CHAPTER VIII

MEASUREMENT OF ANTIGENIC POTENCY OF VACCINE AND STABILITY OF ANTIBODY TITERS

MEASUREMENT OF ANTIGENIC POTENCY OF VACCINE

A primary objective in obtaining specimens of blood from a segment of the study population in each test area was to measure the antigenic potency of different lots of vaccine. Study was, therefore, made of antibody titers in the serum of children before and after vaccination in comparison with parallel titrations of serum from unvaccinated controls. The data could then be used to seek correlations between antibody response to lots of vaccine or to type-specific components of lots, and the capacity of vaccine to prevent poliomyelitis. It was hoped, in addition, that differences in naturally acquired antibody levels in various sections of the country would be displayed, that changes occurring as a result of natural exposure during the poliomyelitis season would be detectable, and that a view of the persistence over the study period of antibody response to vaccine could be obtained.

The plan was to obtain samples of blood at the time of the first vaccination clinic and two weeks after the third clinic, or seven weeks after the first specimen, from 2 percent of those who received vaccine or placebo and, in observed areas, from 2 percent of the uninoculated controls of the first and third grades of school. In areas with limited numbers of participants, a minimum of 100 persons was to be bled. Obviously, specimens were not available from those who refused participation. The third specimens were obtained from the same persons in November, 1954, approximately five months after the early post-vaccination second bleeding.

The contingent from whom blood was obtained was not a probability sample. It was selected with an eye to convenience and administrative economy and with a realization that the randomization required to furnish a fully representative distribution was impracticable. It was asked, however, that schools representing variations in the community's characteristics be selected. It was also asked that specimens from vaccinated and controls be obtained from the same school groups in observed areas and from children of the first, second, and third grades of placebo area schools; a review of the records demonstrates that this procedure was regularly followed. The available information does not, however, permit comparison of groups within an area on socio-economic, ethnic, or other than basic age and sex distributions.

A limitation to the comparison of serological responses from one area with those from another resides in the fact that the serological tests for any one area were usually conducted in a single laboratory which received all of the specimens from the county unit. The materials from different counties frequently represented different lots of vaccine as well. Efforts to establish uniformity of performance and to measure interlaboratory variation with control materials and exchanged sera are discussed in Chapter VII. Variations in the procurement and shipping of specimens, in the frequency with which toxic sera were encountered, in details of technical methodology contribute other limitations to stringent statistical treatment of the results. The data were, therefore, not suitable for certain of the definitive analyses originally planned.

In placebo areas all available data indicate the close similarity of controls and vaccinated groups, and the similarity applies also to the groups from which blood specimens were

obtained (Table 55). In observed areas, different school grades constituted the vaccinated and controls but there, too, bloods were collected from proportionate numbers of vaccinated and unvaccinated children in the same schools. Since the successive specimens of blood for comparison of titers before and after vaccination were taken from the same persons each time, the response to vaccine could be measured by grouping results in persons of like serological status originally, with or without relation to other known characteristics. The size of the collection was adequate to permit an estimate of antibody response for most lots. In placebo areas the number of paired samples from those receiving a specified lot of vaccine was essentially the same as the number receiving the designated lot of placebo.

THE SEROLOGICAL MATERIAL USED

In all study areas combined, 40,881 first bloods were collected, representing 2.2 percent of the total study population of 1,829,916. Somewhat fewer, 32,428, second bloods were taken. Prior to the collection of the third bloods, the decision was made to take bloods from children who had given either first or second specimens with the result that 33,862 third bloods were collected. Table 53 shows summary counts of bloods drawn, tested, and subsequently tabulated at VEC for all study areas combined.

There was considerable reduction in the number of bloods at each stage of processing. Of the bloods reported to have been collected,

Table 53

PRE- AND POST-VACCINATION BLOODS DRAWN, TESTED, AND TABULATED
PLACEBO AND OBSERVED AREAS COMBINED

	1st Bloods	2nd Bloods	3rd Bloods
Number Drawn (Per Field Clinic Records)	40,881	32,428	33,862
Percent of Total Study Population Bled	2.2	1.8	1.9
Number Received by Laboratories (Per Lab Count)	36,045	28,086	28,863
Percent Received of Number Drawn	88.2	86.6	85.2
Number Tested (Per Laboratory Count)*	33,862	29,137	28,006
Percent Tested of Number Received	93.9	103.7	97.0
Number Tabulated at VEC**	20,067	20,067	14,783
Percent Tabulated of Number Tested	59.3	68.9	52.8
Percent Tabulated of Total Population	1.1	1.1	0.8

* Includes repeat tests.

** Of 29,178 first and/or second blood reports received at VEC, 4,734 were "unpaired," incomplete, or unsatisfactory; 4,377 were reported toxic in tests to one or more virus types; and 20,067 paired first and second blood results were tabulated. The exclusion of the 9,111 toxic or unsatisfactory first and second test results caused further reduction in the number of second and third paired sera.

88 percent, 87 percent, and 85 percent of first, second, and third bloods, respectively, were reported to have been received by the laboratories. Since several laboratories received specimens for storage and later transshipped them elsewhere for testing, losses or errors in recording might account for some of the differences between number drawn and number received by the laboratories. Virtually all second and third bloods received by the laboratories were tested, and 94 percent of all first bloods received were tested.

Punch cards were prepared for all reports received at VEC but only paired first and second bloods, paired second and third bloods, and matched first, second, and third bloods were used in the summary tabulations for studies of comparative antibody levels which appear in this chapter. Bloods from children who received mixed, indeterminate, or odd lot combinations were excluded. Further, in order to have uniformity in the character of data used for analysis, bloods with reported toxicity in tests to one or more virus types were excluded.

The extent of these losses could not be predicted in advance nor is it possible to accurately gauge their impact on the data. However, they were of such magnitude to suggest that much of the benefit which might be gained from a random sample could well be vitiated by irregularities of the nature encountered in the procurement and utilization of the serological results. Summary tabulations with first and second blood specimens included 20,067 readings, or 1.1 percent of the total study population; 14,783 readings, 0.8 percent, were used in the tabulation of results with paired second and third bloods. First, second, and third bloods which were matched and tested simultaneously were tabulated for 10,958 children.

ANTIBODY STATUS PRIOR TO VACCINATION CLINICS

Of 20,067 pairs of sera tested and tabulated from all study areas combined, 52 percent, 54 percent, and 56 percent had no demonstrable antibodies to poliomyelitis virus Types I, II, and III, respectively (Table 54).

The frequency distribution of antibody titers at different levels is not strikingly dif-

Table 54

PRE-VACCINATION ANTIBODY LEVELS BY VIRUS TYPE
PLACEBO AND OBSERVED AREAS COMBINED

Antibody Levels	Type I		Type II		Type III	
	Number	Percent	Number	Percent	Number	Percent
Pre-vaccination Sera - Total	20,067	100.0	20,067	100.0	20,067	100.0
< 4	10,429	52.0	10,878	54.2	11,242	56.0
4 & 8	1,088	5.4	1,324	6.6	1,370	6.8
16	1,565	7.8	1,320	6.6	2,234	11.1
64	2,540	12.7	1,976	9.8	2,485	12.4
256	2,580	12.9	2,261	11.3	1,648	8.2
1024	1,865	9.3	2,308	11.5	1,088	5.4

Number < 4 to all three types = 4,306 or 21.5 percent.

ferent for the several types. It is of interest, in view of the large proportion of negatives, that the percentage at levels of 4 and 8 combined is quite low, suggesting that persons who have had earlier infection with poliomyelitis are more likely to retain substantial levels rather than low levels of antibody. There is, within these measurements, no assurance that persons with recorded titers of less than 4 have not declined from high levels to minimal residuals which are not detected by the methods employed. It may also be that those with the highest levels have had repeated experiences or, possibly, the most recent experience. In any event, only about 40 percent of the children have antibody titers of 16 or greater to virus of a given type. Demonstrable titers of 64 and 256 are most frequently present to Type I while Type III titers center about the 16 and 64 levels.

A reasonable inference from the above data might be that the three virus types have been of about equal prevalence in the history of this group of children. A further inference might be that in unvaccinated children the 1954 case incidence would be about the same for each virus type. However, this did not prove to be the case. The following figures, excerpted from Table 8, Chapter I, show all virus-positive poliomyelitis cases in unvaccinated control children in observed and placebo control areas combined.

Of 285 virus-positive poliomyelitis cases in unvaccinated control children, 155, 54 percent, were Type I, about one-third were Type III, and only 15 percent were Type II. This is in keeping with previous epidemiological experience that while equally prevalent, Type II poliomyelitis virus creates less overt disease than the other types. It is possible, of course, that isolation of Type II virus is more difficult. The frequency of Type III cases was greater than earlier data on the distribution of that virus would anticipate, but its wide dissemination is evidenced by the basic antibody levels. Type I, however, appears to have been the most frequently encountered; it is the type which has been involved in most epidemics of recent years.

VIRUS-POSITIVE POLIOMYELITIS CASES

	Total	Type I	Type II	Type III
Control Children	285	155	42	88
Total (Including Controls, Vaccinated, and Others)	433	241	55	137

Source: Table 8. (Chap. I)

Table 55 presents the proportions of total tabulated bloods taken before vaccination, grouped according to the pattern of antibody exhibited. The data include results for children to be vaccinated and for controls from placebo and observed areas combined and separately. No antibody to any of the three types of virus was detected in 20.7 percent of the total subsequently vaccinated and in 22.1 percent of the controls; the difference existed in both placebo and observed areas. This proportion is small in comparison with the absence of antibody to any single type. Naturally acquired antibody to but one type of virus was present in 35.3 percent of the vaccinated and 34.9 percent of the controls; antibody to two types was found in 27.9 and 27.4 percent of the two groups, respectively. Interestingly, 16.1 and 15.6 percent of the total specimens in the two groups had antibody to the three types of poliomyelitis virus; that pattern was more common than antibody to any one type or to any one combination of two types. Type I antibody was the most frequently present alone or in combination with others. The data as a whole demonstrate a remarkable similarity between the pre-existing antibody status of these vaccinated and control children. The differences noted between the pre-vaccination and pre-control series are of small moment which could scarcely exert a significant influence upon the subsequent behavior of the two; they appear to be chance variations. For instance, in placebo areas, the vaccinated had initial antibody to one type more frequently than the controls, but the latter had antibody

ANTIGENIC POTENCY OF VACCINE

Table 55

PRE-VACCINATION ANTIBODY STATUS BY VACCINATION STATUS
PLACEBO AREAS, OBSERVED AREAS, AND TOTAL STUDY AREAS

Pre-vaccination Antibody Status*	Total		Vaccinated		Controls	
	Number	Percent	Number	Percent	Number	Percent
All Areas Paired Sera - Total	20,067	100.0	9,161	100.0	10,906	100.0
No Antibodies to Any Type - Total	4,306	21.5	1,898	20.7	2,408	22.1
Antibodies to One Type Only - Total	7,040	35.1	3,230	35.3	3,810	34.9
Type I	2,586	12.9	1,160	12.7	1,426	13.1
Type II	2,276	11.3	1,033	11.3	1,243	11.4
Type III	2,178	10.9	1,037	11.3	1,141	10.5
Antibodies to Two Types Only - Total	5,539	27.6	2,554	27.9	2,985	27.4
Types I & II	2,070	10.3	951	10.4	1,119	10.3
Types I & III	1,804	9.0	809	8.8	995	9.1
Types II & III	1,665	8.3	794	8.7	871	8.0
Antibody to All Three Types - Total	3,182	15.9	1,479	16.1	1,703	15.6
Placebo Areas Paired Sera - Total	9,166	100.0	4,646	100.0	4,520	100.0
No Antibodies to Any Type - Total	2,166	23.6	1,061	22.8	1,105	24.4
Antibodies to One Type Only - Total	3,370	36.8	1,737	37.4	1,633	36.1
Type I	1,229	13.4	629	13.5	600	13.3
Type II	1,110	12.1	563	12.1	547	12.1
Type III	1,031	11.2	545	11.7	486	10.8
Antibodies to Two Types Only - Total	2,443	26.7	1,210	26.0	1,233	27.3
Types I & II	992	10.8	491	10.6	501	11.1
Types I & III	752	8.2	362	7.8	390	8.6
Types II & III	699	7.6	357	7.7	342	7.6
Antibodies to All Three Types	1,187	13.0	638	13.7	549	12.1
Observed Areas Paired Sera - Total	10,901	100.0	4,515	100.0	6,386	100.0
No Antibodies to Any Type - Total	2,140	19.6	837	18.5	1,303	20.4
Antibodies to One Type Only - Total	3,670	33.7	1,493	33.1	2,177	34.1
Type I	1,357	12.4	531	11.8	826	12.9
Type II	1,166	10.7	470	10.4	696	10.9
Type III	1,147	10.5	492	10.9	655	10.3
Antibodies to Two Types Only - Total	3,096	28.4	1,344	29.8	1,752	27.4
Types I & II	1,078	9.9	460	10.2	618	9.7
Types I & III	1,052	9.7	447	9.9	605	9.5
Types II & III	966	8.9	437	9.7	529	8.3
Antibodies to All Three Types	1,995	18.3	841	18.6	1,154	18.1

* Based on presence of antibody at level of 4 or

to two types more frequently than the vaccinated. The situation was reversed in observed areas.

There is, however, a consistent indication in this body of accumulated data that antibody was more commonly present in the specimens from children in observed areas than in those tabulated from placebo areas. This is particularly seen in the proportions of those with antibody to all three types of virus. This may be a reflection of the commonly recognized greater prevalence of infection with poliomyelitis virus in southern areas.

RESPONSE TO VACCINE

The results of antibody titrations with paired pre- and two-weeks post-vaccination sera from 4,646 vaccinated children in placebo areas and 4,515 vaccinated children in observed control areas have been combined to demonstrate the composite response to all lots of vaccine against each of the three virus types as shown by the distribution of titers before and after. The percentages shown in the following table were derived from figures presented in Tables 59 and 60 and are based on 9,161 total paired sera from vaccinated children.

The response to the Type I component was clearly less than to Type II or III antigen; about 60 percent of those listed without antibody to Type I originally, developed antibody to that type after vaccination, whereas, about 80 percent of comparable persons responded to Types II or III. Not only were the conversions from antibody-negative to antibody-positive more frequent with Types II and III, but the accessions into the higher ranges of titer were also much greater. This is well seen in the proportionate increases at the levels of 64 and 256. Even in these data, however, the suggestion arises that when Type I

PRE- AND POST-VACCINATION TITERS AS PERCENTAGE OF TOTAL PAIRED SERA
VACCINATED CHILDREN
PLACEBO AND OBSERVED AREAS COMBINED

Antibody Level	Type I		Type II		Type III	
	1st Sera	2nd Sera*	1st Sera	2nd Sera*	1st Sera	2nd Sera*
<4	51.9	20.0	53.5	10.9	55.0	9.9
4 or 8	5.5	9.2	7.2	7.1	7.3	10.0
16	7.6	13.0	6.4	15.0	11.0	18.1
4 or 8 & 16	13.2	22.2	13.6	22.1	18.4	28.1
64	12.1	14.2	9.7	19.2	12.1	17.0
256	12.8	15.0	11.2	15.8	8.7	14.4
64 & 256	24.9	29.2	20.9	35.1	20.8	31.4
64 or >	34.9	57.8	32.9	67.0	26.6	62.0
1024 or >	10.0	28.6	12.0	31.9	5.9	30.5

9,161 paired sera = 100%

* These proportions include instances of titer drops or rises to the given level as well as those who were at the given level in the first serum and remained unchanged.

Source: Tables 59 and 60.

antigen was stimulative, the resultant titers were of the same order as those observed with the other types.

Variation in Response to Lots of Vaccine

At the time of the Summary Report, the available evidence gave clear indication of wide variations in antigenic potency of different preparations of vaccine and emphasized that the lots of material under test were not uniform. The defectiveness of the Type I component was particularly prominent. From the accumulated serological tests, an attempt was made to grade the antigenic potency of a lot or combination of vaccine lots as a unit

Table 56

CHILDREN REPORTED WITHOUT ANTIBODY TO ANY VIRUS TYPE IN FIRST SERUM AND WITH ANTIBODY TO ALL THREE TYPES IN SECOND SERUM, BY VACCINE LOT

Lot Numbers	Vaccinated <4 to All 3 Types in 1st Serum			Controls <4 to All 3 Types in 1st Serum		
	Total	4 or > to All 3 Types in 2nd Serum		Total	4 or > to All 3 Types in 2nd Serum	
		Number	Percent		Number	Percent
Placebo Area Lots - Total	1,061	460	43	1,105	15	1
302	187	4	2	196	1	1
304	137	127	93	139	3	2
306	114	80	70	130	1	1
308	55	40	73	52	3	6
503	69	-	-	79	-	-
505	176	66	38	197	2	1
512	179	77	43	223	4	2
514	144	66	46	89	1	1
Observed Area Lots - Total	837	295	35	1,303	18	1
303-303-307	28	16	57	69	-	-
303-303-303	96	70	73	178	6	3
305-305-307	54	44	81	74	4	5
305-305-305	73	30	41	93	2	2
307-307-307	3	2	-	2	-	-
502-502-502	3	-	-	-	-	-
502-502-307	86	8	9	147	-	-
502-502-309	33	9	27	34	-	-
506-506-506	64	11	17	147	3	2
506-506-307	101	39	39	173	2	1
506-506-309	14	12	86	6	-	-
507-507-507	161	-	-	226	-	-
507-507-307	7	6	86	3	-	-
507-507-309	37	5	14	45	-	-
508-508-508	40	15	38	60	1	2
508-508-307	4	2	50	2	-	-
508-508-309	33	26	79	44	-	-
All Study Areas - Total	1,898	755	40	2,408	33	1

and also according to the individual types of virus. Various levels of host sensitivity, already referred to in this chapter, were considered.

Examinations of the larger body of data subsequently accumulated from the laboratories' reports have resulted in few changes of the basic interpretations reached earlier. The designated gradings have, however, required occasional alterations. For example, Lot 512 was not as good in Type I antigen, as limited early data suggested. Much additional effort has been given to deriving numerical values which will reasonably represent the observed antigenic potency of the lots.

Conversion of Triple Negatives to Triple Positives

Since the purpose of the vaccine was to induce antibody to the three types of virus, the most succinct measure of complete antigenic potency is the capacity of a preparation to stimulate antibody to all types in children who had no antibody to any of the types before vaccination. Moreover, the number of observations required for such an estimate is not great. In Table 56, the lots are listed on this basis. Lot 304 was successful in inducing antibody to the three types of virus in 93 percent of the subjects; seven lots and lot combinations varied between 70 and 86 percent. It is seen, however, that Lots 502, 503, and 507 are completely deficient on this basis, and five other lots and lot combinations were less than 30 percent effective. The total percentage of conversion in these series from negative to the three types to positive to the three types was but 40 percent, which is far from satisfactory in terms of the ultimate objective.

Response in Children Without Antibody to Any Type Before Vaccination

Further indication of the relative potency of the Type I, II, and III components of the vaccine is provided by a study of antibody change in vaccinated children who, prior to vaccination, had no demonstrable antibody to any type of poliomyelitis virus. For this purpose, figures for vaccinated children from Table 57 were combined with figures from Table 58; the combined data are shown in the following table.

Considering a report of antibody at a level of 4 or greater to be positive, the total percentage response of these presumably immunological virgins is seen to be far from uniform even at this level, and the response to Type I is clearly inferior to those for Types II and III. The right half of the table indi-

SECOND SERUM ANTIBODY LEVELS OF VACCINATED CHILDREN WHO HAD NO ANTIBODY TO ANY TYPE PRIOR TO VACCINATION PLACEBO AND OBSERVED AREAS

Area	Pre-vaccination Sera With No Antibody to Any Type												
	Total	Titers of 4 or > in 2nd Serum						Titers of 16 or > in 2nd Serum					
		Type I		Type II		Type III		Type I		Type II		Type III	
		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Placebo Areas	1,061	501	47	755	71	842	79	316	30	628	59	593	56
Observed Areas	837	344	41	570	68	579	69	186	22	449	54	425	51
Total	1,898	845	45	1,325	70	1,421	75	502	26	1,077	57	1,018	54

Source: Tables 57 and 58.

cates, however, that when response was obtained the titers were more likely to reach levels of 16 or greater than to fall in the minimal range of 4 and 8. This effect, of itself, points strongly to the probability that the primary defect lies in antigenic variability of the vaccine preparations rather than in the responsiveness of the host population.

Of 1,898 children without antibody to any type, only 40 percent developed antibody to all three types of virus after vaccination (Table 56). These groups presumably represent persons at greatest risk immunologically in whom the complete vaccine effect is most desirable.

Response According to Original Antibody Pattern

Tables 57 and 58 present summaries of the patterns of antibody observed before vaccination and provide material for estimating their effects upon the response to vaccination. The results with control sera collected and tested in the same manner again furnish a stability control. If one considers the response of persons with no recognized antibody prior to vaccination to be a standard of inexperience, the difference between the results in that group and in those with previous experience, as marked by the presence of antibody to one or more types, may be taken as the influence of a previous experience upon antibody response to heterologous types.

The presence of antibody for Type I virus at a level of 4 or greater before vaccination appears to enhance somewhat the percentage of positives to Types II and III after vaccination, particularly when titers of 16 or greater are considered. In the presence of pre-vaccination antibody to Type II only, 85 percent of the children whose bloods were studied developed Type I antibody, compared with 41 to 47 percent becoming Type I positives among those children who had no antibody to any type prior to vaccination. In the presence of antibody to Type II before vaccination, 87 to 94 percent became positive to Type III as opposed

Table 57

PRE-VACCINATION ANTIBODY STATUS BY POST-VACCINATION ANTIBODY STATUS, BY VIRUS TYPE AND VACCINATION STATUS
PLACEBO AREAS

Pre-vaccination Antibody Status*	1st Sera Total		Titers of 4 or > in 2nd Serum						Titers of 16 or > in 2nd Serum					
			Type I		Type II		Type III		Type I		Type II		Type III	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Vaccinated Paired Sera - Total	4,646	100.0	3,654	78.6	4,113	88.5	4,251	91.5	3,180	68.4	3,755	80.8	3,696	79.6
No Antibodies to Any Type	1,061	22.8	501	47.2	755	71.2	842	79.4	316	29.8	628	59.2	593	55.9
Antibodies to Type I Only	629	13.5	605	96.2	547	87.0	537	85.4	590	93.8	486	77.3	399	63.4
Antibodies to Type II Only	563	12.1	476	84.5	559	99.3	531	94.3	399	70.9	549	97.5	467	82.9
Antibodies to Type III Only	545	11.7	314	57.6	453	83.1	536	98.3	209	38.3	385	70.6	527	96.7
Antibodies to Types I & II Only	491	10.6	480	97.8	489	99.6	461	93.9	472	96.1	478	97.4	403	82.1
Antibodies to Types I & III Only	362	7.8	354	97.8	326	90.1	357	98.6	340	93.9	277	76.5	349	96.4
Antibodies to Types II & III Only	357	7.7	292	81.8	354	99.2	354	99.2	251	70.3	346	96.9	350	98.0
Antibodies to All Three Types	638	13.7	632	99.1	630	98.7	633	99.2	603	94.5	606	95.0	608	95.3
Placebo Paired Sera - Total	4,520	100.0	2,109	46.7	2,013	44.5	1,845	40.8	1,839	40.7	1,737	38.4	1,547	34.2
No Antibodies to Any Type	1,105	24.4	64	5.8	62	5.6	59	5.3	40	3.6	42	3.8	44	4.0
Antibodies to Type I Only	600	13.3	565	94.2	59	9.8	46	7.7	533	88.8	29	4.8	27	4.5
Antibodies to Type II Only	547	12.1	52	9.5	516	94.3	40	7.3	15	2.7	498	91.0	27	4.9
Antibodies to Type III Only	486	10.8	35	7.2	39	8.0	456	93.8	22	4.5	21	4.3	420	86.4
Antibodies to Types I & II Only	501	11.1	472	94.2	459	91.6	56	11.2	421	84.0	414	82.6	25	5.0
Antibodies to Types I & III Only	390	8.6	365	93.6	56	14.4	362	92.8	335	85.9	24	6.2	305	78.2
Antibodies to Types II & III Only	342	7.6	45	13.2	317	92.7	317	92.7	17	5.0	284	83.0	262	76.6
Antibodies to All Three Types	549	12.1	511	93.1	505	92.0	509	92.7	456	83.1	425	77.4	437	79.6

* Based on presence of antibody at titer level of 4 or >.

to 69-79 percent among those initially without antibody to any type.

At levels of 16 or greater, the influence of existing Type II antibody on heterologous responses is still more marked and far beyond any range of variation in serological procedure; the positives for Type I are 2.5 to 3.5 times greater than in those with no antecedent antibody, while those for Type III are 50 percent greater. Pre-vaccination antibody to Type III virus appears to have a moderate and equal influence upon the heterologous Type I and II responses. Essentially, the same heterogenic effect is observed if antibody to two types is present before vaccination.

The data readily suggest that Type II virus contains antigenic components related to Types I and III in sufficient amount to prepare the antibody mechanism for increased response when exposed to those stimuli, and that Types I and III have a limited influence upon heterologous response as measured by neutralization tests. The question might be raised whether heterologous antibody might have a distinct influence in limiting disease caused by Type II virus because of its broader antigenic structure.

