpose of social classification of the vaccinees,

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using the Hollingshead two-factor scale.[2] This classification designates five social classes, class I being the highest and class V the lowest. For our purposes it was sufficient to consider combined classes I and II as "upper," III and IV as "middle," and class V as "lower" socio-economic groups. The composition of the population surveyed serologically is shown by age and social class in Table 1, and by the number of doses of Salk-type vaccine received, in Table 2.

TABLE 1. COMPOSITION OF GROUPS SURVEYED SEROLOGICALLY, BY AGE AND SOCIAL CLASS

		Number in each age group			
Social class	*Number*	*<1-4*	*5-9*	*10-14*	*15-19*
I & II	165	74	31	34	26
III & IV	321	157	44	65	55
V	185	73	31	51	30
Total	671	304	106	150	111

TABLE 2. VACCINATION HISTORY, BY AGE AND DOSES OF INACTIVATED VACCINE

		Number of doses—per cent with:				
Age	*Number*	*0*	*1*	*2*	*3*	*4*
<1-4	304	4	5	14	41	36
5-9	106	0	0	5	34	61
10-14	150	3	0	1	34	62
15-19	111	2	2	6	53	37
Total	671	3	3	8	40	46

Antibody determinations. The micromethod of Green and Opton[3] using finger blood collected on filter paper was employed. Paired specimens were tested in monkey-kidney tissue-culture tubes, with appropriate challenge doses of the three types of poliovirus. The sensitivity of this method is roughly comparable to that of the tube neutralization test in which dilutions of serum and 100 TCD_{50} of virus are incubated for one hour at room temperature before inoculation. Both methods depend upon inhibition of cytopathic effect (CPE), and as has been pointed out previously[4,5] low

titers of antibody (1 : 8 or less) which would be revealed by the colorimeteric (pH) method of measuring neutralizing antibody may be missed.

RESULTS

Pre-vaccinal antibody survey. As shown in Table 2, the children had been well vaccinated with Salk-type vaccine, 86 per cent having received three or more injections. Their antibody patterns for the three types of poliovirus

TABLE 3. ANTIBODY PATTERNS (EXPRESSED QUALITATIVELY AS POSITIVE OR NEGATIVE) AFTER SALK-TYPE VACCINE, BUT PRIOR TO ORAL VACCINE ADMINISTRATION.

Age	*Number of doses*	*Number of children*	*Per cent with antibodies to:**		
			Type I	*Type II*	*Type III*
<1-4	0-2	71	25	37	23
	3	124	59	72	47
	4	109	69	83	48
5-9	0-2	5	(80)*	(80)	(60)
	3	36	64	92	44
	4	65	82	98	46
10-14	0-2	5	(60)	(80)	(20)
	3	52	81	96	52
	4	93	95	99	71
15-19	0-2	11	70	90	50
	3	59	85	97	61
	4	41	90	100	68

* Figures in parentheses are not of statistical significance.

are shown in Table 3, by age and the number of injections of inactivated vaccine which they had received. As had been observed in a previous study carried out in New Haven, Conn.,[5] a considerable percentage of the children, particularly the preschool group, lacked antibody to one or more types in spite of multiple doses of Salk-type vaccine. The less satisfactory response of this youngest age group to inactivated vaccine as compared to school-age children is also evident from this table. The low per cent with type III antibodies is doubtless in part due to the test method used,[5] although the relatively poorer antigenicity of type III Salk vaccine is probably also a factor. Analysis of antibody patterns in terms of social class showed no significant differences.

Antibody responses induced by oral vaccine. Following the administration of two doses of oral vaccine, homotypic negative children showed high conversion rates for all three types, as shown in Table 4. From 99 to 100 per cent of children aged <1 to 9 years developed antibodies to types I and II, and 89 per cent to type III. A lower percentage of older individuals (15-19 years) develop antibodies—81 per cent for type I, and 66 per cent for type III. In general, post-oral-vaccine antibody titers were high, the majority being 1:512 or greater.* These results confirm many

TABLE 4. ANTIBODY CONVERSIONS* IN HOMOTYPIC NEGATIVES AFTER ORAL VACCINE

		Type I		*Type II*		*Type III*	
Age	*No.*	*No. neg.***	*Per cent conversions*	*No. neg.***	*Per cent conversions*	*No. neg.***	*Per cent conversions*
<1-4	304	146	99	99	100	178	89
5-9	106	26	100	5	100	57	89
10-14	150	17	100	4	100	56	79
15-19	111	16	81	3	100	41	66
Total	671	205	98	111	100	332	83

* To a level of 1:16 or higher.
** Neg. = lacking pre-oral-vaccination antibodies.

previous observations on the high degree of immunological effectiveness of the Sabin vaccine,[4] particularly in young children. The excellent responses to two doses, i.e. type I followed after six weeks by types II and III together, are in line with our earlier observations[5] and with the experience of others.[6]

The lower rate of conversions among older individuals as compared with younger children, has been noted by others.[7] An explanation for this is not entirely clear, but several possible factors may be involved. One is that certain adults who lack demonstrable antibody nevertheless have been infected previously and, as a result, have a high degree of intestinal resistance to re-infection.[4] Another point to be considered is that the greater probability of contact infection among young children may be responsible for increasing the conversion rates in this age group. However, if this latter factor played a major role, one might expect a greater difference

* In the following discussion, "titers" refer to estimated neutralizing antibody levels based on standards worked out for the filter paper micromethod.[3]

between preschool and older children;[8] instead the decline in conversion rates is striking only in those over 14 years, and particularly in young adults.