Comparability in Controls

The variation in titers among the controls in these series is of interest in that the greatest constancy, 94-97 percent, exists in those without antibody to any type. The variation between first and second sera of controls is somewhat greater with each type if antibody to one type was previously present; when antibody to two types was noted in the first sera, 10 to 14 percent of negatives to the third type were recorded as positive in the second sera. This increasing variation may indicate either that marginal amounts of heterologous antibody to the third type arise from experiences with the other two types, or that persons who by this age have been infected with two types are more likely to have had some exposure to the third type also. A decrease in number recorded as positive - antibody titers of 4 or

Table 58

PRE-VACCINATION ANTIBODY STATUS BY POST-VACCINATION ANTIBODY STATUS BY VIRUS TYPE AND VACCINATION STATUS
OBSERVED AREAS

Pre-vaccination Antibody Status*	1st Sera Total		Titers of 4 or > in 2nd Serum						Titers of 16 or > in 2nd Serum					
			Type I		Type II		Type III		Type I		Type II		Type III	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Vaccinated Paired Sera - Total	4,515	100.0	3,678	81.5	4,054	89.8	4,000	88.6	3,310	73.3	3,758	83.2	3,639	80.6
No Antibodies to Any Type	837	18.5	344	41.1	570	68.1	579	69.2	186	22.2	449	53.6	425	50.8
Antibodies to Type I Only	531	11.8	530	99.8	447	84.2	406	76.5	523	98.5	406	76.5	313	58.9
Antibodies to Type II Only	470	10.4	406	86.4	469	99.8	410	87.2	368	78.3	463	98.5	366	77.9
Antibodies to Type III Only	492	10.9	280	56.9	426	86.6	489	99.4	185	37.6	377	78.6	474	96.3
Antibodies to Types I & II	460	10.2	458	99.6	457	99.3	400	87.0	450	97.8	445	96.7	364	79.1
Antibodies to Types I & III	447	9.9	447	100.0	410	91.7	445	99.6	440	98.4	368	82.3	439	98.2
Antibodies to Types II & III	437	9.7	381	87.2	436	99.8	434	99.3	333	78.2	432	98.9	429	98.2
Antibodies to All Three Types	841	18.6	832	98.9	839	99.8	837	99.5	825	98.1	818	97.3	829	98.6
Control Paired Sera - Total	6,386	100.0	3,295	51.6	3,148	49.3	3,060	47.9	2,980	46.7	2,729	42.7	2,649	41.5
No Antibodies to Any Type	1,303	20.4	50	3.8	71	5.4	67	5.1	32	2.5	42	3.2	39	3.0
Antibodies to Type I Only	826	12.9	803	97.2	75	9.1	52	6.3	776	93.9	35	4.2	28	3.4
Antibodies to Type II Only	696	10.9	48	6.9	671	96.4	37	5.3	21	3.0	646	92.8	21	3.0
Antibodies to Type III Only	655	10.3	37	5.6	56	8.5	641	97.9	18	2.7	25	3.8	595	90.8
Antibodies to Types I & II Only	618	9.7	603	97.6	582	94.2	64	10.4	550	89.0	518	83.8	25	4.0
Antibodies to Types I & III Only	605	9.5	586	96.9	82	13.6	582	96.2	560	92.6	32	5.3	521	86.1
Antibodies to Types II & III Only	529	8.3	51	9.6	511	96.6	507	95.8	24	4.5	481	90.9	441	83.4
Antibodies to All Three Types	1,154	18.1	1,117	96.8	1,100	95.3	1,110	96.2	999	86.6	950	82.3	979	84.8

* Based on presence of antibody at titer level of 4 or >.

greater–to a given type between first and second bleedings is noted consistently to be 6 to 7 percent in placebo area data and 2 to 4 percent in those from observed areas. Hence, the increasing number of positives in the previously recorded negative controls is not attributable to a technical variation always leaning to a higher titer in the second of a pair of sera.

Response in Relation to Initial Level of Antibody

Attention can again be directed to the data of Tables 57 and 58 which show the percentage distribution of pre-existing titers and the comparatively low frequency at levels of 4, 8, and 16. Moreover, this gap is consistently present in the initial titers of vaccinated and control subjects from both placebo and observed areas. The tendency for Type III titers to collect at the level of 16 is also consistently present. The prevalence of recorded titers of 64 or greater is highest for Type I and lowest for Type III. Titers of this height are more common for each type in subjects from observed areas, again suggesting their greater experience.

Additional detail of antibody response is presented in Tables 59 and 60 for the vaccinated and control groups of the placebo and observed study areas separately. The control data demonstrate the degree of variation encountered in the levels of antibody reported by the laboratories based on pairs of sera taken seven weeks apart but tested simultaneously; theoretically, they should be essentially the same. The titers in the controls fluctuate rather evenly about the designated first titer so that approximately 90 percent remain within the range of one serum dilution. In the vaccinated, however, the second titers move selectively into the higher levels.

Table 59

PRE-VACCINATION SERUM ANTIBODY LEVELS
BY POST-VACCINATION LEVELS BY VIRUS TYPE AND VACCINATION STATUS
PLACEBO AREAS

Antibody Levels by Virus Type	Vaccinated Children																Placebo Children													
	1st Serum Titers		2nd Serum Titers														1st Serum Titers		2nd Serum Titers											
			< 4		4 & 8		16		64		256		1024		Mean				< 4		4 & 8		16		64		256		1024		Mean
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Titers**		No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Titers**
Type I																															
< 4	2,526	54	939	37	408	16	474	19	381	15	187	7	137	5	8		2,480	55	2,283	92	97	4	25	1	24	1	32	1	19	1	< 4
4 & 8	256	6	20	8	47	18	48	19	40	16	55	21	46	18	30		258	6	58	22	123	48	42	16	21	8	8	3	6	2	6
16	312	7	9	3	12	4	54	17	79	25	59	19	99	32	67		312	7	11	4	41	13	171	55	66	21	14	4	9	3	12
64	497	11	9	2	3	1	22	4	108	22	127	26	228	46	144		507	11	23	5	3	1	74	15	277	55	102	20	28	6	35
256	519	11	7	1	3	1	7	1	30	6	140	27	332	64	256		533	12	22	4	3	1	8	2	107	20	290	54	103	19	100
1024	536	12	8	1	1	*	8	1	10	2	25	5	484	90	391		430	10	14	3	3	1	5	1	17	4	75	17	316	73	277
Total	4,646	100	992	21	474	10	613	13	648	14	593	13	1,326	29	31		4,520	100	2,411	53	270	6	325	7	512	11	521	12	481	11	9
Type II																															
< 4	2,597	56	516	20	305	12	588	23	662	25	336	13	190	7	15		2,581	57	2,367	92	98	4	34	1	23	1	26	1	33	1	< 4
4 & 8	320	7	8	3	37	12	51	16	94	29	63	20	67	21	44		265	6	73	28	135	51	34	13	10	4	6	2	7	3	5
16	280	6	2	1	7	2	42	15	59	21	84	30	86	31	86		286	6	13	5	37	13	162	57	53	19	16	6	5	2	11
64	432	9	3	1	4	1	16	4	70	16	112	26	227	53	180		368	8	12	3	4	1	34	9	232	63	72	20	14	4	37
256	435	9	3	1	3	1	6	1	20	5	89	20	314	72	298		462	10	17	4	-	-	9	2	75	16	274	59	87	19	108
1024	582	13	1	*	2	*	6	1	8	1	26	4	539	93	432		558	12	25	4	2	*	5	1	14	3	75	13	437	78	293
Total	4,646	100	533	11	358	8	709	15	913	20	710	15	1,423	31	46		4,520	100	2,507	55	276	6	278	6	407	9	469	10	583	13	9
Type III																															
< 4	2,744	59	373	14	509	19	800	29	651	24	258	9	153	6	13		2,753	61	2,552	93	78	3	49	2	41	1	21	1	12	*	< 4
4 & 8	312	7	10	3	23	7	48	15	51	16	78	25	102	33	71		302	7	61	20	154	51	66	22	14	5	4	1	3	1	5
16	465	10	4	1	12	3	47	10	41	9	105	23	256	55	162		442	10	21	5	51	12	268	61	72	16	21	5	9	2	11
64	490	11	6	1	9	2	16	3	46	9	100	20	313	64	222		472	10	23	5	10	2	84	18	263	56	68	14	24	5	29
256	350	8	2	1	1	*	5	1	15	4	74	21	253	72	306		316	7	8	3	4	1	10	3	77	24	169	53	48	15	89
1024	285	6	-	-	1	*	5	2	6	2	17	6	256	90	406		235	5	10	4	1	*	4	2	12	5	42	18	166	71	250
Total	4,646	100	395	9	555	12	921	20	810	17	632	14	1,333	29	40		4,520	100	2,675	59	298	7	481	11	479	11	325	7	262	6	6

* Less than 1 percent.
** Geometric mean of titers in which $Log_2 < 4$ was taken as 1.0000 and Log_2 4 & 8 was taken as 1 Log_2 above < 4 and 1 Log_2 below 16.

That effect is well seen in the total distribution of antibody levels to each type of virus and in each initial antibody group; the increased number with titers of 1024 or greater, even among the Type I vaccinated, is quite marked. In these data the influence of pre-existing antibody on response to vaccine is readily observed by comparison of the resultant titers in those with pre-vaccination levels of less than 4, 4 or 8, and 16. Of those with less than 4 initially to Type III in placebo areas, 9 percent and 6 percent reached 256 and 1024 or greater levels, respectively; of those initially with 4 or 8 titers, it was 25 percent and 33 percent; with initial titers of 16, it was 23 and 55 percent. Although the efficiency of Type I as a primary stimulus was less, its effect upon persons with antibody to begin with was not much different from antigens of the other types. But with no type did the presence of antibody at low levels result in uniform exaltation of titers into the highest ranges after vaccination. The geometric mean titers summarize the influence of vaccine upon the responses of those with or without pre-existing antibody. The median values presented on the following page again show the superior effect of Type II stimulus in persons without pre-vaccination antibody. The median titers in the second sera of vaccinated subjects are strikingly higher for each type and for each pre-vaccination level than those of the controls.

Response in Children With No Antibody to a Given Type

Study of the actual antibody levels attained after vaccination by children who had no demonstrable antibody to a specific type prior to vaccination gives further information of the relative antigenicity of the type-specific components of the vaccines. Included in the 9,161 total paired sera from vaccinated children in placebo and observed areas combined, 4,757

Table 60

PRE-VACCINATION SERUM ANTIBODY LEVELS
BY POST-VACCINATION LEVELS BY VIRUS TYPE AND VACCINATION STATUS
OBSERVED AREAS

Antibody Levels by Virus Type	Vaccinated Children															Control Children												
	1st Serum Titers		2nd Serum Titers													1st Serum Titers		2nd Serum Titers										
			< 4		4 & 8		16		64		256		1024		Mean			< 4		4 & 8		16		64		256		1024		Mean
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Titers**	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	Titers**
Type I																														
< 4	2,231	49	828	37	334	15	472	21	365	16	175	8	57	3	7	3,192	50	3,006	94	91	3	39	1	24	1	19	1	13	*	< 4
4 & 8	252	6	5	2	24	10	49	19	59	23	66	26	49	19	47	322	5	57	18	166	52	66	20	16	5	6	2	11	3	6
16	385	9	2	1	8	2	44	11	96	25	116	30	119	31	92	556	9	10	2	47	8	336	60	130	23	22	4	11	2	12
64	613	14	2	*	-	-	11	2	104	17	199	32	297	48	186	923	14	9	1	9	1	112	12	587	64	171	19	35	4	37
256	652	14	-	-	1	*	3	*	28	4	181	28	439	67	301	876	14	5	1	2	*	6	1	166	19	555	63	142	16	117
1024	382	8	-	-	1	*	1	*	3	1	44	12	333	87	417	517	8	4	1	-	-	3	1	12	2	152	29	346	67	299
Total	4,515	100	837	19	368	8	580	13	655	15	781	17	1,294	29	38	6,386	100	3,091	48	315	5	562	9	935	15	925	14	558	9	10
Type II																														
< 4	2,302	51	451	20	254	11	563	24	630	27	312	14	92	4	14	3,398	53	3,111	92	152	4	39	1	42	1	35	1	19	1	< 4
4 & 8	343	8	4	1	30	9	65	19	84	24	110	32	50	15	46	396	6	101	26	217	54	54	14	12	3	8	2	4	1	4
16	307	7	1	*	9	3	23	7	66	21	75	24	133	43	126	447	7	9	2	44	10	257	57	108	24	14	3	15	3	13
64	457	10	2	*	2	*	12	3	51	11	116	25	274	60	226	719	11	9	1	3	*	62	11	440	61	159	22	26	4	39
256	588	13	3	1	-	-	1	*	13	2	103	18	468	80	365	776	12	5	1	2	*	8	1	130	17	487	63	144	19	123
1024	518	11	-	-	1	*	1	*	6	1	25	5	485	94	456	650	10	3	*	1	*	1	*	10	2	126	19	509	78	361
Total	4,515	100	461	10	296	7	665	15	850	19	741	16	1,502	33	54	6,386	100	3,238	51	419	7	441	7	742	12	829	13	717	11	10
Type III																														
< 4	2,293	51	502	22	324	14	645	28	533	23	201	9	88	4	11	3,452	54	3,230	94	109	3	54	2	31	1	13	*	15	*	< 4
4 & 8	361	8	5	1	29	8	53	15	68	19	85	24	121	34	75	395	6	88	17	217	55	75	19	16	4	10	3	9	2	5
16	547	12	5	1	5	1	28	5	74	14	136	25	299	55	183	780	12	14	2	71	9	499	64	156	20	23	3	17	2	11
64	615	14	3	*	1	*	8	1	59	10	146	24	398	65	258	908	14	10	1	14	2	116	13	585	64	144	16	39	4	35
256	448	10	-	-	-	-	1	*	13	3	103	23	331	74	340	534	8	4	1	-	-	10	2	122	23	322	60	76	14	105
1024	251	6	-	-	2	1	2	1	3	1	18	7	226	90	417	317	5	-	-	-	-	1	*	18	6	74	23	224	71	312
Total	4,515	100	515	11	361	8	737	16	750	17	689	15	1,463	32	48	6,386	100	3,326	52	411	6	755	12	928	15	586	9	380	6	8

* Less than 1 percent.
** Geometric mean of titers in which $\text{Log}_2 < 4$ was taken as 1.0000 and Log_2 4 & 8 was taken as 1 Log_2 above <4 and 1 Log_2 below 16.

MEDIAN TITERS IN SECOND SERA BY FIRST SERUM ANTIBODY LEVELS
BY VACCINATION STATUS
PLACEBO AND OBSERVED AREAS

First Serum Antibody Levels	Median Titers of Second Sera by Virus Type					
	Type I		Type II		Type III	
	Vaccinated	Controls	Vaccinated	Controls	Vaccinated	Controls
Placebo Areas						
<4	28		53		28	
4 & 8	87	7	101	7	271	7
16	170	23	270	23	563	22
64	464	89	540	90	628	80
256	629	310	672	322	672	271
1024	745	687	748	712	739	677
Observed Areas						
<4	27		49		29	
4 & 8	114	7	117	7	254	7
16	272	24	410	24	560	23
64	496	87	599	91	630	84
256	644	309	704	322	677	287
1024	730	644	751	699	740	662

Computed from data presented in Tables 59 and 60; second serum titers of <4 were excluded from the distributions before computations were made.

(52 percent), 4,899 (53 percent), and 5,037 (55 percent), had no antibody to Type I, II or III, respectively. Post-vaccination antibody levels for those children are shown on page 163.

The quantitative effect of vaccination upon antibody titers is clearly seen in addition to the reduction in antibody-negatives in that the levels attained by those who did respond are well distributed and reach the greatest concentration at substantial titers of 16 and 64. A greater proportion of high antibody levels is achieved in those who responded to Type II antigen than in responders to antigens of Types I and III whose effects were consistently of the same order when the production of antibody occurred. It is of interest to speculate whether the highest titers may represent persons with previous antibody which was below the level recognized by the serological procedure employed.

POST-VACCINATION ANTIBODY LEVELS FOR VACCINATED CHILDREN WITHOUT ANTIBODY TO SPECIFIC TYPE PRIOR TO VACCINATION BY TYPE PLACEBO AND OBSERVED AREAS COMBINED

Poliomyelitis	Pre-vaccination Sera <4	Post-vaccination Antibody Levels					
		<4	4 & 8	16	64	256	1024
Type I							
Number	4,757	1,767	742	946	746	362	194
Percent	100.0	37.1	15.6	19.9	15.7	7.6	4.1
Type II							
Number	4,899	967	559	1,151	1,292	648	282
Percent	100.0	19.7	11.4	23.5	26.4	13.2	5.8
Type III							
Number	5,037	875	833	1,445	1,184	459	241
Percent	100.0	17.4	16.5	28.7	23.5	9.1	4.8

Source: Tables 59 and 60.

Relative Antigenic Effect of Different Vaccine Lots

It has been repeatedly emphasized that with a given preparation one antigenic component could be of poor potency while others retained a good antigenic efficiency. The type-specific effect was then estimated for each of the lots and combinations with corrections for the degree of intrinsic change in reported titers as reflected in the controls for the same lots, whether related to natural or technical irregularities. These relative antibody responses to the preparations employed in subjects who were without antibody to a given type before vaccination are listed in Tables 61 and 62. Since the results comprise those from subjects with no antibody to any type and those with antibody before vaccination to one or two types other than that under consideration, the degree of response to a given antigen recorded here is presumably enhanced, as earlier indicated, by the influence of previous experience with virus of another type.

It is seen that the response to Type I is the lowest in all but one instance and that those lots noted in Table 56 to be least effective as complete antigenic stimuli are also the least effective against Type I.

The difference in potency of antigens within a lot is well illustrated by these same lots, especially 302, the Type III component of which had a high antigenic effect. Lot 304, however, is seen to be of good potency throughout. It is of interest that in the poorest lots the Type III antigen was the best, indicating its greater stability. The deficiency of Type II antigen in a few lots reduces the average response to that type although it was generally better than the Type III stimulus.

In Table 62 the type-specific antigenic ef-

fects of lots or combinations are listed according to potency. Fifteen lots had estimated effect of 90 percent or greater for Type II, 10 for Type III, and only 3 for Type I. The problems confronting efforts to amalgamate these results in order to provide a single estimate of potency or effect is clearly seen.

Table 61

VACCINE LOTS BY PERCENT RELATIVE ANTIGENIC EFFECT TO EACH POLIOMYELITIS VIRUS TYPE*

Lot Number	Percent Relative Antigenic Effect		
	Type I	Type II	Type III
Placebo Areas			
302-302-302	27	49	86
304-304-304	93	98	98
306-306-306	84	90	89
308-308-308	78	90	79
503-503-503	3	18	46
505-505-505	66	88	88
512-512-512	61	94	84
514-514-514	67	96	91
Observed Areas			
303-303-303	88	93	88
303-303-307	74	86	76
305-305-305	72	92	96
305-305-307	83	97	91
307-307-307	83	100	83
502-502-502	71	43	100
502-502-307	50	85	88
502-502-309	60	86	76
506-506-506	57	96	98
506-506-307	67	93	90
506-506-309	95	100	94
507-507-507	7	21	24
507-507-307	47	98	90
507-507-309	49	71	48
508-508-508	67	92	80
508-508-307	64	89	69
508-508-309	92	99	94

* See Glossary.

In addition, Tables 63 and 64 present the type-specific antibody levels attained two weeks after vaccination with the various lots, by persons without preceding antibody to either the given type or to any type.

Series A, those without pre-vaccination antibody to a specific type, includes Series B, those without antibody to any type. For Lot 302 it is seen that while 54 percent of all original specimens had no antibody to Type I (Series A), 22 percent of the total, or 42 percent of Series A, was also included in Series B. Consequently, results in the former are heavily influenced by the behavior of the presumably inexperienced B group. It can be seen by examination of almost any segment of the data that the stimulus required to induce antibodies in those with no original antibodies to the three types is greater than for persons who do not exhibit antibody to the one type under analysis but possess antibody to one or more heterologous types. The total experience with Type I shows that nearly 50 percent more of Group A than of Group B developed detectable antibody after vaccination.

There is a distinct parallelism between the capacity of a lot of vaccine to change the negatives to positives and the proportion of titers which reach a level of 16 or greater. That effect is more generally noted in the resultant titers of persons responding to antigens of Type II or III; 50 percent of those responding reach levels of 64 or greater. With lots having good antigens, the response in the majority of persons without antibody to any of the types may also reach 64 or greater. The latter then constitute a more critical test of the antigenic capacity of a vaccine. In fact, inspection of responses of the triple negatives to a lot or type is probably the readiest single method of estimating antigenic effect.

RELATION OF ANTIGENIC POTENCY TO PROPHYLACTIC EFFECTIVENESS

Results condensed in a number of ways for estimating antigenic effect of lots of vaccine on the component types are assembled in Tables 65 and 66. They include data showing the extent of conversion from negative to

Table 62

VACCINE LOTS ARRANGED BY RELATIVE ANTIGENIC EFFECT TO EACH POLIOMYELITIS VIRUS TYPE*

Type I		Type II		Type III	
Lot Number	Percent Relative Antigenic Effect	Lot Number	Percent Relative Antigenic Effect	Lot Number	Percent Relative Antigenic Effect
506-506-309	95	307-307-307	100	502-502-502	100
304-304-304	93	506-506-309	100	304-304-304	98
508-508-309	92	508-508-309	99	506-506-506	98
303-303-303	88	304-304-304	98	305-305-305	96
306-306-306	84	507-507-307	98	506-506-309	94
307-307-307	83	305-305-307	97	508-508-309	94
305-305-307	83	514-514-514	96	305-305-307	91
308-308-308	78	506-506-506	96	514-514-514	91
303-303-307	74	512-512-512	94	506-506-307	90
305-305-305	72	506-506-307	93	507-507-307	90
502-502-502	71	303-303-303	93	306-306-306	89
506-506-307	67	508-508-508	92	505-505-505	88
514-514-514	67	305-305-305	92	502-502-307	88
508-508-508	67	308-308-308	90	303-303-303	88
505-505-505	66	306-306-306	90	302-302-302	86
508-508-307	64	508-508-307	89	512-512-512	84
512-512-512	61	505-505-505	88	307-307-307	83
502-502-309	60	502-502-309	86	508-508-508	80
506-506-506	57	303-303-307	86	308-308-308	79
502-502-307	50	502-502-307	85	303-303-307	76
507-507-309	49	507-507-309	71	502-502-309	76
507-507-307	47	302-302-302	49	508-508-307	69
302-302-302	27	502-502-502	43	507-507-309	48
507-507-507	7	507-507-507	21	503-503-503	46
503-503-503	3	503-503-503	18	507-507-507	24

* Relative antigenic effect: See Glossary.

positive antibody status for children without antibody to any type of virus before vaccination and children without initial antibody to a specific type; geometric means of titers, by type, of all persons tested regardless of the initial antibody level are also shown. Estimates of relative antigenic effectiveness according to antibody response are presented for each lot with respect to type. Estimates of prophylactic effectiveness based upon the occurrence of cases of poliomyelitis related to each lot and type are also included. The purpose is to relate these several measures of antigenic potency to prophylactic effect. The results in placebo controls or in unvaccinated controls of observed areas are presented for comparison and for indication of variation inherent in the test procedures.

The percentage response of the serological negatives is clearly seen in the percentages remaining negative after vaccination. The comparative sensitivity of the two groups considered in Tables 63 and 64 can again be reviewed. They both provide ready differentiation of relative antigenic effect.

Table 63

SERUM ANTIBODY TITERS FOR PAIRED SERA WHERE FIRST BLOOD TITER LEVEL IS LESS THAN FOUR, BY VACCINE LOT, VIRUS TYPE AND VACCINATION STATUS PLACEBO AREAS

A = Sera <4 for first blood to type specified B = Sera <4 for first blood to all three types

Vaccine Lot by Vaccination Status			Total Paired Sera	Type I								Type II								Type III							
				1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers					
				No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024
302	Vaccinated	A	833	449	54	312	66	44	22	1	4	449	54	217	82	86	47	13	4	517	62	74	117	152	117	42	15
		B		187	22	177	5	3	2	-	-	187	22	157	20	5	2	2	1	187	22	43	50	56	27	7	4
	Placebo	A	851	429	50	405	12	2	2	6	2	526	62	495	21	3	4	-	3	542	64	509	15	11	3	2	2
		B		196	23	192	1	-	1	2	-	196	23	192	2	-	2	-	-	196	23	188	4	3	-	1	-
304	Vaccinated	A	621	295	48	18	40	81	100	42	14	370	60	9	27	92	128	77	37	384	62	7	18	97	157	79	26
		B		137	22	8	25	52	36	13	3	137	22	4	16	39	50	23	5	137	22	5	6	35	63	18	10
	Placebo	A	553	299	54	275	17	1	2	2	2	335	61	303	21	3	3	3	2	324	59	300	13	5	3	3	-
		B		139	25	132	4	1	1	1	-	139	25	133	2	1	1	1	1	139	25	132	1	3	1	2	-
306	Vaccinated	A	543	302	56	45	65	63	57	40	32	262	48	23	41	63	68	50	17	328	60	33	50	81	97	45	22
		B		114	21	27	35	38	10	1	3	114	21	15	15	30	32	17	5	114	21	19	21	27	31	10	6
	Placebo	A	532	307	58	280	21	4	-	-	2	276	52	248	18	4	1	3	2	344	65	324	10	4	3	3	-
		B		130	24	123	7	-	-	-	-	130	24	128	-	1	1	-	-	130	24	127	1	1	-	1	-
308	Vaccinated	A	270	145	54	29	14	33	30	18	21	137	51	13	12	38	34	17	23	131	49	25	18	42	25	16	5
		B		55	20	12	6	16	10	7	4	55	20	7	4	21	14	4	5	55	20	11	12	15	12	4	1
	Placebo	A	255	152	60	140	6	2	2	2	-	124	49	112	5	2	1	1	3	143	56	128	9	1	3	1	1
		B		52	20	47	2	1	1	1	-	52	20	46	2	-	1	-	3	52	20	46	2	1	2	-	1
503	Vaccinated	A	405	186	46	162	14	8	-	1	1	222	55	173	31	13	3	2	-	200	49	99	41	29	17	11	3
		B		69	17	68	1	-	-	-	-	69	17	68	1	-	-	-	-	69	17	47	13	6	1	1	1
	Placebo	A	452	213	47	192	14	4	1	1	1	223	49	212	6	1	-	2	2	207	46	192	7	3	2	1	2
		B		79	17	72	5	1	-	-	1	79	17	73	5	1	-	-	-	79	17	77	-	-	1	1	-
505	Vaccinated	A	773	434	56	141	65	94	71	34	29	424	55	46	60	114	104	57	43	434	56	48	89	130	104	33	30
		B		176	23	102	30	30	7	3	4	176	23	33	38	57	33	7	8	176	23	32	49	60	23	5	7
	Placebo	A	721	410	57	388	9	4	4	4	1	413	57	387	12	5	1	1	7	438	61	417	8	3	9	-	1
		B		197	27	191	2	1	2	1	-	197	27	190	4	1	-	-	2	197	27	191	1	-	4	-	1
512	Vaccinated	A	642	399	62	134	74	77	47	35	32	405	63	22	33	78	145	74	53	401	62	56	71	139	82	19	34
		B		179	28	90	39	27	4	8	11	179	28	14	18	48	63	20	16	179	28	41	37	55	25	7	14
	Placebo	A	677	441	65	385	12	5	13	16	10	420	62	364	7	11	10	15	13	459	68	401	10	19	14	10	5
		B		223	33	198	2	1	9	7	6	223	33	198	2	6	5	5	7	223	33	200	5	7	6	4	1
514	Vaccinated	A	559	316	57	98	70	74	54	16	4	328	59	13	19	104	133	46[a]	13	349	62	31	105	130	52	13	16
		B		144	26	76	44	19	3	-	2	144	26	8	15	54	52	14	1	144	26	21	61	44	15	2	1
	Placebo	A	479	229	48	218	6	3	-	1	1	264	55	246	8	5	3	1	1	296	62	281	6	3	4	1	1
		B		89	19	86	1	-	-	1	1	89	19	83	3	1	1	-	1	89	19	85	1	1	1	1	-

Table 64

SERUM ANTIBODY TITERS FOR PAIRED SERA WHERE FIRST BLOOD TITER LEVEL IS LESS THAN FOUR, BY VACCINE LOT, VIRUS TYPE AND VACCINATION STATUS OBSERVED AREAS

A = Sera <4 for first blood to type specified B = Sera <4 for first blood to all three types

Vaccine Lot by Vaccination Status			Total Paired Sera	Type I								Type II								Type III							
				1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers					
				No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024
502-502-307	Vaccinated	A	230	129	56	63	23	13	15	13	2	118	51	17	23	31	29	16	2	144	63	18	18	45	37	22	4
		B		86	37	68	15	3	-	-	-	86	37	22	19	27	15	2	1	86	37	14	11	30	18	12	1
	Controls	A	332	229	69	224	2	3	-	-	-	224	67	215	-	1	4	3	1	227	68	222	3	-	-	1	1
		B		147	44	146	-	1	-	-	-	147	44	142	-	1	3	1	-	147	44	144	-	1	1	-	1
502-502-309	Vaccinated	A	182	77	42	29	16	11	6	7	8	94	52	13	22	21	21	12	5	86	47	20	18	22	16	7	3
		B		33	18	22	7	2	-	-	2	33	18	11	12	7	2	-	1	33	18	11	7	7	3	3	2
	Controls	A	227	90	40	85	1	-	3	1	-	92	41	89	2	-	1	-	-	97	43	93	1	1	1	-	1
		B		34	15	34	-	-	-	-	-	34	15	34	-	-	-	-	-	34	15	34	-	-	-	-	-
502-502-502	Vaccinated	A	11	7	64	2	1	1	1	2	-	7	64	4	2	-	-	-	1	7	64	3	1	2	1	-	-
		B		3	27	2	1	-	-	-	-	3	27	3	-	-	-	-	-	3	27	3	-	-	-	-	-
	Controls	A	2	2	100	2	-	-	-	-	-	1	50	1	-	-	-	-	-	-	-	-	-	-	-	-	-
		B		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
506-506 -506	Vaccinated	A	483	239	49	100	42	56	28	11	2	215	45	8	29	86	64	24	4	193	40	4	25	81	59	13	11
		B		64	13	50	8	3	-	3	-	64	13	6	19	29	8	1	1	64	13	3	13	31	13	1	3
	Controls	A	771	400	52	386	9	2	-	1	2	369	48	345	15	3	1	5	-	388	50	365	16	3	2	2	-
		B		147	19	144	3	-	-	-	-	147	19	141	3	1	1	1	-	147	19	140	4	2	-	1	-
506-506-307	Vaccinated	A	486	246	51	76	42	75	41	9	3	267	55	16	14	88	85	52	12	281	54	23	30	114	65	16	13
		B		101	21	46	30	17	8	-	-	101	21	11	8	43	30	9	-	101	21	18	20	45	13	4	1
	Controls	A	784	393	50	370	8	9	2	3	1	448	57	403	25	8	7	3	2	444	57	418	15	8	3	-	-
		B		173	22	165	3	4	-	-	1	173	22	157	8	2	5	1	-	173	22	163	4	5	1	-	-
506-506-309	Vaccinated	A	57	37	65	2	9	11	14	-	1	35	61	-	3	14	11	7	-	33	58	2	6	16	6	2	1
		B		14	25	1	6	2	5	-	-	14	25	-	2	9	2	1	-	14	25	1	4	8	1	-	-
	Controls	A	11	9	82	9	-	-	-	-	-	8	73	8	-	-	-	-	-	8	73	8	-	-	-	-	-
		B		6	55	6	-	-	-	-	-	6	55	6	-	-	-	-	-	6	55	6	-	-	-	-	-
507-507-507	Vaccinated	A	608	309	51	278	10	10	5	3	3	385	63	292	48	28	12	2	3	372	61	270	42	35	12	6	7
		B		161	26	156	1	2	-	1	1	161	26	155	3	2	1	-	-	161	26	133	15	11	-	1	1
	Controls	A	907	482	53	468	5	4	1	2	2	561	62	538	12	6	3	1	1	542	60	521	11	4	1	2	3
		B		226	25	223	-	1	-	1	1	226	25	222	-	-	3	-	1	226	25	221	2	1	-	2	-
507-507-307	Vaccinated	A	121	71	59	37	12	8	4	7	3	69	57	8	8	16	20	8	9	74	61	7	10	24	18	10	5
		B		7	6	6	1	-	-	-	-	7	6	1	1	2	3	-	-	7	6	3	-	3	-	-	1
	Controls	A	96	55	57	54	1	-	-	-	-	55	57	53	1	1	-	-	-	60	62	56	-	1	1	1	1
		B		3	3	3	-	-	-	-	-	3	3	3	-	-	-	-	-	3	3	3	-	-	-	-	-

(Continued on next page.)

Table 64 Continued

Vaccine Lot by Vaccination Status			Total Paired Sera	Type 1								Type II								Type III							
				1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers						1st Sera <4		2nd Serum Titers					
				No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024	No.	%	<4	4&8	16	64	256	1024
507-507-309	Vaccinated	A	233	100	43	47	13	14	12	10	4	124	53	35	20	27	19	16	7	101	43	51	26	16	5	2	1
		B		37	16	31	3	2	1	-	-	37	16	22	8	6	1	-	-	37	16	21	9	5	1	-	1
	Controls	A	239	119	50	110	4	2	2	1	-	135	56	128	1	1	1	1	3	136	57	130	1	3	1	1	-
		B		45	19	45	-	-	-	-	-	45	19	45	-	-	-	-	-	45	19	43	1	1	-	-	-
508-508-508	Vaccinated	A	357	165	46	47	31	31	34	16	6	162	45	12	15	47	46	35	7	168	47	31	36	49	29	15	8
		B		40	11	23	11	3	1	2	-	40	11	5	7	16	8	4	-	40	11	12	13	9	3	1	2
	Controls	A	487	209	43	180	17	2	5	3	2	211	43	179	14	5	6	3	4	237	49	210	8	10	5	2	2
		B		60	12	55	1	1	1	2	-	60	12	53	2	2	2	-	1	60	12	56	1	2	1	-	-
508-508-307	Vaccinated	A	18	11	61	4	3	2	2	-	-	9	50	1	-	3	4	1	-	13	72	4	2	3	4	-	-
		B		4	22	2	1	1	-	-	-	4	22	-	-	2	2	-	-	4	22	1	1	1	1	-	-
	Controls	A	9	5	56	5	-	-	-	-	-	4	44	4	-	-	-	-	-	6	67	6	-	-	-	-	-
		B		2	22	2	-	-	-	-	-	2	22	2	-	-	-	-	-	2	22	2	-	-	-	-	-
508-508-309	Vaccinated	A	208	100	48	8	7	28	39	17	1	102	49	1	3	20	46	23	9	112	54	7	19	34	40	10	2
		B		33	16	6	5	13	7	2	-	33	16	1	2	10	15	3	2	33	16	2	14	9	5	2	1
	Controls	A	262	120	46	119	1	-	-	-	-	140	53	129	9	-	1	-	1	143	55	133	9	1	-	-	-
		B		44	17	43	1	-	-	-	-	44	17	43	1	-	-	-	-	44	17	41	3	-	-	-	-
303-303-303	Vaccinated	A	473	248	52	28	38	74	65	32	11	241	51	15	10	50	99	48	19	233	49	25	26	67	76	25	14
		B		96	20	16	25	32	16	5	2	96	20	5	6	28	38	15	4	96	20	13	14	33	25	8	3
	Controls	A	755	410	54	385	7	7	6	3	2	399	53	365	11	2	9	9	3	423	56	386	14	11	8	2	2
		B		178	24	166	-	4	5	2	1	178	24	165	4	1	3	3	2	178	24	162	5	4	6	-	1
303-303-307	Vaccinated	A	85	57	67	15	7	17	12	4	2	53	62	7	3	11	21	9	2	48	56	11	7	11	13	6	-
		B		28	33	8	4	7	7	1	1	28	33	5	1	7	9	4	2	28	33	8	4	3	8	5	-
	Controls	A	223	139	62	137	2	-	-	-	-	145	65	139	2	1	1	2	-	152	68	146	-	-	3	-	3
		B		69	31	68	1	-	-	-	-	69	31	68	-	1	-	-	-	69	31	67	-	-	1	-	1
305-305-305	Vaccinated	A	598	265	44	67	41	76	49	25	7	233	39	17	36	64	70	35	11	271	45	12	22	72	99	52	14
		B		73	12	40	21	9	1	2	-	73	12	16	24	20	10	3	-	73	12	7	11	21	25	6	3
	Controls	A	777	300	39	271	19	4	3	1	2	321	41	266	37	10	4	3	1	336	43	305	17	8	4	2	-
		B		93	12	85	6	1	1	-	-	93	12	82	6	3	1	-	1	93	12	89	2	1	1	-	-
305-305-307	Vaccinated	A	355	164	46	24	39	43	37	17	4	184	52	5	18	55	83	22	1	171	48	13	36	51	51	15	5
		B		54	15	15	19	9	7	3	1	54	15	4	9	17	18	6	-	54	15	7	18	11	14	3	1
	Controls	A	492	222	45	193	15	6	2	4	2	280	57	244	23	1	4	5	3	247	50	225	14	4	2	-	2
		B		74	15	66	3	3	1	-	1	74	15	67	5	-	1	1	-	74	15	63	6	3	1	-	1
307-307-307	Vaccinated	A	10	6	60	1	-	2	1	2	-	4	40	-	-	2	-	2	-	6	60	1	-	3	2	-	-
		B		3	30	1	-	1	1	-	-	3	30	-	-	1	-	2	-	3	30	1	-	1	1	-	-
	Controls	A	12	8	67	8	-	-	-	-	-	5	42	5	-	-	-	-	-	8	50	6	-	-	-	-	-
		B		2	17	2	-	-	-	-	-	2	17	2	-	-	-	-	-	2	17	2	-	-	-	-	-

Table 65

SEROLOGY AND CLINICAL DATA BY VACCINATION STATUS AND VACCINE LOT
PLACEBO AREAS

Item	Total For Placebo Area Lots		Lot 302		Lot 304		Lot 306		Lot 308		Lot 503		Lot 505		Lot 512		Lot 514		Mixed Lots	
	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.	Vacc.	Plac.
Study Population - Total	200,745	201,229	24,020	24,236	21,760	21,880	28,748	28,629	17,423	17,244	18,188	18,299	36,000	36,382	34,063	34,124	20,530	20,456	33	19
Paired 1st and 2nd Sera - Total	4,646	4,520	833	851	621	553	543	532	270	255	405	452	773	721	642	677	559	479	-	-
<4 to All Three Types in 1st Serum																				
Number	1,061	1,105	187	198	137	139	114	130	55	52	69	79	176	197	179	223	144	89	-	-
Percent	23	24	22	23	22	25	21	24	20	20	17	17	23	27	28	33	28	19	-	-
% <4 in 2nd Serum																				
Type 1	53	94	95	98	6	95	24	95	22	90	99	91	58	97	50	89	53	97	-	-
Type II	29	94	84	98	3	96	13	98	13	88	99	92	19	96	8	89	6	93	-	-
Type III	21	95	23	96	4	95	17	98	20	88	68	97	18	97	23	90	15	96	-	-
% <4 to Type I in 1st Serum	54	55	54	50	48	54	56	58	54	80	46	47	58	57	62	65	57	48	-	-
% <4 to Type I in 2nd Serum	21	53	38	49	3	52	10	58	12	55	42	44	19	56	24	64	18	47	-	-
% <4 to Type II in 1st Serum	56	57	54	62	60	61	48	52	51	49	55	49	55	57	63	62	59	55	-	-
% <4 to Type II in 2nd Serum	11	55	26	60	2	58	5	49	5	46	43	50	6	58	4	62	2	52	-	-
% <4 to Type III in 1st Serum	59	61	62	64	62	59	60	65	49	56	49	46	56	61	62	68	62	62	-	-
% <4 to Type III in 2nd Serum	9	59	9	61	1	58	7	63	9	52	26	46	7	60	9	66	6	60	-	-
Geometric Mean Titers - Type 1*																				
1st Serum	106	94	114	106	99	78	64	71	155	164	86	81	119	89	137	121	109	91	-	-
2nd Serum	298	83	220	97	462	77	203	70	412	193	116	92	445	86	246	46	541	87	-	-
Geometric Mean Titers - Type II																				
1st Serum	101	110	91	88	78	79	95	129	107	113	91	86	159	198	119	139	78	75	-	-
2nd Serum	362	93	288	88	372	76	344	119	384	123	169	81	503	171	402	54	529	72	-	-
Geometric Mean Titers - Type III																				
1st Serum	57	52	68	69	78	47	38	69	91	126	57	39	73	54	59	42	33	29	-	-
2nd Serum	383	45	415	68	418	41	271	88	490	119	254	37	568	48	273	20	437	30	-	-
Relative Antigenic Effect**																				
Type I	61		27		93		84		78		3		66		61		67		-	
Type II	80		49		98		90		90		18		88		94		96		-	
Type III	85		88		98		89		79		46		88		84		91		-	
Paralytic and Nonparalytic Cases - Total	56	138	8	32	4	19	4	18	1	7	6	5	9	14	11	24	15	19	-	-
Nonparalytic Cases	23	28	2	3	1	4	2	4	1	1	2	1	3	1	4	8	8	6	-	-
Paralytic Cases	33	110	4	29	3	15	2	14	-	6	4	4	6	13	7	16	7	13	-	-
Paralytic - Rate/100,000	16	55	17	120	14	69	7	49	-	35	22	22	17	38	21	47	34	64	-	-
Virus Positive Paralytic Cases - Total	11	62	3	17	-	12	-	8	-	1	2	2	4	9	2	12	-	1	-	-
Type 1 - Number	10	35	3	2	-	5	-	6	-	1	2	2	3	7	2	12	-	-	-	-
Rate/100,000	5	17	12	8	-	23	-	21	-	8	11	11	8	19	6	35	-	-	-	-
Type II - Number	-	4	-	1	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Rate/100,000	-	2	-	4	-	14	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Type III - Number	1	23	-	14	-	4	-	2	-	-	-	-	1	2	-	-	-	1	-	-
Rate/100,000	****	11	-	58	-	18	-	7	-	-	-	-	3	6	-	-	-	5	-	-
% Estimate of Effectiveness***																				
Paralytic Cases - Total	71		86		80		86		100		0		53		55		47		-	
Virus Positive Paralytic Cases																				
Type I	71		Neg.		100		100		100		0		58		83		-		-	
Type II	100		100		100		-		-		-		-		-		-		-	
Type III	95		100		100		100		-		-		50		-		100		-	

* Geometric mean titers in which $Log_2 < 4$ was taken as 1.0000.
** See Glossary.
*** Percent estimate of effectiveness determined by means of the following:

$$100\left(1 - \frac{R_1}{R_2}\right)\% \qquad \text{Where: } R_1 = \text{rate for vaccinated}, \; R_2 = \text{rate for controls}$$

**** Less than 1 per 100,000.

\- = No challenge

Neg. = Higher rate in vaccinated than in controls

Table 66

SEROLOGY AND CLINICAL DATA BY VACCINATION STATUS AND VACCINE LOT
OBSERVED AREAS

Item	Total for Observed Area Lots		Lot 303		Lot 303-307		Lot 305		Lot 305-307		Lot 307		Lot 502-307		Lot 502-309		Lot 502		Lot 506-307	
	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.
Study Population - Total	221,998	725,173	22,601	86,900	8,449	23,411	16,207	59,254	14,340	42,819	1,234	4,046	7,865	23,807	13,698	49,740	341	1,243	29,052	88,221
Paired 1st and 2nd Sera - Total	4,515	6,386	473	755	85	223	598	777	355	492	10	12	230	332	182	227	11	2	486	784
<4 to All Three Types in 1st Serum																				
Number	837	1,303	96	178	28	69	73	93	54	74	3	2	86	147	33	34	3	-	101	173
Percent	19	20	20	24	33	31	12	12	15	15	30	17	37	44	18	15	27	-	21	22
% <4 in 2nd Serum																				
Type I	59	98	17	93	29	99	55	91	28	89	33	100	79	99	67	100	67	-	46	95
Type II	32	95	5	93	18	99	22	88	7	91	0	100	26	97	33	100	100	-	11	91
Type III	31	95	14	91	29	97	10	96	13	85	33	100	18	98	33	100	100	-	18	94
% <4 to Type I in 1st Serum	49	50	52	54	67	62	44	39	46	45	60	67	56	69	42	40	64	100	51	50
% <4 to Type I in 2nd Serum	19	48	6	52	18	63	11	37	7	42	10	67	27	68	16	37	18	100	16	48
% <4 to Type II in 1st Serum	51	53	51	53	62	65	39	41	52	57	40	42	51	67	52	41	64	50	55	57
% <4 to Type II in 2nd Serum	10	51	3	50	9	65	3	38	2	52	-	42	7	65	7	41	36	50	3	53
% <4 to Type III in 1st Serum	51	54	49	56	56	68	45	43	48	50	60	50	63	68	47	43	64	-	54	57
% <4 to Type III in 2nd Serum	11	52	6	53	13	66	2	41	4	48	20	50	8	67	11	42	27	-	5	54
Geometric Mean Titers - Type I*																				
1st Serum	88	87	102	80	58	120	91	85	75	79	128	181	89	101	145	181	32	-	66	67
2nd Serum	367	89	540	87	420	118	379	84	332	66	256	128	386	103	726	193	512	-	388	74
Geometric Mean Titers - Type II																				
1st Serum	95	94	119	100	146	84	126	99	51	62	256	312	117	111	143	190	45	64	78	65
2nd Serum	428	96	620	107	395	79	490	94	282	54	645	172	587	104	648	155	1,024	1,024	498	77
Geometric Mean Titers - Type III																				
1st Serum	52	53	72	58	141	148	66	70	43	44	64	51	57	55	59	74	32	128	36	35
2nd Serum	425	56	518	61	653	151	496	72	331	43	91	51	611	65	618	74	362	1,024	480	42
Relative Antigenic Effect**																				
Type I	61		88		74		72		83		83		50		60		71		67	
Type II	80		93		86		92		97		100		85		86		43		93	
Type III	78		88		76		96		91		83		88		76		100		90	
Paralytic and Nonparalytic Cases - Total	55	391	3	36	2	11	6	24	2	27	1	2	4	15	3	16	-	-	6	62
Nonparalytic Cases	17	60	-	5	-	-	-	3	1	-	-	-	3	6	-	4	-	-	2	5
Paralytic Cases	38	331	3	31	2	11	6	21	1	27	1	2	1	9	3	12	-	-	4	57
Paralytic - Rate/100,000	17	46	13	36	24	47	37	35	7	63	81	49	13	38	22	24	-	-	14	65
Virus Positive Paralytic Cases - Total	14	190	-	13	-	2	2	16	1	19	-	-	1	7	2	6	-	-	2	33
Type I - Number	8	104	-	8	-	1	2	11	-	12	-	-	1	3	1	1	-	-	2	16
Rate/100,000	4	14	-	9	-	4	12	19	-	28	-	-	13	13	7	2	-	-	7	18
Type II - Number	2	29	-	2	-	-	-	1	-	2	-	-	-	3	-	3	-	-	-	2
Rate/100,000	1	4	-	2	-	-	-	2	-	5	-	-	-	13	-	6	-	-	-	2
Type III - Number	4	57	-	3	-	1	-	4	1	5	-	-	-	1	1	2	-	-	-	15
Rate/100,000	2	8	-	3	-	4	-	7	7	12	-	-	-	4	7	4	-	-	-	17
% Estimate of Effectiveness***																				
Paralytic Cases - Total	63		64		49		Neg.		89		Neg.		66		8		-		78	
Virus Positive Paralytic Cases																				
Type I	71		100		100		37		100		-		0		Neg.		-		61	
Type II	75		100		-		100		100		-		100		100		-		100	
Type III	75		100		100		100		42		-		100		Neg.		-		100	

(Continued on next page.)

Table 66 Continued

Item	Lot 506-309		Lot 506		Lot 507-307		Lot 507-309		Lot 507		Lot 508-307		Lot 508-309		Lot 508		Mixed Lots	
	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.	Vacc.	Cont.
Study Population - Total	3,447	10,090	19,815	63,959	7,367	19,976	11,178	36,218	21,635	64,614	572	2,090	9,194	25,838	18,031	67,603	16,972	55,346
Paired 1st and 2nd Sera - Total	57	11	483	771	121	96	233	239	608	907	18	9	208	262	357	487	-	-
<4 to All Three Types in 1st Serum																		
Number	14	6	64	147	7	3	37	45	161	226	4	2	33	44	40	60	-	-
Percent	25	55	13	19	6	3	16	19	26	25	22	22	16	17	11	12	-	-
% <4 in 2nd Serum																		
Type I	7	100	78	98	88	100	84	100	97	99	50	100	18	98	58	92	-	-
Type II	0	100	9	96	14	100	59	100	96	98	0	100	3	98	12	88	-	-
Type III	7	100	5	95	43	100	57	96	83	98	25	100	6	93	30	93	-	-
% <4 to Type I in 1st Serum	65	82	49	52	59	57	43	50	51	53	61	56	48	46	46	43	-	-
% <4 to Type I in 2nd Serum	4	91	21	52	31	56	21	47	46	52	28	89	4	47	13	38	-	-
% <4 to Type II in 1st Serum	81	73	44	48	57	57	53	56	63	62	50	44	49	53	45	43	-	-
% <4 to Type II in 2nd Serum	4	73	2	46	7	55	15	55	49	61	6	44	1	52	3	39	-	-
% <4 to Type III in 1st Serum	58	73	40	50	81	62	43	57	61	60	72	67	54	55	47	49	-	-
% <4 to Type III in 2nd Serum	4	73	1	49	6	58	22	56	45	59	22	67	3	53	9	45	-	-
Geometric Mean Titers - Type I*																		
1st Serum	52	32	73	59	121	108	102	88	119	132	43	4	97	128	66	71	-	-
2nd Serum	158	4	309	60	526	130	641	88	152	129	256	3	605	122	378	83	-	-
Geometric Mean Titers - Type II																		
1st Serum	47	406	65	86	131	165	106	161	119	132	64	147	64	86	95	69	-	-
2nd Serum	396	161	397	103	555	189	496	158	183	121	188	147	473	69	439	79	-	-
Geometric Mean Titers - Type III																		
1st Serum	29	40	36	39	81	114	41	47	77	73	21	10	60	66	42	33	-	-
2nd Serum	431	64	429	41	678	108	344	43	271	70	446	25	490	67	305	38	-	-
Relative Antigenic Effect**																		
Type I	95		57		47		49		7		64		92		67		-	
Type II	100		98		98		71		21		89		99		92		-	
Type III	94		98		90		48		24		69		94		80		-	
Paralytic and Nonparalytic Cases - Total	-	3	2	39	-	15	3	25	10	44	-	2	1	5	5	36	7	29
Nonparalytic Cases	-	-	-	4	-	2	1	4	3	15	-	-	1	-	3	8	3	4
Paralytic Cases	-	3	2	35	-	13	2	21	7	29	-	2	-	5	2	28	4	25
Paralytic - Rate/100,000	-	30	10	55	-	65	18	58	32	45	-	96	-	19	11	41	24	45
Virus Positive Paralytic Cases - Total	-	1	-	22	-	10	-	2	4	25	-	1	-	3	1	16	1	14
Type I - Number	-	1	-	14	-	7	-	1	1	7	-	-	-	-	1	11	-	11
Rate/100,000	-	10	-	22	-	35	-	3	5	11	-	-	-	-	6	16	-	20
Type II - Number	-	-	-	1	-	-	-	-	1	9	-	1	-	1	-	2	1	2
Rate/100,000	-	-	-	2	-	-	-	-	5	14	-	48	-	4	-	3	6	4
Type III - Number	-	-	-	7	-	3	-	1	2	9	-	-	-	2	-	3	-	1
Rate/100,000	-	-	-	11	-	15	-	3	9	14	-	-	-	8	-	4	-	2
% Estimate of Effectiveness***																		
Paralytic Cases - Total	100		82		100		69		29		100		100		73		47	
Virus Positive Paralytic Cases																		
Type I	100		100		100		100		55		-		-		62		100	
Type II	-		100		-		-		64		100		100		100		Neg.	
Type III	-		100		100		100		36		-		100		100		100	

* Geometric mean titers in which $\text{Log}_2 < 4$ was taken as 1.0000.