Antibody rises in children with low level pre-oral-vaccine titers. As indicated in Table 5, a high percentage of children with titers of 1:8 to 1:32 against one or more types of poliovirus showed sharp rises in titer after oral vaccination, the levels reached being in the 1:512 — 1:1024 or higher range in the majority of instances. In general, it is likely that such low pre-oral-vaccinal titers represent antibodies induced by Salk-type

TABLE 5. ANTIBODY RISES (FOURFOLD OR GREATER) IN CHILDREN WITH PRE-ORAL-VACCINE TITERS OF 1:8 TO 1:32

	Type I		*Type II*		*Type III*	
Age group	*Number of children*	*Per cent with antibody rise*	*Number of children*	*Per cent with antibody rise*	*Number of children*	*Per cent with antibody rise*
<1-4	38	94	37	97	39	90
5-9	13	92	8	100	19	74
10-14	16	94	14	100	20	70
15-19	21	76	9	67	12	67
Total	88	90	68	94	90	79

vaccine alone, while levels of 1:64 or higher are more apt to have been induced by previous natural inapparent infection enhanced, in some, by vaccine injections. It is not surprising, therefore, that the majority of children listed in Table 5 showed sharp antibody rises after receiving oral vaccine, since it has been well established that inactivated vaccine does not confer significant intestinal resistance to infection. Thus in 90 per cent of the children, rises to type I occurred, in 94 per cent to type II, and in 79 per cent to type III. In previous studies, such rises have been shown to be associated invariably with virus excretion; it is thus likely that the present results are due to actual infection, and not to heterotypic responses.

Comparison between responses to oral vaccine and to Salk-type vaccine. As has been observed previously,[5,9] in spite of multiple doses of Salk-type vaccine given prior to the oral vaccine campaign, a significant number of children lacked adequate antibody levels against one or more types of poliovirus (Table 3). This was most striking in the preschool age group, i.e. among young children who had not yet had time to experience natural in-

fection with wild polioviruses to enhance their antibody levels acquired from Salk-type vaccine (or vice-versa). Thus in spite of four doses of inactivated vaccine, 31, 17, and 52 per cent of children aged <1-4 lacked antibody to type I, II, and III respectively. Among older children with comparable vaccine histories, these figures were considerably lower, particularly for types I and II; presumably, these differences reflected the greater opportunity with increasing age to acquire natural infection. A higher per cent of all age groups lacked type III antibody as compared with the other types, a pattern observed before, and related in part at least to the poorer antigenicity of the type III component of Salk-type vaccine.

Following oral vaccination, the responses were remarkably good in terms of antibody conversions and rises, and high titers were the rule. Based on our previous experiences with immunization of young children[5] there is reason to expect that the high titers reached will persist without greater decline than would be expected to follow natural infection with wild poliovirus strains.

These results emphasize the desirability of oral poliovirus vaccine, even in a community as well covered by inactivated vaccine as was Middletown.

SUMMARY

The immunological effectiveness of the Sabin strains of oral poliovirus vaccine given in two doses (type I, followed after six weeks by types II and III) was determined by measuring the serological responses of 671 vaccinees of different age and social class. Even though 86 per cent had received three or more doses of Salk-type vaccine, a number of children lacked significant antibody to one or more types. The responses to oral vaccine were certainly satisfactory. Conversion rates in antibody-negative children were uniformly high: 98 per cent for type I, 100 per cent for type II, and 83 per cent for type III. The highest rates were observed in preschool children, and the lowest in those aged 15-19 years. Children with low level pre-oral-vaccine titers (presumably resulting from Salk-type vaccine) responded with rises to high titers: 90 to 94 per cent for types I and II, and 79 per cent for type III. No significant differences were noted in the pre- or post-oral-vaccine antibody patterns according to social class.

The results again emphasize the immunological effectiveness of the oral poliovirus vaccine and its superiority over the Salk-type vaccine in achieving higher conversion rates and higher antibody levels. This was evident in Middletown, even though inactivated vaccine had been widely used, for many children lacked antibodies in spite of having received multiple in-

jections. In contrast, a single exposure to each of the three types of oral vaccine corrected the deficits in a high percentage of children.

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