** See Glossary.

*** Percent estimate of effectiveness determined by means of the following:

$$100\left(1 - \frac{R_1}{R_1}\right)\% \qquad \text{Where: } R_1 = \text{rate for vaccinated}, \; R_2^1 = \text{rate for controls}$$

**** Less than 1 per 100,000

\- = No challenge

Neg. = Higher rate in vaccinated than in controls

The mean titers achieved by a group who received a given lot of vaccine also reflect in the aggregate the potency of an antigenic stimulus; major effects and defects are discernible. When good antigens were used, the mean post-vaccination titer for a group appears to be in the same range as that for convalescent patients. Certain reservations must be maintained on this point, however, since a large proportion of the patients are persons without original antibody to any type while only a minority of vaccinated belong in that class; moreover, the titration procedures for the pre- and post-vaccination titers employed larger increments of measurements. The initial mean titers are essentially the same for vaccinated and controls. The shifts in mean titers after vaccination provide a reasonable measurement of antigenic effect, especially when they are considered in relation to the later titers of the control specimens which are practically unchanged. The view of comparative antigenicity is well seen with Lots 302 and 503 where the variation between Types I, II, and III is clearly detected by the mean titers.

The relation between the relative antibody response observed in the serological results and the estimates of prophylactic effectiveness based upon the occurrence of virus positive paralytic cases can be seen according to lot and type. There is general agreement between the two although certain disagreements in either direction occur.

RELATIONSHIP OF "EXPECTED" TO "ACTUAL" CASES IN VACCINATED CHILDREN

Data from the placebo areas demonstrate that practically all Type I virus-positive paralytic cases in vaccinated children occurred in lots of which the Type I antigenic effectiveness was computed to be less than 70 percent. Similar findings suggested that a study of the correlation between "expected" and "actual" cases in vaccinated children might be useful in assessing the relationship of antigenic effect to clinically recognized cases of poliomyelitis.

Several computing procedures for estimating "expected cases" or "expected rates" were possible. The one chosen was the simple procedure of applying the rate of "ineffectiveness" to the number of cases reported for each combination of laboratory demonstrated cases (poliomyelitis virus recovered and/or serological evidence of poliomyelitis infection) by the respective lot-type. Since the population which received vaccine for each lot-type remains constant, expected rates were not computed. The studies of correlation will give the same results whether cases or rates are used. Ineffectiveness by lot-type was estimated as $V_2 \div V_1$, wherein V_2 was the proportion of second blood readings less than 4, and V_1 was the proportion of first bloods less than 4. For example, from Table 67, of the first serum Type I titer readings reported as less than 4 for children vaccinated with Lot 302, 69.5 percent remained less than 4 in the second bloods drawn seven weeks later. As in Table 61, this method of computation of ineffectiveness was demonstrated to be essentially the same as $V_2 \div V_1$ divided by $C_2 \div C_1$, since $C_2 \div C_1$ approximated unity for each of the lot-type results.

The decision to use the less-than-4 readings in this evaluation resulted from studies in which the various levels of antibody readings were subjected to computations of ineffectiveness by lot-type and used for calculation of expected cases. These studies established that the ratio of post-vaccination readings less than 4 to pre-vaccination readings less than 4, among vaccinated children by lot-type was more closely correlated with the number of laboratory-demonstrated cases than similar ratios for any other antibody level.

Application of the ratios selected to express ineffectiveness by lot-type, computation of expected cases and resulting correlation coefficients are shown in Tables 67 and 68. The correlation coefficients were computed from the lot-type expected cases and actual cases. The correlation coefficient "r" was used in order to provide a basis for comparison of the relationships between paired groupings of expected and actual cases over all types of poliomyelitis.

Table 67

EXPECTED AND ACTUAL CASES IN VACCINATED CHILDREN
BY VACCINE LOT AND VIRUS TYPE
PLACEBO AREAS

Virus Type by Lot	Poliomyelitis Virus Positive Cases				Poliomyelitis Virus Positive and/or Serologically Positive Cases				Poliomyelitis Virus Positive and/or Serologically Positive or Serologically Probable Cases			
	Percent Ineffectiveness	Placebo Cases	Expected Vaccinated Cases	Actual Vaccinated Cases	Percent Ineffectiveness	Placebo Cases	Expected Vaccinated Cases	Actual Vaccinated Cases	Percent Ineffectiveness	Placebo Cases	Expected Vaccinated Cases	Actual Vaccinated Cases
Type I												
302	69.5	3	2.1	3	69.5	3	2.1	3	69.5	5	3.5	4
304	6.1	6	0.4	-	6.1	7	0.4	-	6.1	7	0.4	-
306	14.9	6	0.9	-	14.9	7	1.0	-	14.9	8	1.2	-
308	20.0	1	0.2	-	20.0	2	0.4	-	20.0	3	0.6	-
503	87.1	2	1.7	2	87.1	2	1.7	2	87.1	3	2.6	4
505	32.5	8	2.6	4	32.5	8	2.6	5	32.5	9	2.9	5
512	33.6	13	4.4	3	33.6	14	4.7	3	33.6	18	6.0	3
514	31.0	1	0.3	2	31.0	2	0.6	2	31.0	3	0.9	2
Total		40	12.6	14		45	13.5	15		56	18.1	18
Weighted Estimate:												
All Lots	35.4	40	14.2	14	35.4	45	15.6	15	35.4	56	19.8	18
Challenged Lots	35.4	40	14.2	14	35.4	45	15.6	15	35.4	56	19.8	18
Type II												
302	48.3	2	1.0	-	48.3	3	1.4	-	48.3	3	1.4	-
304	2.4	4	0.1	-	2.4	4	0.1	-	2.4	4	0.1	-
306	8.8	-	-	-	8.8	-	-	-	8.8	2	0.2	-
308	9.5	-	-	-	9.5	-	-	-	9.5	-	-	-
503	77.9	-	-	-	77.9	-	-	1	77.9	-	-	2
505	10.8	-	-	-	10.8	-	-	-	10.8	-	-	-
512	5.4	-	-	-	5.4	1	0.1	1	5.4	3	0.2	2
514	4.0	-	-	-	4.0	-	-	-	4.0	1	-	-
Total		6	1.1	-		8	1.6	2		13	1.9	4
Weighted Estimate:												
All Lots	18.4	6	1.1	-	18.4	8	1.5	2	18.4	13	2.4	4
Challenged Lots	26.5	6	1.6	-	17.5	8	1.4	1	13.4	13	1.7	2
Type III												
302	14.3	14	2.0	-	14.3	16	2.3	-	14.3	17	2.4	-
304	1.8	4	0.1	-	1.8	5	0.1	-	1.8	5	0.1	-
306	10.1	3	0.3	-	10.1	4	0.4	-	10.1	5	0.5	1
308	19.1	1	0.2	-	19.1	1	0.2	-	19.1	1	0.2	-
503	49.5	-	-	-	49.5	-	-	-	49.5	1	0.5	-
505	11.1	2	0.2	1	11.1	2	0.2	2	11.1	3	0.3	2
512	14.0	-	-	-	14.0	1	0.1	-	14.0	2	0.3	-
514	8.9	1	0.1	-	8.9	2	0.2	-	8.9	3	0.3	-
Total		25	2.9	1		31	3.5	2		37	4.6	3
Weighted Estimate:												
All Lots	14.8	25	3.7	1	14.6	31	4.6	2	14.8	37	5.5	3
Challenged Lots	10.7	25	2.7	1	11.3	31	3.5	2	14.8	37	5.5	3
Correlation Coefficient			r = .77				r = .78				r = .65	

This method of calculating expected cases among vaccinated children is obviously independent of the method of determining the number of clinical and/or laboratory diagnosed cases as reported in the Field Trial. Hence, if estimates of effectiveness based on the two independent methods are found to agree, credence is added to those obtained from the clinical experience alone. Furthermore, close agreement between the two sets of estimates would demonstrate that the reduction of poliomyelitis incidence among the vaccinated resulted from the administration of vaccine.

Evaluation of the total effect of the eight vaccine lots in the placebo area study (Table 67) against Type I, for example, from the laboratories' appraisal of the ability of the vaccine to cause changes in antibody level from less than 4 to greater than 4 was approached by three different computations:

Table 68

EXPECTED AND ACTUAL CASES IN VACCINATED CHILDREN BY VACCINE LOT AND VIRUS TYPE OBSERVED AREAS

Virus Type by Lot	Poliomyelitis Virus Positive Cases						Poliomyelitis Virus Positive and/or Serologically Positive Cases						Poliomyelitis Virus Positive and/or Serologically Positive or Serologically Probable Cases					
	Percent Ineffectiveness	Control Cases	Control/ Vaccinated Population Ratio	Population Adjusted Control Cases	Expected Vaccinated Cases	Actual Vaccinated Cases	Percent Ineffectiveness	Control Cases	Control/ Vaccinated Population Ratio	Population Adjusted Control Cases	Expected Vaccinated Cases	Actual Vaccinated Cases	Percent Ineffectiveness	Control Cases	Control/ Vaccinated Population Ratio	Population Adjusted Control Cases	Expected Vaccinated Cases	Actual Vaccinated Cases
Type I																		
303	11.3	10	3.85	2.6	0.3	-	11.3	12	3.85	3.1	0.4	-	11.3	15	3.85	3.9	0.4	-
303-303-307	26.3	-	2.77	-	-	-	26.3	-	2.77	-	-	-	26.3	-	2.77	-	-	-
305	25.3	26	3.66	7.1	1.8	5	25.3	26	3.66	7.1	1.8	5	25.3	26	3.66	7.1	1.8	5
305-305-307	14.6	-	2.99	-	-	-	14.6	-	2.99	-	-	-	14.6	1	2.99	0.3	-	-
307	16.7	-	3.28	-	-	-	16.7	-	3.28	-	-	-	16.7	-	3.28	-	-	-
502	28.6	8	3.65	2.2	0.6	2	28.8	8	3.65	2.2	0.6	2	28.6	8	3.65	2.2	0.6	2
502-502-307	48.8	-	3.03	-	-	-	48.8	1	3.03	0.3	0.1	-	48.8	1	3.03	0.3	0.1	-
502-502-309	37.7	-	3.63	-	-	-	37.7	-	3.63	-	-	-	37.7	-	3.63	-	-	-
506	41.8	31	3.23	9.8	4.0	2	41.8	34	3.23	10.5	4.4	3	41.8	38	3.23	11.8	4.9	3
506-506-307	30.9	-	3.04	-	-	-	30.9	-	3.04	-	-	-	30.9	2	3.04	0.7	0.2	-
506-506-309	5.4	-	2.93	-	-	-	5.4	-	2.93	-	-	-	5.4	-	2.93	-	-	-
507	90.0	18	3.00	8.0	5.4	3	90.0	23	3.00	7.7	6.9	4	90.0	24	3.00	8.0	7.2	5
507-507-307	52.1	-	2.71	-	-	-	52.1	-	2.71	-	-	-	52.1	-	2.71	-	-	-
507-507-309	47.0	-	3.24	-	-	-	47.0	-	3.24	-	-	-	47.0	3	3.24	0.9	.4	-
508	26.5	11	3.75	2.9	0.6	1	26.5	14	3.75	3.7	1.1	1	28.5	16	3.75	4.3	1.2	1
508-508-307	36.4	-	3.65	-	-	-	36.4	-	3.65	-	-	-	36.4	1	3.65	0.3	0.1	-
508-508-309	8.0	-	2.81	-	-	-	8.0	-	2.81	-	-	-	8.0	-	2.81	-	-	-
Total		104		30.4	12.9	13		118		34.6	15.3	15		135		39.8	16.9	16
Weighted Estimate:																		
All Lots	35.3	104	3.27	31.8	11.2	13	35.3	118	3.27	38.1	12.7	15	35.3	135	3.27	41.3	14.6	16
Challenged Lots	40.2	104	3.27	31.8	12.8	13	40.8	118	3.27	36.1	14.7	15	37.1	135	3.27	41.3	15.3	16
Type II																		
303	8.2	2	3.85	0.5	-	-	6.2	3	3.85	.8	-	1	6.2	4	3.85	1.0	0.1	2
303-303-307	13.2	-	2.77	-	-	-	13.2	-	2.77	-	-	-	13.2	1	2.77	0.4	0.1	-
305	7.3	4	3.66	1.1	0.1	1	7.3	4	3.66	1.1	0.1	1	7.3	6	3.66	1.8	0.1	1
305-305-307	2.7	-	2.99	-	-	-	2.7	1	2.99	0.3	-	-	2.7	1	2.99	0.3	-	-
307	-	-	3.28	-	-	-	-	-	3.28	-	-	-	-	-	3.28	-	-	-
502	57.1	-	3.85	-	-	-	57.1	-	3.85	-	-	-	57.1	-	3.85	-	-	-
502-502-307	14.4	9	3.03	3.0	0.4	-	14.4	9	3.03	3.0	0.4	-	14.4	9	3.03	3.0	0.4	-
502-502-309	13.8	-	3.63	-	-	-	13.8	-	3.63	-	-	-	13.8	-	3.63	-	-	-
506	3.7	4	3.23	1.2	-	-	3.7	4	3.23	1.2	-	-	3.7	4	3.23	1.2	-	-
506-506-307	8.0	-	3.04	-	-	-	8.0	-	3.04	-	-	-	8.0	2	3.04	0.7	-	-
506-506-309	-	-	2.93	-	-	-	-	-	2.93	-	-	-	-	-	2.93	-	-	-
507	75.8	12	3.00	4.0	3.0	1	75.8	12	3.00	4.0	3.0	1	75.8	17	3.00	5.7	4.3	1
507-507-307	11.8	-	2.71	-	-	-	11.8	1	2.71	0.4	-	-	11.8	1	2.71	0.4	-	-
507-507-309	28.2	-	3.24	-	-	-	28.2	1	3.24	0.3	0.1	-	28.2	5	3.24	1.5	0.4	-
508	7.4	4	3.75	1.1	0.1	-	7.4	4	3.75	1.1	0.1	-	7.4	5	3.75	1.3	0.1	-
508-508-307	11.1	-	3.65	-	-	-	11.1	-	3.65	-	-	-	11.1	-	3.65	-	-	-
508-508-309	1.0	-	2.81	-	-	-	1.0	-	2.81	-	-	-	1.0	1	2.81	0.4	-	-
Total		35		10.9	3.6	2		39		12.2	3.7	3		56		17.5	5.5	4
Weighted Estimate:																		
All Lots	15.5	35	3.27	10.7	1.7	2	15.5	39	3.27	11.9	1.8	3	15.5	56	3.27	17.1	2.7	4
Challenged Lots	20.9	35	3.27	10.7	2.2	2	19.1	39	3.27	11.9	2.3	3	18.7	56	3.27	17.1	2.9	4
Type III																		
303	10.7	4	3.85	1.0	0.1	-	10.7	8	3.85	2.1	0.2	-	10.7	9	3.85	2.3	0.1	-
303-303-307	22.9	-	2.77	-	-	-	22.9	-	2.77	-	-	-	22.9	3	2.77	1.1	0.3	1
305	4.4	9	3.66	2.5	0.1	1	4.4	9	3.66	2.5	0.1	1	4.4	10	3.66	2.7	0.1	1
305-305-307	7.6	-	2.99	-	-	-	7.6	-	2.99	-	-	-	7.8	2	2.99	0.7	0.1	-
307	18.7	-	3.28	-	-	-	16.7	1	3.28	0.3	0.1	-	16.7	1	3.28	0.3	0.1	1
502	42.8	-	3.65	-	-	-	42.8	-	3.85	-	-	-	42.8	-	3.65	-	-	-
502-502-307	12.5	4	3.03	1.3	0.2	1	12.5	4	3.03	1.3	0.2	1	12.5	5	3.03	1.7	0.2	1
502-502-309	23.2	-	3.63	-	-	-	23.2	1	3.63	0.3	0.1	-	23.2	2	3.63	0.8	0.2	-
506	2.1	23	3.23	7.1	0.1	-	2.1	27	3.23	8.4	0.2	-	2.1	28	3.23	8.7	0.2	-
506-506-307	8.8	-	3.04	-	-	-	8.8	-	3.04	-	-	-	8.8	2	3.04	0.7	0.1	-
506-506-309	6.1	-	2.93	-	-	-	6.1	-	2.93	-	-	-	6.1	-	2.93	-	-	-
507	72.9	15	3.00	5.0	3.8	2	72.9	17	3.00	5.7	4.2	2	72.9	18	3.00	6.0	4.4	2
507-507-307	9.4	-	2.71	-	-	-	9.4	-	2.71	-	-	-	9.4	-	2.71	-	-	-
507-507-309	50.5	-	3.24	-	-	-	50.5	-	3.24	-	-	-	50.5	2	3.24	0.6	0.3	-
508	18.4	8	3.75	1.8	0.3	-	18.4	8	3.75	2.1	0.4	-	18.4	10	3.75	2.7	0.5	-
508-508-307	30.8	-	3.65	-	-	-	30.8	-	3.85	-	-	-	30.8	-	3.65	-	-	-
508-508-309	6.2	-	2.81	-	-	-	8.2	-	2.81	-	-	-	6.2	1	2.81	0.4	-	-
Total		61		18.5	4.4	4		75		22.7	5.5	4		94		28.7	6.6	6
Weighted Estimate:																		
All Lots	19.5	61	3.27	18.7	3.6	4	19.5	75	3.27	22.9	4.5	4	19.5	94	3.27	28.7	5.8	6
Challenged Lots	22.2	61	3.27	18.7	4.2	4	22.3	75	3.27	22.9	5.1	4	20.7	94	3.27	28.7	5.9	6
Correlation Coefficient					r = .72						r = .77						r = .75	

1. Summing up for each type the expected vaccinated cases computed for each lot-type and comparing with the sum of the actual cases (unweighted estimate of ineffectiveness).

2. A "weighted percent ineffectiveness" for each type of poliomyelitis was computed by:

   a. multiplying each lot-type percent ineffectiveness by the number vaccinated,

   b. summing these products, and

   c. dividing by the total number vaccinated;

   d. multiplying this weighted percent ineffectiveness by the total "control" cases of the type of poliomyelitis to generate

Table 69

EXPECTED AND ACTUAL CASES IN VACCINATED CHILDREN, BY VIRUS TYPE PLACEBO AND OBSERVED AREAS

Study Areas	Poliomyelitis Virus Type	Poliomyelitis Virus Positive Cases		Poliomyelitis Virus Positive and/or Serologically Positive Cases		Poliomyelitis Virus Positive and/or Serologically Positive or Serologically Probable	
		Actual Cases	Expected Cases	Actual Cases	Expected Cases	Actual Cases	Expected Cases
All Lots (Using "Unweighted Ineffectiveness" by Virus Type)							
Placebo	I	14	12.6	15	13.5	18	18.1
	II	-	1.1	2	1.6	4	1.9
	III	1	2.9	2	3.5	3	4.6
Observed	I	13	12.9	15	15.3	16	16.9
	II	2	3.8	3	3.7	4	5.5
	III	4	4.4	4	5.5	6	6.6
Total		34	37.5	41	43.1	51	53.6
Correlation Coefficient		r = .99		r = .99		r = .98	
All Lots (Using "Weighted Ineffectiveness" by Virus Type)*							
Placebo	I	14	14.2	15	15.6	18	19.8
	II	-	1.1	2	1.5	4	2.4
	III	1	3.7	2	4.6	3	5.5
Observed	1	13	11.2	15	12.7	16	14.6
	II	2	1.7	3	1.8	4	2.7
	III	4	3.6	4	4.5	6	5.6
Total		34	35.5	41	40.7	51	50.6
Correlation Coefficient		r = .97		r = .96		r = .97	
Challenged Lots (Using "Weighted Ineffectiveness" by Virus Type)**							
Placebo	I	14	14.2	15	15.6	18	19.8
	II	-	1.6	2	1.4	4	1.7
	III	1	2.7	2	3.5	3	5.5
Observed	1	13	12.8	15	14.7	16	15.3
	II	2	2.2	3	2.3	4	2.9
	III	4	4.2	4	5.1	6	5.9
Total		34	37.7	41	42.6	51	51.2
Correlation Coefficient		r = .99		r = .99		r = .97	

* Expected cases calculated on the basis of actual cases among controls multiplied by (ratio of readings: <4 in 2nd serum/ <4 in 1st serum). In observed areas this quantity was divided by the population ratio of control/vaccinated. Sums of the lot-type expected cases are used in the calculation of "r".

** Expected or predicted cases are obtained by getting a weighted estimate of ineffectiveness (based on titers <4 in 2nd serum/ <4 in 1st serum) for challenged control lots. Using this over-all estimate and multiplying times total number of control cases, one gets predicted cases. For observed areas, control cases are divided by population ratio. Vaccinated population used as basis of estimating ineffectiveness of vaccine.

the total expected vaccinated cases of that type.

3. Compute as in "2" but use only those lot-type units in which at least one actual case appeared, that is, those lot-type units for which there was known to have been some challenge (presence of disease according to laboratory reports).

Each of the three methods of computing over-all ineffectiveness was carried out for each type of poliomyelitis, and the results in summary form are shown in Table 69.

Tables 67 and 68 show that there were great variations in ineffectiveness between the various lot-type units of the study. For example, in Table 67, ineffectiveness calculated from the laboratory readings of pre- and post-vaccination bloods varied for Type I from 6 percent for Lot 304 to 87 percent for Lot 503; for Type II, Lot 304 was estimated at 2 percent, while Lot 503 was 78 percent ineffective. Furthermore, these data demonstrate that the estimates of ineffectiveness from laboratory readings are associated with the occurrence of type-specific laboratory-demonstrated cases.

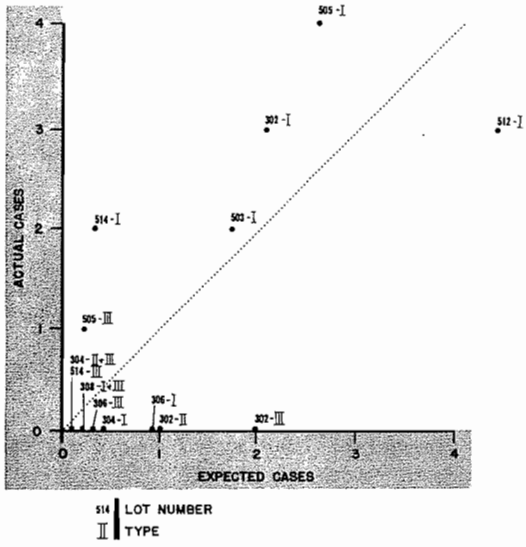
Correlation coefficients calculated from the pairs of expected and actual cases are

also included in Tables 67 and 68. The correlation coefficients presented may all be shown to be significantly different from zero correlation, and not significantly different from each other. In other words, these mathematical expressions of relationship may be viewed as meaningful, and the relationships are of the same order of magnitude. These coefficients approximate 0.7 for each of the lot-types for both the placebo and the observed studies and may be interpreted as explaining approximately 50 percent of the occurrence of the laboratory-demonstrated cases. The tables show that there were usually very few such cases by lot of vaccine, and it follows that considerable variation might be expected.

The total estimated cases by type of poliomyelitis should be less subject to variation than those by lot-type, and the correlation coefficient calculated from total cases for each type of poliomyelitis should have increased efficiency in estimating the total influence of ineffectiveness. Table 69 shows that the results of these calculations yield coefficients approximating 0.98, which may be interpreted as explaining practically all of the cases occurring in the vaccinated populations by type of poliomyelitis during the 1954 Field Trial. The effect of using the expected and actual cases by type of poliomyelitis in the correlation calculations appears to have allowed the variations which were present in the individual lot-type calculations to balance out in such a manner that a very high positive correlation resulted.

Figure 11

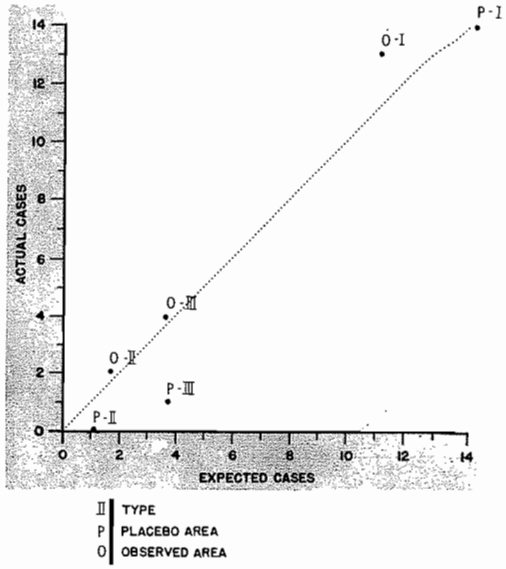
VIRUS-POSITIVE POLIOMYELITIS CASES
BY VACCINE LOT & VIRUS TYPE



Source: Table 67.

Figure 12

VIRUS-POSITIVE POLIOMYELITIS CASES
BY VIRUS TYPE
PLACEBO & OBSERVED AREAS



Source: Table 69, Weighted Ineffectiveness.

Correlation coefficients are often misleading in analyses, and many persons prefer to see graphs of related data. Figure 11 shows the data of Table 67 indicating an obvious positive correlation but not nearly so consistent as that of the relationships depicted in Figure 12, prepared from the data of Table 69.

Several inferences may be drawn from these studies:

1. Laboratory reports of changes in antibody levels between the pre- and post-

vaccination bleedings are valuable in estimating the effectiveness of the vaccine lots used.

2. These studies imply that laboratory-demonstrated cases in vaccinated children occurred primarily in those who had no demonstrable type-specific antibody following vaccination and that antibody level of 4 or greater seems sufficient for prevention of laboratory-demonstrable cases.

3. Over all areas and conditions existing in the Field Trial, the vaccines were estimated by this procedure to have been approximately 65 percent effective against Type I poliomyelitis, and 80 to 85 percent effective against both Types II and III. Great variation existed between the lot-type ability of vaccine to produce changes in levels of antibody from titers of less than 4 according to the laboratory readings of first and second bloods.

Inferences from this study are related to many subjects reported in the Summary Report of April 12, 1955. For example, on page 32 of the text of the Summary Report, mention was made that some 67 percent of paralytic cases may have occurred among those having no antibody to any of the three types of poliomyelitis. Again, Table 67 shows that 14 of the 15 virus-positive cases among the vaccinated children in the placebo study areas were Type I, and these 14 cases occurred in children who received vaccine lots which were relatively ineffective (more than 25 percent) in producing antibody as judged from laboratory readings of pre- and post-vaccination bloods. Similarly, for the observed areas, 16 of the 19 virus-positive cases occurred in children who received vaccine which was relatively ineffective as judged by the same laboratory criterion (Table 68).

The entire correlation procedure was also performed with laboratory readings of less than 4 to all three types of poliomyelitis virus in the pre-vaccination blood as the basis for the serological side of the comparison. The results of this study were nearly identical with those of the type-specific data given above.

These studies leave little doubt that the effectiveness of the vaccines in the Field Trial of 1954 was closely associated with, perhaps entirely dependent upon, the ability of the lots of vaccine used to produce discernible type-specific antibody rise in children who previously had no discernible type-specific antibody.

STABILITY OF ANTIBODY TITERS

The number of specimens of serum available for comparison of antibody titers two weeks after completion of vaccination and five months after vaccination was smaller than that for comparison of the pre- and early post-vaccination levels. Results with 14,783 pairs of sera, excluding the toxics, were tabulated in the later series, 26 percent less than the 20,067 in the first series of paired sera. The data were tabulated in a number of different ways in order to present various comparisons.

Relation of Antibody Stability to Lots of Vaccine

Table XVIII of the Summary Report gave the percentage distribution of second and third titers then available for representative lots of vaccine. The influence of variations in antigenic potency of lots or components upon the durability of the antibody titers has been further examined. Tables 70 and 71 contain the summary distributions of the pre- and two-weeks-post-vaccination titers and those for the two-weeks- and five-months-post-vaccination specimens. Two lines of data are presented for the two-weeks-post-vaccination sera; the first line is based on readings obtained in tests of paired first and second sera; the second line presents readings obtained in tests of paired second and third sera or matched first, second, and third sera. In some instances there were fewer pairs of first and second sera than paired second and third sera; this resulted from an excess of toxic specimens in the first collection. Variations in the numbers involved also relate to the attrition, to incomplete series of specimens or tests, etc. Limitations in direct comparisons are imposed by the fact that different laboratories had material from persons receiving different lots of vaccine, but the serial specimens related to a given lot were regularly tested by the same laboratories.

Table 70

PERCENT DISTRIBUTION OF ANTIBODY LEVELS AT FIRST, SECOND AND THIRD BLEEDINGS BY VACCINE LOT, VIRUS TYPE, AND VACCINATION STATUS
PLACEBO AREAS

Lots by Virus Type and Bleeding			Vaccinated							Placebo						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
302	I	1st	833	54	4	6	12	14	9	851	50	4	8	13	15	10
		2nd*	833	38	10	9	11	15	18	851	49	6	7	12	16	10
		2nd**	247	31	13	9	13	17	17	275	46	6	8	8	19	13
		3rd	247	32	10	8	13	21	16	275	41	7	8	13	16	15
	II	1st	833	54	7	6	12	12	10	851	62	5	6	8	10	8
		2nd*	833	26	11	14	12	14	23	851	60	6	6	10	9	9
		2nd**	247	23	12	15	11	15	23	275	58	9	4	10	9	10
		3rd	247	25	13	14	11	15	23	275	53	11	5	11	10	11
	III	1st	833	62	6	8	10	7	7	851	64	6	8	9	7	7
		2nd*	833	9	14	21	16	14	25	851	61	7	8	9	8	7
		2nd**	247	6	15	21	17	17	23	275	52	11	7	8	13	10
		3rd	247	13	21	17	14	13	22	275	41	12	8	10	18	12
304	I	1st	621	48	7	9	12	12	13	553	54	7	6	13	11	8
		2nd*	621	3	7	16	21	14	39	553	52	7	8	12	11	10
		2nd**	477	3	6	14	20	13	44	398	57	3	5	9	14	13
		3rd	477	7	16	15	11	15	36	398	53	6	3	10	14	14
	II	1st	621	60	9	5	7	9	10	553	61	8	5	7	8	10
		2nd*	621	2	5	18	25	21	30	553	58	8	5	8	9	11
		2nd**	477	2	3	12	26	20	37	398	62	4	3	7	10	14
		3rd	477	3	13	21	21	13	30	398	57	5	5	9	10	15
	III	1st	621	62	8	7	11	8	4	553	59	9	9	10	9	4
		2nd*	621	1	4	18	29	20	29	553	58	8	11	10	8	5
		2nd**	477	2	4	18	28	17	32	398	64	3	8	12	9	4
		3rd	477	11	26	14	12	10	27	398	60	5	7	13	10	5
306	I	1st	543	56	12	8	6	5	13	532	58	10	7	7	7	11
		2nd*	543	10	15	15	17	14	29	532	56	10	8	7	7	12
		2nd**	364	12	14	17	15	13	29	399	62	7	5	7	8	12
		3rd	364	19	17	15	15	9	25	399	61	7	5	8	8	10
	II	1st	543	48	10	7	9	7	18	532	52	7	8	6	8	19
		2nd*	543	5	10	15	19	16	36	532	49	8	7	7	9	19
		2nd**	364	3	12	16	16	13	40	399	51	8	6	6	8	21
		3rd	364	8	18	16	14	9	35	399	50	8	7	6	8	21
	III	1st	543	60	12	9	7	5	6	532	65	6	7	9	7	6
		2nd*	543	7	11	19	23	13	27	532	63	7	7	10	7	8
		2nd**	364	8	10	21	23	11	27	399	67	5	6	10	5	8
		3rd	364	17	20	23	12	7	21	399	64	6	8	9	6	7

(Continued on next page.)

* Second blood readings were obtained when first and second bloods were tested simultaneously.
** Second blood readings came from either second and third blood tests or first, second, and third blood tests.

Table 70 Continued

Lots by Virus Type and Bleeding			Vaccinated							Placebo						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
308	I	1st	270	54	5	6	8	8	18	255	60	3	7	6	8	16
		2nd*	270	12	6	16	13	14	39	255	55	5	3	11	9	16
		2nd**	244	12	6	16	12	16	38	226	56	5	4	9	9	17
		3rd	244	11	11	21	13	10	34	226	51	8	3	9	10	19
	II	1st	270	51	7	8	11	7	16	255	49	8	8	8	9	18
		2nd*	270	5	6	17	17	15	39	255	46	8	10	8	7	22
		2nd**	244	6	5	20	16	16	37	266	45	8	10	8	7	22
		3rd	244	5	9	22	19	11	34	226	41	9	9	10	9	23
	III	1st	270	49	7	10	10	9	14	255	56	5	7	9	9	14
		2nd*	270	9	8	18	12	11	40	255	52	6	8	11	9	14
		2nd**	244	10	9	18	13	12	39	226	50	7	8	11	8	16
		3rd	244	11	16	18	13	6	37	226	48	7	10	11	8	18
503	I	1st	405	46	8	8	12	14	11	452	47	7	9	15	12	10
		2nd*	405	42	7	8	15	14	14	452	44	7	11	13	13	12
		2nd**	197	43	5	8	25	13	7	223	39	6	10	19	16	9
		3rd	197	43	5	11	19	16	7	223	41	4	12	18	16	9
	II	1st	405	55	7	7	10	11	11	452	49	7	9	11	13	11
		2nd*	405	43	11	7	12	12	16	452	50	6	8	12	14	11
		2nd**	197	38	9	8	13	13	19	223	42	7	10	12	17	13
		3rd	197	38	12	8	10	18	15	223	43	6	11	7	19	15
	III	1st	405	49	7	12	16	10	6	452	46	12	14	14	7	7
		2nd*	405	26	11	10	12	19	22	452	46	9	16	15	8	6
		2nd**	197	15	15	14	9	23	24	223	46	7	20	16	7	4
		3rd	197	24	14	8	15	25	14	223	42	9	17	16	11	5
505	I	1st	773	56	4	6	11	12	11	721	57	6	6	11	11	9
		2nd*	773	19	9	14	13	11	34	721	56	4	8	12	9	11
		2nd**	630	20	9	13	13	10	35	602	58	2	7	12	9	11
		3rd	630	27	9	11	12	13	27	602	55	4	7	11	11	12
	II	1st	773	55	5	5	8	10	18	721	57	3	5	6	11	18
		2nd*	773	6	8	16	18	12	39	721	56	4	4	7	11	18
		2nd**	630	6	7	16	17	12	42	602	57	3	3	6	11	20
		3rd	630	11	12	17	14	11	34	602	54	4	4	6	12	20
	III	1st	773	56	4	10	12	11	6	721	61	5	8	15	8	3
		2nd*	773	7	12	18	16	10	38	721	60	6	10	12	8	4
		2nd**	630	7	11	18	16	9	39	602	63	5	9	11	8	4
		3rd	630	22	13	15	7	14	29	602	60	5	8	13	10	4

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Table 70 Continued

Lots by Virus Type and Bleeding			Vaccinated							Placebo						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
512	I	1st	642	62	3	5	9	10	11	677	65	4	3	8	13	7
		2nd*	642	24	12	15	10	11	28	677	64	5	3	8	11	8
		2nd**	545	26	11	15	9	11	28	573	65	5	3	8	11	8
		3rd	545	31	12	12	8	12	25	573	61	4	6	9	12	9
	II	1st	642	63	6	5	5	8	13	677	62	5	2	8	11	11
		2nd*	642	4	6	14	26	16	34	677	62	4	5	7	12	11
		2nd**	545	4	6	14	27	15	33	573	64	4	5	6	12	9
		3rd	545	8	11	23	16	14	27	573	62	5	5	7	10	10
	III	1st	642	62	4	11	10	6	6	677	68	6	9	10	5	3
		2nd*	642	9	13	26	15	9	27	677	66	5	9	10	5	3
		2nd**	545	9	12	25	15	10	28	573	65	4	11	12	6	3
		3rd	545	24	18	12	11	13	21	573	64	5	10	12	5	4
514	I	1st	559	57	3	6	14	11	10	479	48	3	11	15	15	8
		2nd*	559	18	13	14	13	11	31	479	47	4	10	16	13	9
		2nd**	491	19	13	15	13	11	30	424	49	4	10	16	12	8
		3rd	491	29	10	14	11	14	22	424	47	4	10	17	15	7
	II	1st	559	59	4	7	14	10	6	479	55	5	9	13	12	6
		2nd*	559	2	4	20	27	17	30	479	52	7	9	14	12	7
		2nd**	491	2	4	20	26	17	30	424	52	6	8	15	12	7
		3rd	491	4	15	23	18	16	24	424	51	6	10	12	13	8
	III	1st	559	62	7	15	9	3	4	479	62	6	18	7	4	2
		2nd*	559	6	19	25	12	14	25	479	60	7	17	9	4	4
		2nd**	491	6	19	27	12	13	23	424	61	7	17	9	4	2
		3rd	491	26	19	15	8	16	16	424	59	7	16	11	5	2

* Second blood readings were obtained when first and second bloods were tested simultaneously.
** Second blood readings came from either second and third blood tests or first, second, and third blood tests.

Table 71

PERCENT DISTRIBUTION OF ANTIBODY LEVELS AT FIRST, SECOND AND THIRD BLEEDINGS BY VACCINE LOT, VIRUS TYPE, AND VACCINATION STATUS OBSERVED AREAS

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
303-303-303	I	1st	473	52	4	8	13	13	9	755	54	3	10	14	13	5
		2nd*	473	6	8	16	17	18	34	755	52	3	9	16	13	7
		2nd**	208	6	10	13	18	16	38	293	43	3	10	18	19	6
		3rd	208	13	12	13	12	23	28	293	41	2	10	18	18	10
	II	1st	473	51	4	7	12	14	12	755	53	5	6	14	13	9
		2nd*	473	3	2	12	23	20	40	755	50	4	7	15	14	11
		2nd**	208	4	2	12	25	25	32	293	53	3	6	13	16	8
		3rd	208	4	10	16	23	22	25	293	47	4	5	13	18	12
	III	1st	473	49	7	11	12	12	9	755	56	5	11	14	10	4
		2nd*	473	6	7	15	19	12	40	755	53	6	10	15	11	5
		2nd**	208	6	6	10	20	19	40	293	51	4	12	18	10	6
		3rd	208	11	15	14	6	19	36	293	47	3	14	16	15	5
303-303-307	I	1st	85	67	5	8	9	6	5	223	62	3	5	10	13	7
		2nd*	85	18	9	20	19	12	22	223	63	2	4	9	13	8
		2nd**	48	6	6	8	25	15	40	58	34	7	16	21	14	9
		3rd	48	2	6	21	19	23	29	58	34	2	22	17	14	10
	II	1st	85	62	2	6	6	14	9	223	65	4	6	10	9	6
		2nd*	85	9	5	15	27	14	30	223	65	3	5	12	9	6
		2nd**	48	-	4	12	17	6	60	58	48	7	7	19	10	9
		3rd	48	-	8	23	4	15	50	58	48	5	14	12	10	10
	III	1st	85	56	4	5	12	11	13	223	68	2	3	9	8	9
		2nd*	85	13	9	13	16	14	34	223	66	1	3	10	9	10
		2nd**	48	2	6	8	27	8	48	58	52	3	10	10	14	10
		3rd	48	4	17	15	12	8	44	58	52	2	7	16	12	12
305-305-305	I	1st	598	44	6	10	13	17	9	777	39	7	10	17	18	10
		2nd*	598	11	8	15	14	19	32	777	37	7	9	19	19	9
		2nd**	582	14	10	13	14	17	32	670	39	6	8	20	18	9
		3rd	582	17	12	12	13	20	26	670	35	8	9	17	20	12
	II	1st	598	39	9	6	10	17	19	777	41	9	8	10	16	15
		2nd*	598	3	7	14	17	16	44	777	38	12	8	11	16	16
		2nd**	582	3	10	13	18	13	42	670	39	10	8	11	15	16
		3rd	582	5	15	16	13	13	38	670	33	13	8	11	18	16
	III	1st	598	45	8	11	15	14	7	777	43	6	11	18	14	7
		2nd*	598	2	4	14	22	19	39	777	41	8	11	17	14	9
		2nd**	582	2	4	15	20	19	40	670	42	7	11	17	13	11
		3rd	582	9	13	16	13	15	34	670	38	6	13	19	13	11

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* 2nd blood readings were obtained when 1st and 2nd bloods were tested simultaneously.

** 2nd blood readings came from either 2nd and 3rd blood tests or 1st, 2nd and 3rd blood tests.

*** Less than one-tenth of 1 percent.

Table 71 Continued

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
305-305-307	I	1st	355	46	9	7	14	14	9	492	45	9	8	15	14	10
		2nd*	355	7	12	15	18	20	28	492	42	10	9	14	15	9
		2nd**	304	6	15	15	18	19	26	409	43	8	10	17	14	9
		3rd	304	13	20	13	13	19	22	409	38	9	7	19	16	10
	II	1st	355	52	15	6	7	13	7	492	57	10	5	10	11	6
		2nd*	355	2	7	19	30	17	25	492	52	13	5	10	12	8
		2nd**	304	2	5	20	27	19	27	409	49	15	5	10	13	9
		3rd	304	5	16	22	16	19	22	409	43	15	7	11	16	9
	III	1st	355	48	11	13	13	10	5	492	50	8	16	13	8	5
		2nd*	355	4	12	17	20	18	30	492	48	9	13	17	7	6
		2nd**	304	4	11	19	21	15	30	409	49	10	12	17	9	4
		3rd	304	12	24	13	11	17	23	409	47	10	12	17	9	5
305-305-508	I	1st	-							-						
		2nd*	-							-						
		2nd**	7	14	29	14	-	-	43	4	-	25	25	25	25	-
		3rd	7	29	14	-	14	29	14	4	25	-	50	-	25	-
	II	1st	-							-						
		2nd*	-							-						
		2nd**	7	14	29	14	14	-	29	4	50	-	-	25	-	25
		3rd	7	29	14	14	14	-	29	4	50	-	-	25	25	-
	III	1st	-							-						
		2nd*	-							-						
		2nd**	7	14	-	-	14	29	43	4	75	-	25	-	-	-
		3rd	7	14	14	-	29	14	29	4	75	25	-	-	-	-
307-307-307	I	1st	10	60	-	10	10	10	10	12	67	-	17	8	8	-
		2nd*	10	10	-	20	20	40	10	12	67	-	-	16	16	-
		2nd**	19	5	-	5	16	26	47	16	56	-	-	19	19	6
		3rd	19	5	-	21	16	16	42	16	56	-	-	12	-	31
	II	1st	10	40	-	-	30	-	30	12	42	-	-	8	33	17
		2nd*	10	-	-	20	10	20	50	12	42	-	8	8	33	8
		2nd**	19	-	5	11	21	11	53	16	44	-	12	12	19	12
		3rd	19	-	5	21	5	16	53	16	19	6	12	19	12	31
	III	1st	10	60	10	10	-	10	10	12	50	8	17	8	8	8
		2nd*	10	20	-	30	30	-	20	12	50	8	8	16	16	-
		2nd**	19	11	5	26	21	5	32	16	62	-	12	12	12	-
		3rd	19	16	11	37	-	5	32	16	56	-	12	12	6	12

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* 2nd blood readings were obtained when 1st and 2nd bloods were tested simultaneously.
** 2nd blood readings came from either 2nd and 3rd blood tests or 1st, 2nd and 3rd blood tests.
*** Less than one-tenth of 1 percent.

Table 71 Continued

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
502-502-307	I	1st	230	56	7	6	8	14	8	332	69	2	4	12	10	3
		2nd*	230	27	10	6	13	23	21	332	68	2	5	11	11	3
		2nd**	145	34	7	6	10	17	26	287	68	2	6	9	11	3
		3rd	145	38	6	8	14	17	18	287	70	1	4	10	11	5
	II	1st	230	51	6	5	8	19	10	332	67	2	5	9	12	5
		2nd*	230	7	10	14	16	16	36	332	65	3	4	11	14	4
		2nd**	145	10	12	13	18	15	32	287	63	3	4	12	14	4
		3rd	145	16	10	14	14	14	32	287	54	3	5	12	16	8
	III	1st	230	63	5	7	12	11	2	332	68	3	9	10	8	2
		2nd*	230	8	8	20	17	19	28	332	67	4	7	11	8	4
		2nd**	145	11	7	26	15	14	27	287	66	3	6	13	8	4
		3rd	145	22	17	15	10	14	22	287	61	4	5	13	12	5
502-502-309	I	1st	182	42	6	6	10	22	14	227	40	4	4	16	14	22
		2nd*	182	16	9	8	4	11	52	227	37	4	5	15	18	21
		2nd**	211	13	8	6	4	12	56	218	37	4	6	15	16	23
		3rd	211	14	8	5	11	17	45	218	36	4	4	15	17	24
	II	1st	182	52	3	8	9	16	13	227	41	3	7	14	13	23
		2nd*	182	7	13	12	14	16	39	227	41	2	8	15	16	18
		2nd**	211	6	11	11	13	15	45	218	39	2	7	13	18	20
		3rd	211	9	9	15	13	16	37	218	35	3	8	14	17	24
	III	1st	182	47	6	12	21	10	4	227	43	4	14	18	14	7
		2nd*	182	11	10	12	15	11	41	227	42	4	14	20	12	9
		2nd**	211	10	9	12	15	9	46	218	44	4	14	19	11	7
		3rd	211	18	9	8	10	19	35	218	39	4	11	20	13	12
502-502-502	I	1st	11	64	9	9	9	9	-	2	100	-	-	-	-	-
		2nd*	11	18	9	9	9	36	18	2	100	-	-	-	-	-
		2nd**	2	-	50	-	-	50	-	2	100	-	-	-	-	-
		3rd	2	50	-	-	-	50	-	2	100	-	-	-	-	-
	II	1st	11	64	18	-	-	9	9	2	50	-	-	50	-	-
		2nd*	11	36	18	-	-	-	46	2	50	-	-	-	-	50
		2nd**	2	50	-	-	-	-	50	2	50	-	-	-	-	50
		3rd	2	50	-	-	-	-	50	2	50	-	-	-	-	50
	III	1st	11	64	9	-	27	-	-	2	-	-	-	50	50	-
		2nd*	11	27	9	18	18	9	18	2	-	-	-	-	-	100
		2nd**	2	50	-	-	-	-	50	2	-	-	-	-	-	100
		3rd	2	50	-	-	-	-	50	2	-	-	-	-	50	50

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Table 71 Continued

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
506-506-307	I	1st	486	51	5	10	18	11	5	784	50	4	12	17	12	5
		2nd*	486	16	9	18	15	14	28	784	48	4	11	18	14	6
		2nd**	408	15	9	18	13	13	32	618	50	4	11	16	14	6
		3rd	408	22	11	17	10	17	24	618	48	4	13	14	16	6
	II	1st	486	55	7	7	11	12	8	784	57	7	8	12	10	6
		2nd*	486	3	4	20	21	18	34	784	53	8	8	12	10	9
		2nd**	408	4	4	23	21	16	32	618	56	7	9	10	9	9
		3rd	408	4	13	28	16	15	24	618	52	9	9	12	9	10
	III	1st	486	54	10	14	13	5	4	784	57	7	14	15	5	2
		2nd*	486	5	7	26	17	11	35	784	54	7	14	16	7	3
		2nd**	408	5	8	27	15	11	33	618	58	7	12	13	6	3
		3rd	408	13	16	21	6	16	28	618	52	7	14	14	10	4
506-506-309	I	1st	57	65	7	4	12	12	-	11	82	9	-	-	9	-
		2nd*	57	4	19	21	35	7	14	11	91	-	9	-	-	-
		2nd**	67	6	15	25	30	10	13	7	100	-	-	-	-	-
		3rd	67	15	28	10	16	22	7	7	71	-	-	29	-	-
	II	1st	57	61	5	7	19	5	2	11	73	-	-	-	18	9
		2nd*	57	4	10	28	18	16	25	11	73	-	18	-	-	9
		2nd**	67	1	3	16	30	19	30	7	71	-	-	14	14	-
		3rd	67	1	16	27	13	22	19	7	57	14	-	14	14	-
	III	1st	57	58	12	12	7	9	2	11	73	9	9	-	-	9
		2nd*	57	4	10	28	18	16	25	11	73	-	18	-	-	9
		2nd**	67	3	10	16	25	21	24	7	71	-	14	-	-	14
		3rd	67	10	24	12	16	18	19	7	71	-	-	14	-	14
506-506-506	I	1st	483	49	5	11	15	13	6	771	52	7	11	14	11	5
		2nd*	483	21	10	14	13	17	25	771	52	6	12	13	12	6
		2nd**	457	21	10	16	11	18	26	697	52	6	11	15	12	4
		3rd	457	24	9	15	13	20	19	697	49	5	11	18	13	5
	II	1st	483	44	10	12	12	14	9	771	48	5	10	14	14	9
		2nd*	483	2	7	20	21	18	32	771	46	5	9	13	16	11
		2nd**	457	2	7	20	22	17	33	697	48	6	10	11	14	11
		3rd	457	6	10	21	22	16	25	697	46	6	9	12	16	11
	III	1st	483	40	11	20	16	9	4	771	50	8	18	14	6	4
		2nd*	483	1	6	20	18	15	40	771	49	7	18	13	8	5
		2nd**	457	2	6	21	16	17	39	697	50	8	17	13	7	4
		3rd	457	9	15	16	11	20	30	697	46	6	16	16	10	5

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* 2nd blood readings were obtained when 1st and 2nd bloods were tested simultaneously.
** 2nd blood readings came from either 2nd and 3rd blood tests or 1st, 2nd and 3rd blood tests.
*** Less than one-tenth of 1 percent.

Table 71 Continued

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		< 4	4&8	16	64	256	1024		< 4	4&8	16	64	256	1024
507-507-307	I	1st	121	59	2	5	11	17	6	96	57	5	6	10	9	11
		2nd*	121	31	10	7	8	16	29	96	56	5	6	8	11	12
		2nd**	133	29	8	8	8	18	30	101	56	4	8	6	13	13
		3rd	133	29	3	10	16	20	23	101	52	5	9	6	16	12
	II	1st	121	57	6	6	5	13	13	96	57	4	4	7	12	15
		2nd*	121	7	7	15	19	12	40	96	55	4	4	5	20	11
		2nd**	133	8	6	14	17	15	41	101	56	4	4	6	18	12
		3rd	133	10	9	15	20	19	28	101	50	7	7	8	14	14
	III	1st	121	61	6	3	14	10	6	96	62	3	6	8	11	8
		2nd*	121	6	9	21	16	12	36	96	58	4	6	10	11	9
		2nd**	133	5	9	18	17	17	35	101	59	5	7	10	10	9
		3rd	133	20	14	14	15	14	24	101	55	6	9	6	11	13
507-507-309	I	1st	233	43	6	9	13	18	11	239	50	5	6	17	15	7
		2nd*	233	21	6	6	8	16	44	239	47	5	8	17	15	8
		2nd**	199	25	7	9	9	17	34	206	51	6	8	16	14	6
		3rd	199	25	7	7	11	22	29	206	48	8	4	17	12	11
	II	1st	233	53	3	9	14	10	11	239	56	3	5	10	10	16
		2nd*	233	15	9	12	13	16	34	239	55	3	4	12	9	18
		2nd**	199	15	12	12	17	15	29	206	55	4	7	13	11	10
		3rd	199	18	10	15	18	16	24	206	45	8	4	14	15	14
	III	1st	233	43	8	20	16	9	4	239	57	5	12	17	7	2
		2nd*	233	22	12	8	11	22	25	239	56	5	12	18	7	2
		2nd**	199	24	12	7	15	19	24	206	57	4	12	17	8	2
		3rd	199	35	5	7	22	17	15	206	52	3	14	18	10	2
507-507-507	I	1st	608	51	3	8	13	15	10	907	53	3	6	11	16	10
		2nd*	608	46	4	7	14	17	13	907	52	2	7	12	15	11
		2nd**	414	46	3	7	14	18	13	577	54	4	6	11	15	10
		3rd	414	44	5	7	13	17	15	577	50	3	7	14	12	15
	II	1st	608	63	6	4	6	8	12	907	62	5	4	8	9	12
		2nd*	608	49	11	9	7	7	17	907	61	5	4	7	10	13
		2nd**	414	48	12	11	7	7	16	577	62	5	6	7	9	12
		3rd	414	49	10	8	8	10	16	577	54	5	5	7	12	18
	III	1st	608	61	4	8	11	8	7	907	60	5	9	11	7	8
		2nd*	608	45	9	7	7	11	20	907	59	5	8	11	8	8
		2nd**	414	40	10	8	8	14	19	577	63	4	8	12	7	5
		3rd	414	45	6	10	12	12	16	577	58	3	11	12	7	8

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Table 71 Continued

Lots by Virus Type and Bleeding			Vaccinated							Control						
			Total Sera	Titers as Percent of Total Sera						Total Sera	Titers as Percent of Total Sera					
Lot	Type	Bleeding		<4	4&8	16	64	256	1024		<4	4&8	16	64	256	1024
508-508-307	I	1st	18	61	-	17	17	6	-	9	56	44	-	-	-	-
		2nd*	18	28	17	11	11	11	22	9	89	-	-	11	-	-
		2nd**	-							-						
		3rd	-							-						
	II	1st	18	50	-	22	11	11	6	9	44	-	-	22	33	-
		2nd*	18	6	-	17	44	22	11	9	44	-	-	33	11	11
		2nd**	-							-						
		3rd	-							-						
	III	1st	18	72	11	-	17	-	-	9	67	22	-	11	-	-
		2nd*	18	22	11	17	22	17	11	9	67	11	-	22	-	-
		2nd**	-							-						
		3rd	-							-						
508-508-309	I	1st	208	48	7	7	12	15	11	262	46	4	7	16	13	14
		2nd*	208	4	3	15	23	14	40	262	47	3	9	11	18	13
		2nd**	206	4	3	13	20	16	43	263	48	3	8	15	15	11
		3rd	206	9	15	17	10	13	37	263	45	5	7	14	17	12
	II	1st	208	49	12	5	14	11	9	262	53	6	8	9	16	7
		2nd*	208	1	1	12	26	24	36	262	52	8	7	13	14	6
		2nd**	206	1	***	10	24	24	40	263	52	8	6	12	15	6
		3rd	206	1	7	16	21	22	33	263	48	9	8	13	13	10
	III	1st	208	54	8	7	17	10	5	262	55	6	8	16	8	7
		2nd*	208	3	9	19	23	15	31	262	53	8	7	16	11	6
		2nd**	206	3	8	15	24	17	33	263	53	8	9	13	11	5
		3rd	206	9	17	17	12	19	25	263	51	5	10	19	8	7
508-508-508	I	1st	357	46	9	8	18	12	7	487	43	7	12	16	14	8
		2nd*	357	13	10	11	16	20	30	487	38	9	12	17	14	11
		2nd**	290	11	9	10	17	22	32	342	34	8	12	17	16	13
		3rd	290	11	10	12	17	21	30	342	30	7	12	17	18	16
	II	1st	357	45	8	8	12	15	13	487	43	10	10	15	12	10
		2nd*	357	3	5	16	19	22	36	487	39	9	11	14	15	12
		2nd**	290	4	3	10	18	22	43	342	33	8	11	14	17	17
		3rd	290	4	6	9	20	19	41	342	28	9	11	13	19	20
	III	1st	357	47	12	14	10	11	6	487	49	10	16	16	6	3
		2nd*	357	9	12	17	15	20	28	487	45	8	18	16	8	4
		2nd**	290	6	11	17	17	16	34	342	45	8	19	14	10	5
		3rd	290	11	13	13	16	15	31	342	39	9	17	18	11	6

* 2nd blood readings were obtained when 1st and 2nd bloods were tested simultaneously.
** 2nd blood readings came from either 2nd and 3rd blood tests or 1st, 2nd and 3rd blood tests.
*** Less than one-tenth of 1 percent.

Briefly, the data of Tables 70 and 71 indicate the tendency of titers, five months after vaccination, to shift to levels lower than those in the early post-vaccination period, producing, thereby, an increased aggregation of sera with titers of 4 to 16; with Type III the decline is greater so that a significant excess of previously positive titers is reported after five months to be less than 4. In the gross data major differences between lots are not readily observed, although there is a suggestion that the shift to lower but positive titers in third specimen is more frequent with the lots of better potency; this might be expected because they stimulated a larger proportion of subjects to antibody production. Generally, the Type II titers were the most stable with any lot. The greatest decline and the greatest evident variation in durability of effect between lots is observed in Type III titers.

Generally with Types I and II, regardless of the original antigenic effect, an additional 4 to 5 percent was added after five months to the results reported as negative two weeks after vaccination. With Type III, additions of 10 to 12 percent to the negatives were not uncommon, sometimes doubling the proportion present in the second specimens. Results reported from tests of comparable control sera usually showed a decrease in the proportion of negatives in the third sera.

It was mentioned earlier that during the five-months period between the collection of the second and third sera while recessions in titers from positive to negative status were occurring, accessions to positive status were also reported; 10 to 20 percent of the total vaccinated segment from placebo areas who had no antibody to a given type of virus in the second specimen of serum were reported positive in the third serum (Table 77). Many of the titers so reported were of high level and the frequency was considerably greater than in the controls. This frequency according to type was proportionate to the total antigenic efficiency of the type: II, III, I. The results suggest that type-specific rises in antibody took place in these persons during the period between two weeks and five months after vaccination. It is also possible that they represent persons who had minimal responses to vaccine but had received a booster effect from natural exposure. These late responses are also seen to be related characteristically to antigenic potency of lots and their type components.

Tables 72 and 73, prepared from the detailed lot tabulations, present groupings of lots according to relative antigenic effect by virus type for vaccinated children who were bled in placebo and observed areas. Initial response in persons without type-specific antibody prior to vaccination and secondary or delayed response in persons who did not respond initially seem to follow fairly closely the defined categories of relative antigenic effect. This is more concise for Types I and II in placebo areas and for Type III in observed areas; for Type III in placebo areas and Types I and II in observed areas, the pattern is less distinct but even here the secondary or delayed response is greater for the good lots than for the very poor lots.

For Type II in placebo areas and Types II and III in observed areas, the extent of regression to negative status after having attained positive status is less for the good lots than for those of less original antigenic effect. The extent of regression for Type I in observed areas is essentially the same for all lot groups (14 to 20 percent); for Type III in placebo areas it ranged from 20 to 28 percent and for Type I in placebo areas it ranged from 9 percent in the good lots to 24 percent in the fair lots with no regression among the few individuals who responded to the very poor lots.

Inapparent Infection

In addition to determining the persistence of antibody after vaccination it was hoped that some estimate of the frequency of natural infection during the poliomyelitis season might be gained by comparison of the antibody titers in control subjects before and after the poliomyelitis season. As previously noted, in the total compilations, changes from positive to negative and from negative to positive between the first and second titers of controls were of essentially the same magnitude (5 to 6 percent) indicating that they were largely attributable to laboratory variation. Changes

Table 72

FIRST BY SECOND BY THIRD SERUM TITERS OF VACCINATED CHILDREN BY LOT GROUPS ACCORDING TO RELATIVE ANTIGENIC EFFECT, BY VIRUS TYPE PLACEBO AREA LOTS*

Lot Groups by Virus Type	Antibody Levels	1st Serum <4 to Specified Type: 2nd Serum Titers	1st Serum <4 to Specified Type: 3rd Serum Titers <4	4 & 8	16	64 or >	1st Serum 4 & 8 to Specified Type: 2nd Serum Titers	1st Serum 4 & 8 to Specified Type: 3rd Serum Titers <4	4 & 8	16	64 or >	1st Serum 16 to Specified Type: 2nd Serum Titers	1st Serum 16 to Specified Type: 3rd Serum Titers <4	4 & 8	16	64 or >	1st Serum 64 or > to Specified Type: 2nd Serum Titers	1st Serum 64 or > to Specified Type: 3rd Serum Titers <4	4 & 8	16	64 or >	Initial Response %**	Secondary Response %***	Return to Negative Status %****
Type I:																								
Good Lots (304 only)	< 4	6	4	2	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1			
	4 & 8	9	3	3	2	1	1	-	-	1	-	-	-	-	-	-	1	-	1	-	-			
	16	27	4	12	10	1	4	-	2	2	-	-	-	-	-	-	-	-	-	-	-	94.9	33.3	9.0
	64 or >	75	3	12	25	35	6	-	2	2	2	8	-	-	-	8	124	1	2	5	116			
	Total	117	14	29	37	37	11	-	4	5	2	8	-	-	-	8	126	1	3	5	117			
Moderate Lots (306, 308)	< 4	58	45	8	4	1	8	6	-	2	-	1	-	1	-	-	1	1	-	-	-			
	4 & 8	53	21	26	2	4	7	3	2	1	1	4	1	1	1	1	-	-	-	-	-			
	16	72	10	33	23	6	13	2	2	6	3	12	1	-	8	3	4	-	-	2	2	82.4	22.4	11.8
	64 or >	147	1	14	39	93	28	-	1	8	19	24	-	1	1	22	155	1	-	7	147			
	Total	330	77	81	68	104	56	11	5	17	23	41	2	3	10	26	160	2	-	9	149			
Fair Lots (505, 512, 514)	< 4	287	263	13	1	10	1	1	-	-	-	5	5	-	-	-	15	13	-	1	1			
	4 & 8	152	93	39	10	10	3	-	3	-	-	-	-	-	-	-	2	-	1	-	1			
	16	184	38	71	62	13	2	-	1	1	-	6	1	-	2	3	15	1	7	5	2	66.7	8.4	24.1
	64 or >	240	8	17	68	147	44	1	1	3	39	67	-	1	8	58	432	1	1	9	421			
	Total	863	402	140	141	180	50	2	5	4	39	78	6	1	10	61	464	15	9	15	425			
Poor Lots (302 only)	< 4	63	57	-	-	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	21	6	9	2	2	9	1	6	-	2	1	1	-	-	-	-	-	-	-	-			
	16	9	-	5	2	2	2	-	1	1	-	7	-	-	4	3	2	-	-	-	2	36.4	9.5	22.2
	64 or >	6	-	1	3	2	1	-	-	-	1	8	1	-	2	5	90	-	-	3	87			
	Total	99	65	15	7	12	12	1	7	1	3	16	2	-	6	8	92	-	-	3	89			
Very Poor Lots (503 only)	< 4	24	23	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	1	-	1	-	-	2	1	1	-	-	1	-	-	1	-	-	-	-	-	-			
	16	3	-	1	2	-	3	-	1	2	-	-	-	-	-	-	1	-	-	1	-	17.2	4.2	0.0
	64 or >	1	-	-	-	1	-	-	-	-	-	4	-	-	1	3	23	-	-	2	21			
	Total	29	23	2	2	2	5	1	2	2	-	5	-	-	2	3	24	-	-	3	21			
Type II:																								
Good Lots (304, 514, 512, 308, 306)	< 4	55	36	4	7	6	3	-	2	1	-	1	-	-	-	1	-	-	-	-	-			
	4 & 8	85	31	46	4	4	10	4	2	4	-	3	-	2	1	-	6	2	3	1	-			
	16	241	14	102	100	25	7	1	2	3	1	14	1	-	10	3	14	3	5	5	1	94.4	30.9	5.8
	64 or >	608	9	54	189	356	108	-	3	18	87	65	-	1	8	76	505	1	2	12	490			
	Total	989	92	206	300	391	126	5	9	26	86	103	1	3	19	80	525	6	10	18	491			
Moderate Lots (505 only)	< 4	26	25	1	-	-	-	-	-	-	-	-	-	-	-	-	2	1	1	-	-			
	4 & 8	36	22	12	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	16	83	9	35	35	4	4	-	1	3	-	3	-	-	3	-	4	1	1	-	2	91.4	3.6	12.2
	64 or >	159	3	14	52	90	19	-	-	3	16	19	-	1	1	17	204	-	-	2	202			
	Total	304	59	62	88	95	23	-	1	6	16	22	-	1	4	17	210	2	2	2	204			
Fair Lots (None)																								
Poor Lots (302 only)	< 4	44	40	3	-	1	1	1	-	-	-	-	-	-	-	-	1	1	-	-	-			
	4 & 8	23	7	12	2	2	4	1	-	1	2	-	-	-	-	-	1	-	-	1	-			
	16	18	1	6	10	1	10	-	3	6	1	2	-	-	-	2	1	-	-	1	-	53.2	9.1	16.0
	64 or >	9	-	1	3	5	9	-	-	2	7	12	-	-	2	10	84	1	1	4	78			
	Total	94	48	22	15	9	24	2	3	9	10	14	-	-	2	12	87	2	1	6	78			
Very Poor Lots (503 only)	< 4	23	21	2	-	-	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	3	2	1	-	-	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-			
	16	1	-	1	-	-	1	-	-	1	-	1	-	1	-	-	-	-	-	-	-	20.7	8.7	33.3
	64 or >	2	-	1	-	1	1	-	-	1	-	4	-	-	-	4	25	-	-	1	24			
	Total	29	23	5	-	1	4	1	1	2	-	5	-	1	-	4	25	-	-	1	24			
Type III:																								
Good Lots (304, 514)	< 4	31	28	-	1	2	-	-	-	-	-	1	-	-	-	1	-	-	-	-	-			
	4 & 8	89	63	22	2	2	1	-	-	-	1	-	-	-	-	-	-	-	-	-	-			
	16	166	42	75	41	6	3	-	-	2	1	4	-	-	4	-	2	1	1	-	-	93.2	9.7	27.3
	64 or >	173	12	39	56	66	41	-	2	-	39	72	-	1	3	68	106	1	2	1	102			
	Total	459	145	136	100	78	45	-	2	2	41	77	-	1	7	69	108	2	3	1	102			
Moderate Lots (306, 505, 302, 512, 308)	< 4	127	107	12	4	4	5	2	1	1	1	1	1	-	-	-	2	2	-	-	-			
	4 & 8	185	106	60	11	8	10	3	5	2	-	6	6	2	-	-	7	3	3	-	1			
	16	323	79	124	92	28	32	4	7	18	3	19	-	5	9	5	10	3	4	2	1	88.0	15.7	22.0
	64 or >	424	20	82	141	181	77	-	2	11	64	159	2	2	7	146	445	2	5	8	432			
	Total	1,059	312	278	248	221	124	9	15	32	68	187	9	9	16	153	464	10	12	8	434			
Fair Lots (None)																								
Poor Lots (503 only)	< 4	11	10	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	6	2	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	16	5	1	3	1	-	-	-	-	-	-	1	-	-	-	1	1	-	-	1	-	57.7	9.1	20.0
	64 or >	4	-	1	2	1	3	-	-	1	2	10	-	1	2	7	22	-	-	1	21			
	Total	26	13	8	3	2	3	-	-	1	2	11	-	1	2	8	23	-	-	2	21			
Very Poor Lots (None)																								

* All three specimens of sera were tested simultaneously.
"Relative antigenic effect": See Glossary.
Lot groups defined according to relative antigenic effect as follows:

Good - 90% or >
Moderate - 75 to 89%
Fair - 50 to 74%
Poor - 25 to 49%
Very Poor - <25%

** <4 in 1st serum, 4 or > in 2nd serum (%).

*** <4 in 1st and 2nd sera, 4 or > in 3rd serum (%).

**** <4 in 1st serum, 4 or > in 2nd serum, < 4 in 3rd serum (%).

Table 73

FIRST BY SECOND BY THIRD SERUM TITERS OF VACCINATED CHILDREN BY LOT GROUPS ACCORDING TO RELATIVE ANTIGENIC EFFECT, BY VIRUS TYPE OBSERVED AREA LOTS*

Lot Groups by Virus Type	Antibody Levels	1st Serum <4 to Specified Type					1st Serum 4 & 8 to Specified Type					1st Serum 16 to Specified Type					1st Serum 64 or > to Specified Type					Initial Response	Secondary Response	Return to Negative Status
		2nd Serum Titers	3rd Serum Titers				2nd Serum Titers	3rd Serum Titers				2nd Serum Titers	3rd Serum Titers				2nd Serum Titers	3rd Serum Titers						
			<4	4 & 8	16	64 or >		<4	4 & 8	16	64 or >		<4	4 & 8	16	64 or >		<4	4 & 8	16	64 or >	% **	% ***	% ****
Type I:																								
Good Lots (506-309, 508-309)	< 4	9	8	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	11	7	2	-	2	1	-	1	-	-	1	-	1	-	-	-	-	-	-	-			
	16	27	6	16	3	2	3	-	1	1	1	-	-	-	-	-	-	-	-	-	-	91.3	11.1	14.9
	64 or >	56	1	13	26	16	12	-	-	1	11	8	-	-	1	7	71	-	-	-	71			
	Total	103	22	32	29	20	18	-	2	2	12	9	-	1	1	7	71	-	-	-	71			
Moderate Lots (303, 307, 305-307)	< 4	23	18	1	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	29	15	11	2	1	3	-	2	-	1	1	-	-	-	1	1	-	-	-	1			
	16	34	5	15	10	4	5	-	2	1	2	2	-	-	1	1	-	-	-	-	-	83.5	21.7	19.8
	64 or >	53	3	14	11	25	14	-	2	4	8	27	-	-	3	24	107	1	-	4	102			
	Total	139	41	41	25	32	22	-	6	5	11	30	-	-	4	26	108	1	-	4	103			
Fair Lots (303-307, 305, 506-307, 508, 502-309, 506, 502-307)	< 4	253	233	7	2	11	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	111	52	44	7	8	5	2	2	1	-	2	-	1	1	-	-	-	-	-	-			
	16	161	16	55	72	18	19	-	6	11	2	11	-	-	11	-	4	-	1	1	2	63.9	7.9	15.4
	64 or >	175	1	15	57	102	54	-	1	5	48	125	-	1	14	110	547	1	-	6	540			
	Total	700	302	121	138	139	79	3	9	17	50	138	-	2	26	110	551	1	1	7	542			
Poor Lots (507-309, 507-307)	< 4	60	53	-	1	6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	19	8	5	2	4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	16	15	3	3	8	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	49.6	11.7	18.6
	64 or >	25	-	-	6	19	12	-	-	1	11	17	-	1	1	15	89	-	-	-	89			
	Total	119	64	8	17	30	12	-	-	1	11	17	-	1	1	15	89	-	-	-	89			
Very Poor Lots (507 only)	< 4	117	112	2	-	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	5	2	3	-	-	1	-	1	-	-	1	-	1	-	-	-	-	-	-	-			
	16	3	-	-	1	2	-	-	-	-	-	13	-	3	7	3	5	-	-	2	3	10.7	4.3	14.3
	64 or >	6	-	1	1	4	4	-	-	-	4	11	-	1	3	7	99	-	-	3	96			
	Total	131	114	6	2	9	5	-	1	-	4	25	-	5	10	10	104	-	-	5	99			
Type II:																								
Good Lots (303, 307, 506, 506-309, 508-309, 507-307, 305-307, 506-307, 508, 305)	< 4	53	42	4	3	4	-	-	-	-	-	-	-	-	-	-	3	1	-	2	-			
	4 & 8	74	29	33	8	4	8	1	5	1	1	1	-	-	1	-	-	-	-	-	-			
	16	278	14	96	133	35	31	1	9	16	5	5	-	2	1	2	5	-	2	-	3	94.1	20.8	5.8
	64 or >	486	6	46	157	277	116	-	2	18	96	115	-	1	6	108	628	-	-	4	624			
	Total	891	91	179	301	320	155	2	16	35	102	121	-	3	8	110	636	1	2	6	627			
Moderate Lots (502-309, 303-307, 502-307)	< 4	21	14	1	1	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	32	13	15	3	1	-	-	-	-	-	1	1	-	-	-	-	-	-	-	-			
	16	30	7	8	11	4	2	-	1	1	-	-	-	-	-	-	-	-	-	-	-	85.8	33.3	16.5
	64 or >	65	1	4	26	34	5	-	-	-	5	15	-	-	2	13	102	-	-	1	101			
	Total	148	35	28	41	44	7	-	1	1	5	16	1	-	2	13	102	-	-	1	101			
Fair Lots (507-309)	< 4	21	13	1	4	3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	15	4	6	-	5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	16	14	3	5	3	3	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	71.2	38.1	15.4
	64 or >	23	1	1	7	14	3	-	-	1	2	10	-	-	2	8	40	2	-	1	37			
	Total	73	21	13	14	25	3	-	-	1	2	10	-	-	2	8	41	2	-	1	38			
Poor Lots (Only Lot 502 - too few cards to tabulate)																								
Very Poor Lots (507 only)	< 4	128	111	5	2	10	1	1	-	-	-	-	-	-	-	-	2	1	-	-	1			
	4 & 8	23	11	8	1	3	5	1	3	1	-	-	-	-	-	-	-	-	-	-	-			
	16	17	3	9	1	4	6	-	2	2	2	4	-	-	4	-	2	-	-	-	2	26.4	13.3	30.4
	64 or >	6	-	-	4	2	3	-	-	1	2	8	-	-	2	6	60	-	-	1	59			
	Total	174	125	22	8	19	15	2	5	4	4	12	-	-	6	6	64	1	-	1	62			
Type III:																								
Good Lots (506, 305, 506-309, 508-309, 305-307, 506-307, 507-307)	< 4	48	39	4	3	2	-	-	-	-	-	1	-	1	-	-	2	1	-	1	-			
	4 & 8	102	53	39	2	8	5	-	4	-	1	2	-	-	2	-	1	-	-	1	-			
	16	257	45	99	94	19	29	3	6	12	6	9	-	1	4	4	3	-	-	-	3	93.5	18.8	17.5
	64 or >	326	22	64	125	115	102	-	9	9	84	168	-	1	3	164	449	1	1	7	440			
	Total	733	159	206	224	144	136	3	21	21	91	180	-	3	9	168	455	2	1	9	443			
Moderate Lots (502-307, 303, 307, 508, 303-307, 502-309)	< 4	46	42	1	1	2	-	-	-	-	-	1	-	1	-	-	-	-	-	-	-			
	4 & 8	41	23	12	1	5	6	3	2	1	-	-	-	-	-	-	-	-	-	-	-			
	16	80	18	32	23	7	7	-	2	4	1	2	-	-	1	1	2	-	1	-	1	83.1	8.7	22.8
	64 or >	105	10	12	28	55	28	-	-	3	26	62	-	1	1	60	191	-	-	2	189			
	Total	272	93	57	53	89	42	3	4	8	27	65	-	2	2	61	193	-	1	2	190			
Fair Lots (Only Lot 508-307, too few cards to tabulate)																								
Poor Lots (507-309)	<4	27	26	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	15	7	5	1	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
	16	8	4	2	2	-	-	-	-	-	-	1	-	-	-	1	-	-	-	-	-	50.0	3.7	44.4
	64 or >	4	1	-	-	3	11	-	-	4	7	25	-	-	-	25	36	1	-	1	34			
	Total	54	38	7	3	6	11	-	-	4	7	26	-	-	-	26	36	1	-	1	34			
Very Poor Lots (507 only)	< 4	109	100	1	-	8	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-			
	4 & 8	20	13	5	2	-	5	1	3	-	1	1	-	1	-	-	-	-	-	-	-			
	16	17	6	5	6	-	1	-	-	1	-	4	1	-	2	1	1	-	-	1	-	30.8	8.3	41.7
	64 or >	11	1	1	5	4	4	-	-	-	4	21	-	-	3	18	70	1	-	1	68			
	Total	157	120	12	13	12	11	1	4	1	5	26	1	1	5	19	71	1	-	2	66			

* All three specimens of sera were tested simultaneously.
"Relative antigenic effect": See Glossary.
Lot groups defined according to relative antigenic effect as follows:

Good	- 90% or >
Moderate	- 75 to 89%
Fair	- 50 to 74%
Poor	- 25 to 49%
Very Poor	- < 25%

** <4 in 1st serum, 4 or > in 2nd serum (%).

*** <4 in 1st and 2nd sera, 4 or > in 3rd serum (%).

**** <4 in 1st serum, 4 or > in 2nd serum, <4 in 3rd serum (%).

of the same degree were noted between the second and third specimens. Analysis of data for control children who were reported to have no antibody to any type of poliomyelitis virus in the first and second specimens revealed that 5 percent had changed from negative to positive to one type or another in the third specimen. The compilations of titer changes among the triple negatives contained, therefore, approximately the same technical variations as noted for the total data.

It was not possible from these data, therefore, to separate natural from technical influences upon the reported antibody titers. However, changes in the titers of control children which are found to be in excess of the indicated technical variation may provide an indication of subclinical infections.

Increases in Titer Among Controls Without Type-specific Antibody Initially: Reference was first made to results obtained when the three specimens (pre-clinic, two-weeks-post-clinic and five-months-post-clinic) were tested simultaneously by the laboratories. A tabulation was made of the increases in titers to each type of virus observed with specimens of control persons who had no antibody to the specified type of virus in the initial specimen; the data are presented in Table 74. Using the Type I data in placebo controls as an example, it is seen that of 1,439 subjects reported with titers of less than 4 originally, 110 were reported positive in the five-week (second) specimen and 62 of them, 4.3 percent of the total, with titers of 16 or greater. Of the 1,329 whose titers remained negative in the second specimen, 98 were reported to be positive in the third specimen; 64, or 4.4 percent of the total, had titers of 16 or greater. It seems quite unlikely that the extent of reported change in the five weeks between the first and second specimens could be related to infection, particularly when during the next five months the reported increases are of the same order of magnitude. Rather, it suggests technical error in the initial readings in that 87 percent of those reported positive at levels of 16 or greater in the second specimen remained so in the third specimen. Of the 48 reported to have titers of 4 or 8 in the second specimen, 23, or 48 percent, were again reported with titers of less than 4 in the third. The results with Types II and III in placebo controls are of the same general order (Table 83).

If increases of titer from less than 4 to 256 or more are considered, there is no difference between the frequency of occurrence between first and second or second and third specimens with Type I and there is a decrease with Type II. With Type III, 16 percent of those becoming positive between first and second specimens rose to a level of 256 or more, while 48 of the 110 reported to have developed antibodies between second and third bleedings had titers of 256 or more. This may indicate inapparent infection but at most represents only 3 percent of those in the series without initial antibody.

The data from observed controls indicate a somewhat smaller frequency of increases to 16 or greater between the original and five-week titers but distinctly greater percentages of increases between the five-week and five-month titers. Moreover, the percentage of reported changes in titer from less than 4 to 256 or greater increased sharply between the two-week and the five-month bleedings as compared with changes of this extent between the first and second titers. The percentages with titers of 256 or more among those first reported positive in the second and third sera, respectively, were 19 and 30 for Type I, 15 and 42 for Type II, and 10 and 39 for Type III. These high levels, while small segments of the total, may again be indicative of inapparent infection but are not clearly differentiated from laboratory variation.

Changes in Titer Among Controls Without Reported Antibody to Any Type Initially: The titers of controls reported to be without antibody to any of the three types initially were analyzed in the same fashion as the type-specific negatives. The numbers involved are smaller but the results presented in Table 75 are essentially parallel to those of Table 74.

If the changes in titer from less than 4 to 16 or more in the five months interval between the second and third specimens were to be considered totally natural occurrences, it would indicate a 2 to 4 percent infection rate

Table 74

ANTIBODY STATUS IN SECOND AND THIRD SERA OF CONTROL CHILDREN WITHOUT TYPE-SPECIFIC ANTIBODY IN FIRST SERUM, BY VIRUS TYPE PLACEBO AND OBSERVED AREAS

Antibody Status	Controls in Placebo Areas			Controls in Observed Areas		
	Type I	Type II	Type III	Type I	Type II	Type III
No. < 4 in 1st Serum - Total	1,439	1,425	1,582	1,642	1,766	1,781
2nd Serum Titers						
<4	1,329	1,308	1,457	1,545	1,615	1,666
4 & 8	48	48	42	46	78	60
16	11	19	30	19	23	28
64	16	14	33	14	27	16
256	19	16	16	12	17	5
1024	16	20	4	6	6	6
No. 4 or >	110	117	125	97	151	115
% 4 or >*	7.6	8.2	7.9	5.9	8.6	6.5
No. 16 or >	62	69	83	51	73	55
% 16 or >*	4.3	4.8	5.2	3.1	4.1	3.1
No. 256 or >	35	36	20	18	23	11
% 256 or >*	2.4	2.5	1.3	1.1	1.3	0.6
16 or > as % of 4 or >	56.4	59.0	66.4	52.6	48.3	47.8
256 or > as % of 4 or >	31.8	30.8	16.0	18.6	15.2	9.6
No. <4 in 1st and 2nd Sera - Total	1,329	1,308	1,457	1,545	1,615	1,666
3rd Serum Titers						
<4	1,231	1,216	1,347	1,409	1,406	1,505
4 & 8	34	45	35	37	56	30
16	16	14	7	25	35	28
64	17	11	20	33	30	40
256	21	8	26	29	61	36
1024	10	14	22	12	27	27
No. 4 or >	98	92	110	136	209	161
% 4 or >*	6.8	6.5	7.0	8.3	11.8	9.0
No. 16 or >	64	47	75	99	153	131
% 16 or >*	4.4	3.3	4.7	6.0	8.7	7.4
No. 256 or>	31	22	48	41	88	63
% 256 or>*	2.2	1.5	3.0	2.5	5.0	3.5
16 or> as % of 4 or>	65.3	51.1	68.2	72.8	73.2	81.4
256 or > as % of 4 or >	31.6	23.9	43.6	30.1	42.1	39.1
No. <4 in 1st, 4 & 8 in 2nd Sera - Total	48	48	42	46	78	60
% <4 in 3rd Serum	47.9	52.1	31.0	43.5	37.2	40.0
No. <4 in 1st, 16 or > in 2nd Serum - Total	62	69	83	51	73	55
% 16 or > in 3rd Serum	87.1	85.5	75.9	58.8	72.6	70.9

* Percentages based on total number <4 in first serum.

Table 75

ANTIBODY STATUS IN SECOND AND THIRD SERA OF CONTROL CHILDREN WITHOUT TYPE-SPECIFIC ANTIBODY IN FIRST SERUM, BY VIRUS TYPE PLACEBO AND OBSERVED AREAS

Antibody Status	Controls in Placebo Areas			Controls in Observed Areas		
	Type I	Type II	Type III	Type I	Type II	Type III
No. <4 to All 3 Types in 1st Serum - Total	774	774	774	789	789	789
2nd Serum Titers						
<4	731	730	733	755	744	740
4 & 8	15	12	8	13	18	24
16	3	10	10	7	7	12
64	11	7	13	5	12	9
256	7	5	8	6	7	3
1024	7	10	2	3	1	1
No. 4 or >	43	44	41	34	45	49
% 4 or >*	5.6	5.7	5.3	4.3	5.7	6.2
No. 16 or >	28	32	33	21	27	25
% 16 or >*	3.6	4.1	4.3	2.7	3.4	3.2
No. 256 or >	14	15	10	9	8	4
% 256 or >*	1.8	1.9	1.3	1.1	1.0	0.5
16 or > as % of 4 or >	65.1	72.7	80.5	61.8	60.0	51.0
256 or > as % of 4 or >	32.6	34.1	24.4	26.5	17.8	8.2
No. <4 to All 3 Types in 1st and <4 to Specific Type in 2nd Serum - Total	731	730	733	755	744	740
3rd Serum Titers						
<4	697	696	693	693	662	681
4 & 8	12	18	12	18	19	12
16	3	5	4	12	10	5
64	5	3	3	12	6	12
256	8	2	9	14	35	17
1024	6	6	12	6	12	13
No. 4 or >	34	34	40	62	82	59
% 4 or >*	4.4	4.4	5.2	7.9	10.4	7.5
No. 16 or >	22	16	28	44	63	47
% 16 or >*	2.8	2.1	3.6	5.6	8.0	6.0
No. 256 or >	14	8	21	20	47	30
% 256 or >*	1.8	1.0	2.7	2.5	6.0	3.8
No. <4 to All 3 Types in 1st and 4 & 8 to Type in 2nd Serum - Total	15	12	8	13	18	24
%<4 to Type in 3rd Serum	46.7	41.7	12.5	53.8	38.9	37.5
No. <4 to All 3 Types in 1st and 16 or > in 2nd Serum - Total	28	32	33	21	27	25
% 16 or > in 3rd Serum	89.3	93.8	81.8	71.4	77.8	80.0
16 or > as % of 4 or >	64.7	47.1	70.0	71.0	76.8	79.7
256 or > as % of 4 or >	41.2	23.5	52.5	32.3	57.3	50.8

* Percentages based on total number <4 in first serum

for the several types in the placebo controls without antibody to any type originally and 6 to 8 percent in the observed controls with similar lack of experience. If, however, the changes between the first two titers are considered to be primarily the index of technical variation, then there is little evidence of inapparent infection among the placebo controls because the percentage of change in the later period is no greater than technical variations would account for. In the controls of observed areas in this series, however, a considerable excess, 3 to 5 percent over presumed technical variation, occurs during the five-month period. Granting that the observed controls included in this series may be more largely drawn from the southern states in comparison with the northern placebo states, the results, so similar for all three types, would indicate quite a high rate of inapparent infection even though the study areas were selected because of continued high incidence of poliomyelitis. It would point to an accession of approximately 5 percent positives per year for each type. This is not, however, out of keeping with the 50 percent positives among study children.

One of the difficulties encountered is that this group is reduced by various factors so that it may not be truly representative of even the original collection. Moreover, the results are those combined from different areas and from various laboratories with different degrees of consistency in performance. One can speculate as to inferences but firm conclusions are not indicated from the data.

Relation of Titer Changes in Controls to Occurrence of Type-specific Cases in Specific Areas: Attention was then directed to the serological results reported by single laboratories which served specific study areas both for examination of the specimens of serum and for the study of case specimens. In this material inter-laboratory variations are avoided and the alterations encountered in titers among the control segment which was tested could be reviewed in relation to the occurrences of cases from whom poliomyelitis virus was recovered and identified by type or cases identified serologically. Areas of comparatively high prevalence of laboratory-confirmed poliomyelitis were chosen for review. Table 76 presents summaries of observations.

Nassau County, New York, had 15 laboratory-confirmed cases of poliomyelitis in the placebo controls; 14 of them were Type I. Of the paired second and third bloods tested among the controls 17, or 6.1 percent, showed changes in titer from less than 4 to 16 or greater against Type I, while 2.6 and 3.2 percent were reported with similar increases to Types II and III, respectively.

In Utah the dominant virus was Type III. Although only a small number of paired second and third control bloods were tested, it is seen that half of them showed increased titers to Type III, while five showed increases to Type I and only one to Type II.

In Jefferson County, Kentucky, Type III virus was also the dominant virus. Twenty-six percent of the control sera showed changes from less than 4 to 16 or more to Type III, 12 percent to Type II, and 2 percent to Type I.

Harris County, Texas, had 10 Type I, 6 Type III, and 1 Type II cases. The frequency of increases was highest to Type I, 17 percent, but that for Type II was 14 percent, while Type III was 9 percent. In this instance the proportion of Type II conversions was not in line with the frequency of identified cases associated with that type.

In Broward and Palm Beach counties of Florida 5 Type I cases and 1 Type III case occurred in the controls. Here 19 percent of the controls tested changed from less than 4 to 16 or more against Type I, while 5 and 8 percent showed this change to Types II and III, respectively.

In Shelby County, Tennessee, there were 7, 2, and 1 virus-positive cases of Types I, II, and III, respectively. Reported conversions from less than 4 to titers of 16 or greater among the "non-case" controls, however, were greatest for Type III, 27 percent, and least for Type I, 7.5 percent. In St. Joseph County, Indiana, the dominant virus was Type I and conversions for Type I were slightly more frequent than for Types II and III.

Although it is not possible to evaluate the numerical significance of the relationship between values of reported titers and virus typed cases, it seems clear that the frequency with which a specific type of virus was

Table 76

LABORATORY CLASSIFICATION OF REPORTED CASES IN CONTROLS AND CHANGES IN SERUM TITERS OF "NON-CASE" CONTROLS BETWEEN SECOND AND THIRD BLEEDINGS, BY VIRUS TYPE SELECTED STUDY AREAS

Laboratory Classification of Cases for Selected Areas*	Reported Cases in Controls		2nd Serum Titers<4 of "Non-case" Controls						
			Total	16 or > in 3rd Serum		64 or > in 3rd Serum		256 or > in 3rd Serum	
	No.	Rate	No.	No.	%	No.	%	No.	%
Nassau County, New York (Control population - 21,581)									
Type I	14	65	277	17	6.1	12	4.3	8	2.9
Type II	1	5	273	7	2.6	6	2.2	4	1.5
Type III	-	-	277	9	3.2	8	2.9	6	2.2
No Specimen	-	-							
Indeterminate	-	-							
Utah - 8 Counties (Control population - 11,815)									
Type I	1	8	23	5	21.7	5	21.7	4	17.4
Type II	2	17	23	1	4.3	-	-	-	-
Type III	10	85	20	10	50.0	10	50.0	7	35.0
No Specimen	2	17							
Indeterminate	3	25							
Jefferson County, Kentucky (Control population - 21,289)									
Type I	3	14	96	2	2.1	1	1.0	1	1.0
Type II	3	14	106	13	12.3	10	9.4	7	6.6
Type III	17	80	125	33	26.4	30	24.0	21	16.8
No Specimen	1	5							
Indeterminate	11	52							
Harris County, Texas (Control population - 42,771)									
Type I	10	23	125	21	16.8	15	12.0	7	5.6
Type II	1	2	133	19	14.3	12	9.0	8	6.0
Type III	6	14	162	15	9.3	10	6.2	4	2.5
No Specimen	3	7							
Indeterminate	2	5							
Broward and Palm Beach Counties, Florida (Control population - 11,534)									
Type I	5	43	59	11	18.6	8	13.6	4	6.8
Type II	-	-	61	3	4.9	1	1.6	1	1.6
Type III	1	9	72	6	8.3	3	4.2	3	4.2
No Specimen	-	-							
Indeterminate	2	17							

Table 76 Continued

Laboratory Classification of Cases for Selected Areas*	Reported Cases in Controls		2nd Serum Titers <4 of "Non-case" Controls						
			Total	16 or > in 3rd Serum		64 or > in 3rd Serum		256 or > in 3rd Serum	
	No.	Rate	No.	No.	%	No.	%	No.	%
Shelby County, Tennessee (Control population - 23,936)									
Type I	7	29	67	5	7.5	5	7.5	2	3.0
Type II	2	8	70	9	12.9	8	11.4	4	5.7
Type III	1	4	70	19	27.1	17	24.3	11	15.7
No Specimen	1	4							
Indeterminate	5	21							
St. Joseph County, Indiana (Control population - 9,080)									
Type I	10	110	59	13	22.0	12	20.3	7	11.9
Type II	1	11	79	16	20.3	13	16.5	8	10.1
Type III	3	33	58	9	15.5	8	13.8	6	10.3
No Specimen	1	11							
Indeterminate	-	-							

* Typed cases were virus-positive and/or serologically positive or probable.

identified in infection among controls and the frequency with which other members of the group were reported to have distinct changes in titer between June and November, gives support to the interpretation that at least a real proportion of the changes result from infection. The variations from area to area also indicate that the distribution of virus types is not uniform in extent irrespective of their elicitation of clinical manifestations. Rather, the data from these area studies support the concept of limited channels of spread. Jefferson County, Kentucky, was largely affected by Type III virus; Doctors Steigman and Lipton have said that the Type I cases encountered in Louisville had all been visitors in Tennessee, across the river, where Type I virus was the usual one encountered.

Titers of Paired Early and Late Post-vaccination Sera

Tables 77 and 78 contain a total compilation of titers of the third blood specimens (five-months-post-vaccination) in reference to the titers obtained with the second or two-weeks-post-vaccination serum from the same persons. It will be recalled that some of the tests were made with first, second, and third specimens simultaneously; in other instances the first and second were tested at one time and the second and third of a series at another time, hence, for each subject a pre-vaccination titer was also recorded. No matter which procedure was used, the titers presented here are those obtained when the second and third specimens were tested together and a specific endpoint was recorded for both sera. Data from the control subjects can be used to illustrate the intrinsic variations in the laboratory results which appear to be unrelated to vaccination.

Several points of interest stand out in the data of Tables 77 and 78:

Table 77

ANTIBODY LEVELS IN SECOND SERUM BY ANTIBODY LEVELS IN THIRD SERUM
BY VIRUS TYPE AND VACCINATION STATUS
PLACEBO AREAS

Antibody Levels by Virus Type	Vaccinated														Placebo Controls											
	Second Serum Titers		Third Serum Titers												Second Serum Titers		Third Serum Titers									
			<4		4 & 8		16		64		256		1024				<4		4 & 8		16		64		256		1024	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Type I																												
<4	603	18.9	532	88.2	28	4.6	13	2.2	9	1.5	13	2.2	8	1.3	1,742	55.8	1,597	91.7	55	3.2	23	1.3	23	1.3	27	1.5	17	1.0
4 & 8	313	9.8	158	50.5	108	34.5	23	7.3	9	2.9	8	2.6	7	2.2	145	4.6	37	25.5	75	51.7	25	17.2	4	2.8	2	1.4	2	1.4
16	441	13.8	69	15.6	164	37.2	159	36.1	28	6.3	15	3.4	6	1.4	197	6.3	6	3.0	26	13.2	104	52.8	40	20.3	14	7.1	7	3.6
64	457	14.3	11	2.4	60	13.1	176	38.5	163	35.7	33	7.2	14	3.1	330	10.6	3	0.9	7	2.1	39	11.8	197	59.7	71	21.5	13	3.9
256	399	12.5	2	0.5	4	1.0	40	10.0	141	35.3	164	41.1	48	12.0	358	11.5	6	1.7	-	-	10	2.8	79	22.1	194	54.2	69	19.3
1024	982	30.7	4	0.4	3	0.3	11	1.1	35	3.6	198	20.2	731	74.4	348	11.2	2	0.6	1	0.3	2	0.6	18	5.2	77	22.1	248	71.3
Total	3,195	100.0	776	24.3	367	11.5	422	13.2	385	12.1	431	13.5	814	25.5	3,120	100.0	1,651	52.9	164	5.3	203	6.5	361	11.6	385	12.3	356	11.4
Type II																												
<4	241	7.5	190	78.8	21	8.7	12	5.0	4	1.7	8	3.3	6	2.5	1,732	55.5	1,591	91.9	70	4.0	24	1.4	13	0.8	16	0.9	18	1.0
4 & 8	212	6.6	88	41.5	94	44.3	17	8.0	7	3.3	3	1.4	3	1.4	174	5.6	47	27.0	98	56.3	21	12.1	5	2.9	2	1.1	1	0.6
16	493	15.4	34	6.9	199	40.4	208	42.2	36	7.3	8	1.6	8	1.6	174	5.6	9	5.2	21	12.1	108	62.1	27	15.5	6	3.4	3	1.7
64	657	20.6	12	1.8	83	12.6	292	44.4	220	33.5	29	4.4	21	3.2	258	8.3	3	1.2	5	1.9	39	15.1	139	53.9	53	20.5	19	7.4
256	489	15.3	2	0.4	11	2.2	69	14.1	193	39.5	171	35.0	43	8.8	333	10.7	3	0.9	1	0.3	6	1.8	61	18.3	198	59.5	64	19.2
1024	1,103	34.5	2	0.2	1	0.1	10	0.9	46	4.2	205	18.6	839	76.1	449	14.4	4	0.9	-	-	3	0.7	8	1.8	73	16.3	361	80.4
Total	3,195	100.0	328	10.3	409	12.8	608	19.0	506	15.8	424	13.3	920	28.8	3,120	100.0	1,657	53.1	195	6.3	201	6.4	253	8.1	348	11.2	466	14.9
Type III																												
<4	233	7.3	189	81.1	18	7.7	8	3.4	11	4.7	4	1.7	3	1.3	1,894	60.7	1,736	91.7	53	2.8	14	0.7	30	1.6	30	1.6	31	1.6
4 & 8	372	11.6	222	59.7	116	31.2	18	4.8	9	2.4	4	1.1	3	0.8	174	5.6	30	17.2	96	55.2	37	21.3	4	2.3	5	2.9	2	1.1
16	671	21.0	158	23.5	266	39.6	191	28.5	26	3.9	16	2.4	14	2.1	323	10.4	3	0.9	41	12.7	196	60.7	66	20.4	8	2.5	9	2.8
64	546	17.1	43	7.9	155	28.4	200	36.6	112	20.5	23	4.2	13	2.4	335	10.7	7	2.1	6	1.8	59	17.6	192	57.3	60	17.9	11	2.3
256	410	12.8	3	0.7	29	7.1	59	14.4	137	33.4	146	35.6	36	8.8	222	7.1	4	1.8	1	0.5	10	4.5	60	27.0	116	52.3	31	14.0
1024	963	30.1	4	0.4	6	0.6	15	1.6	45	4.7	215	22.3	678	70.4	172	5.5	7	4.1	-	-	5	2.9	15	8.7	43	25.0	102	59.3
Total	3,195	100.0	619	19.4	590	18.5	491	15.4	340	10.6	408	12.8	747	23.4	3,120	100.0	1,787	57.3	197	6.3	321	10.3	367	11.8	262	8.4	186	6.0

Table 78

ANTIBODY LEVELS IN SECOND SERUM BY ANTIBODY LEVELS IN THIRD SERUM
BY VIRUS TYPE AND VACCINATION STATUS
OBSERVED AREAS

Antibody Levels by Virus Type	Vaccinated														Controls											
	Second Serum Titers		Third Serum Titers												Second Serum Titers		Third Serum Titers									
			<4		4 & 8		16		64		256		1024				<4		4 & 8		16		64		256		1024	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Type I																										
<4	669	18.1	597	89.2	23	3.4	17	2.5	12	1.8	10	1.5	10	1.5	2,261	47.4	2,045	90.4	78	3.4	33	1.5	51	2.3	36	1.6	18	0.8
4 & 8	316	8.5	135	42.7	126	39.9	24	7.6	11	3.5	11	3.5	9	2.8	234	4.9	43	18.4	122	52.1	43	18.4	13	5.6	7	3.0	6	2.6
16	452	12.2	42	9.3	164	36.3	182	40.3	39	8.6	12	2.7	13	2.9	436	9.1	13	3.0	31	7.1	262	60.1	91	20.9	26	6.0	13	3.0
64	511	13.8	10	2.0	56	11.0	173	33.9	195	38.2	50	9.8	27	5.3	730	15.3	11	1.5	10	1.4	81	11.1	437	59.9	152	20.8	39	5.3
256	623	16.8	-	-	9	1.4	35	5.6	168	27.0	312	50.1	99	15.9	701	14.7	3	0.4	3	0.4	5	0.7	132	18.8	409	58.3	149	21.3
1024	1,129	30.5	3	0.3	2	0.2	10	0.9	41	3.6	304	26.9	769	68.1	406	8.5	4	1.0	1	0.2	1	0.2	17	4.2	104	25.6	279	68.7
Total	3,700	100.0	787	21.3	380	10.3	441	11.9	466	12.6	699	18.9	927	25.1	4,768	100.0	2,119	44.4	245	5.1	425	8.9	741	15.5	734	15.4	504	10.6
Type II																										
<4	334	9.0	265	79.3	21	6.3	15	4.5	13	3.9	11	3.3	9	2.7	2,385	50.0	2,019	84.7	132	5.5	52	2.2	46	1.9	83	3.5	53	2.2
4 & 8	267	7.2	95	35.6	123	46.1	24	9.0	16	6.0	6	2.2	3	1.1	330	6.9	71	21.5	195	59.1	24	7.3	10	3.0	15	4.5	15	4.5
16	550	14.9	34	6.2	186	33.8	237	43.1	51	9.3	20	3.6	22	4.0	352	7.4	8	2.3	48	13.6	198	56.3	68	19.3	14	4.0	16	4.5
64	693	18.7	4	0.6	69	10.0	285	41.1	263	38.0	56	8.1	16	2.3	522	10.9	7	1.3	8	1.5	69	13.2	293	56.1	102	19.5	43	8.2
256	591	16.0	4	0.7	12	2.0	56	9.5	202	34.2	245	41.5	72	12.2	636	13.3	6	0.9	3	0.5	18	2.8	114	17.9	376	59.1	119	18.7
1024	1,265	34.2	4	0.3	2	0.2	9	0.7	49	3.9	257	20.3	944	74.6	543	11.4	5	0.9	-	-	2	0.4	13	2.4	118	21.7	405	74.6
Total	3,700	100.0	406	11.0	413	11.2	626	16.9	594	16.1	595	16.1	1,066	28.8	4,768	100.0	2,116	44.4	386	8.1	363	7.6	544	11.4	708	14.8	651	13.7
Type III																										
<4	353	9.5	302	85.6	15	4.2	10	2.8	8	2.3	15	4.2	3	0.8	2,505	52.5	2,224	88.8	63	2.5	46	1.8	68	2.7	64	2.6	40	1.6
4 & 8	298	8.0	150	50.7	106	35.8	15	5.1	5	1.7	12	4.1	8	2.7	306	6.4	50	16.3	151	49.3	68	22.2	17	5.6	13	4.2	7	2.3
16	604	16.3	115	19.0	225	37.3	195	32.3	28	4.6	23	3.8	18	3.0	575	12.1	8	1.4	48	8.3	371	64.5	107	18.6	26	4.5	15	2.6
64	629	17.0	44	7.0	129	20.5	232	36.9	148	23.5	38	6.0	38	6.0	686	14.4	4	0.6	11	1.6	101	14.7	431	62.8	106	15.5	33	4.8
256	574	15.5	6	1.0	30	5.2	60	10.5	186	32.4	219	38.2	73	12.7	428	9.0	6	1.4	1	0.2	14	3.3	113	26.4	231	54.0	63	14.7
1024	1,244	33.6	4	0.3	6	0.5	16	1.3	57	4.6	290	23.3	871	70.1	268	5.6	5	1.9	-	-	3	1.1	23	8.6	64	23.9	173	64.6
Total	3,700	100.0	621	16.8	511	13.8	528	14.3	432	11.7	597	16.1	1,011	27.3	4,768	100.0	2,297	48.2	274	5.7	603	12.6	759	15.9	504	10.6	331	6.9

1. The percentage of persons with titers of less than 4 in the second specimen who were reported to have antibody in the third specimen is greater for all types of virus, particularly Type II, among the vaccinated than among the controls as shown by data summarized in the table on the right. Since these persons were reported to have titers of less than 4 in the second specimen, it was assumed that the initial titers were also less than 4 although this was not confirmed in detail.

TITER CHANGES FROM LESS THAN 4 IN SECOND SERUM TO 16 OR GREATER IN THIRD SERUM, EXPRESSED AS PERCENT OF NUMBER LESS THAN 4 IN SECOND SERUM

Poliomyelitis Virus Type	Placebo Areas		Observed Areas	
	Vaccine	Placebo	Vaccine	Controls
Type I	7.1	5.2	7.3	6.1
Type II	12.4	4.1	14.4	9.8
Type III	11.2	5.5	10.2	8.7

Source: Tables 77 and 78.

2. The percentage of subjects with titers of 4 and 8 recorded for the second blood who were then reported to have titers less than 4 in the third specimen is considerably greater in the vaccinated than in the controls, even though the reported decrease in titers to less than 4 among the controls is greater from this level than any other. This trend in the controls may manifest itself because of the technical difficulty in evaluating minimal levels. The excess in diminishing titers at this stage in vaccinated probably reflects the actual declines from low levels acquired after vaccination; it is least with Type II and, surprisingly, greatest with Type III. The excess percentage decline in the vaccinated at the 4 and 8 level by type is closely similar for the children bled in placebo and observed areas:

Poliomyelitis Virus Type	Placebo	Observed
Type I	25.0	24.3
Type II	14.5	14.1
Type III	42.5	34.4

Source: Tables 77 and 78.

3. The higher the titers two weeks after completion of vaccination, the smaller the percentage falling to less than 4 in the late specimen; for example, for Type I in placebo areas 15.6 percent and 2.4 percent of those whose second serum titers were at the levels of 16 and 64, respectively, were reported as less than 4 in the third specimen. The great majority of 1024+ titers remained at 1024+ in the late specimens. The Type II titers appear to be more stable at the low levels of 16 or less; above that, Type I and Type II seem to be equally stable, despite the fact that the response to Type I was less as indicated by the distribution of titers in the second blood. At all levels the decline in Type III titers is the most prominent.

4. Excluding the less than 4 and 1024 titers, it is noted that 49 to 65 percent of the control titers recorded for the third specimens are the same as for the corresponding second specimens. The variation is largely distributed in the next higher or lower dilution so that 86 to 98 percent of the repeats usually fall in that range, similar to the results noted in comparison of the first and second blood control titers. Among the vaccinated, however, there is a consistent deviation from the controls: a smaller percentage of third blood titers maintains the same level as the second, and there is a major shift to the next lower level rather than to either side. This trend is most marked with Type III titers. The behavior of the Type III titers is of interest since that antigen was generally superior to that of Type I and close to that of Type II. One can speculate whether it is evi-

dence of the lesser previous experience of the population with Type III virus or whether the relatively greater decline in low titer Type I antibodies and in Type III antibodies of all levels is a reflection of the heterologous effect from Type II antigen, earlier discussed, which might subside more rapidly.

From these data it can be concluded that, in general, antibody titers tended to fall about 4-fold in the period between two weeks after completion of vaccination and five months thereafter; that the decline was progressively more marked in Types II, I, and III titers; that if levels of 16 to 64 are attained after vaccination the vast majority of subjects of this age will still possess measurable antibody five months later. Finally, it is apparent that the antibody titers in the controls presumably acquired from natural infection have attained a stability much greater than that observed during this interval in titers resulting from vaccination.

Stability of Titers in Persons Without Antibody to Any Type Previous to Vaccination

The preceding tables, 77 and 78, compared the early and late post-vaccination titers without reference to the pre-vaccination status except that the less than 4 titers in the second blood can be presumed to be largely those which were less than 4 before vaccination. They comprised both the triple negatives and negatives to a specific type. A separate compilation was, therefore, made of the antibody levels of those without antibody to any type before vaccination and their relative status in the early and late post-vaccination sera.

It is seen that among placebo controls originally without antibody 5 to 6 percent was reported to have antibody to Types I, II, or III in the second blood, and the same proportion of the negatives in the second blood was reported to have antibody to one or more types in the third blood. Thus, about 10 percent of the original triple negatives among the controls was subsequently reported to have antibody to one or more types of virus. Negative to positive changes between first and second titers of control children are believed to be a result of laboratory variation. The number of controls in the other titer levels is too small for adequate comparisons with the vaccinated, but 7 of the 15 placebo controls reported at levels of 4 or 8 to Type I in the second blood and 5 of 12 with titers of 4 or 8 to Type II were again reported less than 4 in the third specimen. Comparable changes are seen in observed controls.

The numbers of original triple negatives in Tables 79 and 80 are considerably smaller than the totals of negatives to a given type in Tables 77 and 78, but by comparison of the two sets of data some differences can be pointed out.

1. In placebo areas the proportion among the original triple negatives who were vaccinated but remained serologically negative to a given type of virus both two weeks and five months later is considerably greater than when the total among those with original titers of less than 4 to any one type is considered. For Type I it was 44 percent versus 17 percent and for Types II and III, 16 versus 6 percent. It appears that a greater antigenic stimulus is required for the triple negatives than for those negative to only one or two types.
2. The data also demonstrate that titers attained two weeks after vaccination by the triple negatives who responded were predominantly in the 4 to 16 range, 76 percent for Type I, 66 percent for Type III, and 50 percent for Type II. Conversely, the fact that half the Type II responses reached levels of 64 or greater may partly explain the lesser decline in antibody to that type in the five-month period. In Tables 77 and 78, this grouping of post-vaccination titers in the original triple negatives is obscured by combination with other data.
3. The decline in titers between second and third specimens of the vaccinated is more marked among the triple negatives. The percentage of positive titers in the second blood falling to less than 4 in the third blood is greater in the triple negatives; it was 36 percent with Type I, 14 percent with Type

Table 79

SECOND BY THIRD SERUM TITERS OF CHILDREN WITH NO ANTIBODY TO ANY TYPE IN FIRST SERUM, BY VIRUS TYPE AND VACCINATION STATUS
PLACEBO AREAS

Antibody Levels by Virus Type	Vaccinated														Placebo Controls											
	Second Serum Titers		Third Serum Titers												Second Serum Titers		Third Serum Titers									
			<4		4 & 8		16		64		256		1024				<4		4 & 8		16		64		256		1024	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Type I																												
<4	341	48.0	310	90.9	10	2.9	4	1.2	6	1.8	9	2.6	2	0.6	731	94.4	697	95.3	12	1.6	3	0.4	5	0.7	8	1.1	6	0.8
4 & 8	140	19.7	87	62.1	41	29.3	8	5.7	1	0.7	2	1.4	1	0.7	15	1.9	7	46.7	6	40.0	2	13.3	-	-	-	-	-	-
16	141	19.9	39	27.7	61	43.3	34	24.1	2	1.4	1	0.7	4	2.8	3	0.4	1	33.3	1	33.3	1	33.3	-	-	-	-	-	-
64	49	6.9	2	4.1	21	42.9	16	32.7	6	12.2	1	2.0	3	6.1	11	1.4	-	-	1	9.1	1	9.1	7	63.6	2	18.2	-	-
256	20	2.8	1	5.0	3	15.0	6	30.0	3	15.0	5	25.0	2	10.0	7	0.9	-	-	-	-	-	-	2	28.6	4	57.1	1	14.3
1024	19	2.7	2	10.5	1	5.3	-	-	-	-	4	21.1	12	63.2	7	0.9	-	-	-	-	-	-	-	-	2	28.6	5	71.4
Total	710	100.0	441	62.1	137	19.3	68	9.6	18	2.5	22	3.1	24	3.4	774	100.0	705	91.1	20	2.6	7	0.9	14	1.8	16	2.1	12	1.6
Type II																												
<4	135	19.0	112	83.0	9	6.7	6	4.4	2	1.5	5	3.7	1	0.7	730	94.3	696	95.3	18	2.5	5	0.7	3	0.4	2	0.3	6	0.8
4 & 8	91	12.8	45	49.5	36	39.6	6	6.6	2	2.1	-	-	2	2.1	12	1.6	5	41.7	4	33.3	1	8.3	-	-	2	16.7	-	-
16	195	27.5	23	11.8	94	48.2	64	32.8	9	4.6	2	1.0	3	1.5	10	1.3	1	10.0	-	-	7	70.0	1	10.0	1	10.0	-	-
64	190	26.8	10	5.3	52	27.4	85	44.7	33	17.4	3	1.6	7	3.7	7	0.9	1	14.3	-	-	1	14.3	5	71.4	-	-	-	-
256	69	9.7	-	-	5	7.2	28	40.6	19	27.5	11	15.9	6	8.7	5	0.6	-	-	-	-	-	-	-	-	4	80.0	1	20.0
1024	30	4.2	1	3.3	-	-	1	3.3	7	23.3	6	20.0	15	50.0	10	1.3	-	-	-	-	-	-	1	10.0	2	20.0	7	70.0
Total	710	100.0	191	26.9	196	27.6	190	26.8	72	10.1	27	3.8	34	4.8	774	100.0	703	90.8	22	2.8	14	1.8	10	1.3	11	1.4	14	1.8
Type III																												
< 4	136	19.2	112	82.4	10	7.4	6	4.4	7	5.1	-	-	1	0.7	733	94.7	693	94.5	12	1.6	4	0.5	3	0.4	9	1.2	12	1.6
4 & 8	168	23.7	107	63.7	48	28.6	6	3.6	4	2.4	2	1.2	1	0.6	8	1.0	1	12.5	6	75.0	1	12.5	-	-	-	-	-	-
16	208	29.3	90	43.3	75	36.1	30	14.4	7	3.4	2	1.0	4	1.9	10	1.3	1	10.0	3	30.0	3	30.0	3	30.0	-	-	-	-
64	131	18.5	21	16.0	56	42.7	39	29.8	12	9.2	3	2.3	-	-	13	1.7	-	-	1	7.7	2	15.4	7	53.8	2	15.4	1	7.7
256	33	4.6	-	-	11	33.3	12	36.4	8	24.2	-	-	2	6.1	8	1.0	1	12.5	-	-	1	12.5	1	12.5	4	50.0	1	12.5
1024	34	4.8	-	-	2	5.9	3	8.8	8	23.5	4	11.8	17	50.0	2	0.3	-	-	-	-	-	-	-	-	1	50.0	1	50.0
Total	710	100.0	330	46.5	202	28.5	96	13.5	46	6.5	11	1.5	25	3.5	774	100.0	696	89.9	22	2.8	11	1.4	14	1.8	16	2.1	15	1.9

Table 80

SECOND BY THIRD SERUM TITERS OF CHILDREN WITH NO ANTIBODY TO ANY TYPE IN FIRST SERUM, BY VIRUS TYPE AND VACCINATION STATUS
OBSERVED AREAS

Antibody Levels by Virus Type	Vaccinated														Controls											
	Second Serum Titers		Third Serum Titers												Second Serum Titers		Third Serum Titers									
			<4		4 & 8		16		64		256		1024				<4		4 & 8		16		64		256		1024	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Type I																										
<4	311	61.7	292	93.9	5	1.6	1	0.3	3	1.0	6	1.9	4	1.3	755	95.7	693	91.8	18	2.4	12	1.6	12	1.6	14	1.9	6	0.8
4 & 8	104	20.6	61	58.7	30	28.8	5	4.8	2	1.9	2	1.9	4	3.8	13	1.6	7	53.8	5	38.5	1	7.7	-	-	-	-	-	-
16	57	11.3	19	33.3	24	42.1	10	17.5	2	3.5	-	-	2	3.5	7	0.9	2	28.6	-	-	3	42.9	2	28.6	-	-	-	-
64	19	3.8	1	5.3	7	36.8	3	15.8	6	31.6	1	5.3	1	5.3	5	0.6	4	80.0	-	-	-	-	1	20.0	-	-	-	-
256	9	1.8	-	-	2	22.2	2	22.2	-	-	4	44.4	1	11.1	6	0.8	-	-	-	-	-	-	1	16.7	5	83.3	-	-
1024	4	0.8	1	25.0	1	25.0	-	-	1	25.0	-	-	1	25.0	3	0.4	-	-	-	-	-	-	-	-	2	66.7	1	33.3
Total	504	100.0	374	74.2	69	13.7	21	4.2	14	2.8	13	2.6	13	2.6	789	100.0	706	89.5	23	2.9	16	2.0	16	2.0	21	2.7	7	0.9
Type II																										
<4	146	29.0	123	84.2	5	3.4	4	2.7	5	3.4	6	4.1	3	2.1	744	94.3	662	89.0	19	2.6	10	1.3	6	0.8	35	4.7	12	1.6
4 & 8	85	16.9	42	49.4	31	36.5	6	7.1	4	4.7	1	1.2	1	1.2	18	2.3	7	38.9	7	38.9	-	-	-	-	2	11.1	2	11.1
16	150	29.8	19	12.7	70	46.7	40	26.7	10	6.7	5	3.3	6	4.0	7	0.9	2	28.6	1	14.3	4	57.1	-	-	-	-	-	-
64	90	17.9	2	2.2	25	27.8	42	46.7	17	18.9	4	4.4	-	-	12	1.5	2	16.7	-	-	1	8.3	4	33.3	3	25.0	2	16.7
256	27	5.4	-	-	4	14.8	11	40.7	3	11.1	6	22.2	3	11.1	7	0.9	1	14.3	-	-	-	-	-	-	6	85.7	-	-
1024	6	1.2	1	16.7	1	16.7	1	16.7	-	-	1	16.7	2	33.3	1	0.1	-	-	-	-	-	-	-	-	-	-	1	100.0
Total	504	100.0	187	37.1	136	27.0	104	20.6	39	7.7	23	4.6	15	3.0	789	100.0	674	85.4	27	3.4	15	1.9	10	1.3	46	5.8	17	2.2
Type III																										
<4	137	27.2	126	92.0	5	3.6	-	-	1	0.7	4	2.9	1	0.7	740	93.8	681	92.0	12	1.6	5	0.7	12	1.6	17	2.3	13	1.8
4 & 8	95	18.8	58	61.1	28	29.5	2	2.1	-	-	4	4.2	3	3.2	24	3.0	9	37.5	8	33.3	4	16.7	3	12.5	-	-	-	-
16	153	30.4	52	34.0	60	39.2	35	22.9	-	-	3	2.0	3	2.0	12	1.5	2	16.7	-	-	7	58.3	1	8.3	2	16.7	-	-
64	73	14.5	20	27.4	26	35.6	20	27.4	3	4.1	2	2.7	2	2.7	9	1.1	3	33.3	-	-	2	22.2	3	33.3	-	-	1	11.1
256	31	6.2	3	9.7	6	19.4	5	16.1	10	32.3	5	16.1	2	6.5	3	0.4	-	-	-	-	-	-	-	-	2	66.7	1	33.3
1024	15	3.0	1	6.7	1	6.7	3	20.0	-	-	1	6.7	9	60.0	1	0.1	-	-	-	-	-	-	-	-	1	100.0	-	-
Total	504	100.0	260	51.6	126	25.0	65	12.9	14	2.8	19	3.8	20	4.0	789	100.0	695	88.1	20	2.5	18	2.3	19	2.4	22	2.8	15	1.9

II, and 39 percent with Type III. Most of the return-to-negatives came from the groups with titers of 4 to 16 in the second blood; while they were declining, a sizeable proportion of the persons with less than 4 in the second blood was reported positive in the third. It is of interest also that the increase in percentage of negative titers in the vaccinated was observed while the percentage of negatives was decreasing in the controls.

4. In placebo areas the percentage of vaccinated triple negatives with titers of less than 4 in the second blood who remained negatives in the third blood was less than that noted in the controls (Table 79). As previously stated, 5 to 6 percent of the controls was reported to have antibody in the third specimen although reported negative in the second; this may be a measure of the inability of the laboratory procedures to duplicate their results. Among the vaccinated, 9 percent was so reported for Type I, 17 percent for Type II, and 18 percent for Type III.

5. The response two weeks after vaccination of the triple negatives from observed areas, accumulated in Table 80, was generally less than in the segment from placebo areas. Of those who responded, a high proportion congregated at titers of 4 to 16. The differences between second and third titers followed generally the same tendencies noted in placebo areas except that the reported shift from positive to negative in the observed controls is greater, and there is less difference between the vaccinated and controls in this respect.

Because of the desirability of obtaining data concerning the response to vaccines as soon as possible, the laboratories had been asked to proceed promptly with the testing of the sera taken before vaccination and two weeks after vaccination. A number of laboratories were unprepared to carry out a significant amount of testing before the five-months-post-vaccination sera were available. They, therefore, titrated the three specimens of serum at one time. Certain laboratories which had completed tests of their first and second sera included the first sera together with the second in tests necessary for titration of the third specimen.

Antibody Titers Obtained in Simultaneous Tests of First, Second, and Third Bloods

In 10,958 instances, the first, second, and third specimens were titrated at the same time. The titers so obtained should be more comparable than when first and third specimens were tested at different times. There was no selection of sera with respect to vaccination status since that information was not made available to the laboratories. The laboratories which followed this procedure were also unselected.

The results are summarized in Table 81 to show the distribution of titers in the sequential samples of blood. It is seen again that failure to develop measurable antibodies two weeks after the third injection of vaccine was most prominent with Type I antigen while Types II and III failures were essentially the same numerically but greater in observed areas than in the placebo areas. The frequency with which early post-vaccination titers declined to less-than-4 levels by five months is essentially identical with that noted in preceding tabulations made from titrations of the second and third sera alone. The greater decline in Type III titers is again evident. Here, too, it is consistently noted that there is an increased percentage of less-than-4 titers among the vaccinated, while the proportion of less-than-4 titers is decreasing in the controls. Consequently, these data raise the question as to whether the changes in the controls are entirely due to technical variations. The change in percentage of less than 4 is uniformly less between original and seven-week titer than between the seven-week and five-month titers of the same series. It is of further interest that the variation between first and second negative titers in the controls of this series is considerably reduced from that observed in the previous tabulations which combined results with tests of first and second sera alone. The effect may represent improved performance as experience was acquired.

Table 81

PERCENT DISTRIBUTION OF ANTIBODY TITERS IN FIRST, SECOND, AND THIRD SERA TESTED SIMULTANEOUSLY BY VACCINATION STATUS AND VIRUS TYPE PLACEBO AND OBSERVED AREAS

Virus Type by Bleeding	Titers in Vaccinated (%)							Titers in Controls (%)						
	Total Sera*	<4	4 & 8	16	64	256	1024	Total Sera*	<4	4 & 8	16	64	256	1024
Placebo Areas														
Type I														
1st	2,586	55.6	5.2	5.7	10.0	11.6	11.9	2,525	57.0	4.4	6.0	10.1	12.3	10.1
2nd		18.2	10.4	14.2	14.0	12.2	31.1		56.0	4.9	6.3	10.1	11.0	11.7
3rd		24.1	11.8	13.4	12.0	13.0	25.6		53.0	5.3	6.5	11.2	12.2	11.8
Type II														
1st	2,586	54.8	6.9	5.6	9.1	9.4	14.2	2,525	56.4	5.8	5.4	7.8	10.5	14.0
2nd		6.1	6.7	15.6	20.5	16.1	35.1		55.4	5.7	5.3	8.6	10.4	14.6
3rd		9.3	12.6	19.3	16.3	13.5	29.0		53.0	6.3	6.1	8.2	11.0	15.4
Type III														
1st	2,586	59.7	6.7	10.6	9.4	7.3	6.3	2,525	62.7	5.5	9.3	10.1	7.4	5.0
2nd		6.9	11.8	21.9	16.9	12.6	29.9		60.8	5.8	10.1	10.5	7.0	5.7
3rd		19.3	18.0	16.3	10.8	12.2	23.3		57.6	6.4	10.2	11.0	8.4	6.3
Observed Areas														
Type I														
1st	2,468	48.3	5.4	8.9	14.0	14.9	8.5	3,379	48.6	4.7	9.4	14.9	13.9	8.4
2nd		18.8	7.7	12.2	14.1	16.7	30.5		47.1	4.5	9.5	15.2	15.1	8.6
3rd		22.2	9.6	11.9	12.5	19.1	24.8		43.9	4.8	9.5	15.5	15.4	10.8
Type II														
1st	2,468	52.1	7.3	6.4	10.2	12.6	11.3	3,379	52.3	5.8	7.7	11.3	12.5	10.4
2nd		9.3	6.4	16.0	19.0	15.4	33.9		49.6	6.0	7.5	11.9	13.6	11.4
3rd		11.4	10.9	17.5	16.2	15.9	28.1		44.4	7.0	8.0	12.0	15.4	13.2
Type III														
1st	2,468	49.3	8.1	12.0	14.9	10.2	5.5	3,379	52.7	5.6	13.4	14.1	8.7	5.4
2nd		9.5	8.0	17.1	15.1	15.7	34.6		50.6	6.5	12.5	14.8	9.4	6.2
3rd		17.1	12.9	14.5	11.2	16.0	28.3		46.8	5.7	12.8	16.5	10.8	7.4

* Matched sera, tested simultaneously.

Although the data in Table 81 give a view of the distribution of titers and certain major changes, one does not obtain an accurate view of the variation and relative stability within the different titer groups. These details are presented in the cross tabulations, Tables 82 and 83, which show the relations between first, second, and third titers obtained in simultaneous tests of first, second, and third sera of the specific subjects in placebo areas. They provide a perspective of the changes between early and late post-vaccination antibody levels in terms of the original titers. Other tabulations have disclosed the fact that the major recessions in titers after vaccination are most prominent in persons without antibody originally and in those whose early post-vaccination titers were 4 to 16.

The data in Tables 82 and 83 clearly demonstrate that essentially all the decline-to-negative status in the five-months-post-vaccination blood occurred in those without type-specific antibody to start with. The Type III results in placebo areas are most informative (Table 82) because of the good initial response to that antigen and because of the greater decline in the five-month titers of the vaccinated. Of those with no demonstrable antibody to Type III in the first blood, 280 had acquired levels of 4 to 8 in the second; and 171 of the 280, 61 percent, were again recorded as negative in the third. In contrast, of the 1,042 vaccinated who had antibody at some level reported before vaccination, 172 were in the range of 4 to 8 and only 9 of the 172 were reported less than 4 in the third specimen.

Table 82

SECOND BY THIRD SERUM TITERS BY VACCINATION STATUS AND VIRUS TYPE FOR PERSONS WHOSE FIRST SERUM TITERS WERE <4, 4 & 8, AND 16 PLACEBO AREAS*

Antibody Levels	First Serum <4 to Specified Type							First Serum 4 & 8 to Specified Type							First Serum 16 to Specified Type						
	Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers					
		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024
Type I																					
Vaccinated																					
<4	438	392	23	5	4	10	4	9	7	-	2	-	-	-	6	5	1	-	-	-	-
4 & 8	236	125	78	16	8	4	5	23	6	12	2	1	2	-	6	2	1	2	-	-	1
16	295	52	122	99	13	4	5	25	2	7	12	3	1	-	25	2	-	14	6	3	-
64	243	8	41	105	76	7	6	19	-	3	9	5	2	-	30	1	2	8	16	2	1
256	124	2	3	22	59	31	7	32	-	-	3	14	13	2	30	-	-	4	14	10	2
1024	102	2	-	8	16	22	54	26	-	1	1	4	8	12	51	-	-	-	-	13	38
Total	1,438	581	267	255	176	78	81	134	15	23	29	27	26	14	148	10	4	28	36	28	42
Placebo																					
<4	1,329	1,231	34	16	17	21	10	32	22	8	-	-	1	1	6	3	1	1	-	1	-
4 & 8	48	23	19	4	2	-	-	48	8	30	7	-	2	1	22	1	10	10	1	-	-
16	11	1	3	4	1	2	-	19	-	6	8	2	2	1	80	1	8	55	12	3	1
64	16	-	1	1	9	5	-	7	1	1	5	-	-	-	33	-	1	3	25	3	1
256	19	3	-	-	6	8	2	2	-	-	-	1	-	1	9	-	-	2	1	6	-
1024	16	-	-	-	-	3	13	4	-	-	-	-	2	2	2	-	-	-	-	1	1
Total	1,439	1,258	57	25	35	39	25	112	31	45	20	3	7	6	152	5	20	71	39	14	3
Type II																					
Vaccinated																					
<4	148	124	10	7	4	3	-	5	2	2	1	-	-	-	1	-	-	-	-	-	1
4 & 8	147	62	71	7	4	2	1	15	5	3	5	-	1	1	3	-	2	1	-	-	-
16	343	24	144	145	22	4	4	22	1	6	13	2	-	-	20	1	1	13	4	-	1
64	418	9	63	191	133	14	8	46	-	2	20	22	2	-	20	-	2	6	10	2	-
256	225	1	7	47	108	54	8	40	-	1	4	15	16	4	46	-	-	5	20	17	4
1024	135	2	-	6	20	41	66	51	-	-	-	2	18	31	55	-	-	1	2	21	31
Total	1,416	222	295	403	291	118	87	179	8	14	43	41	37	36	145	1	5	26	36	40	37
Placebo																					
<4	1,308	1,216	45	14	11	8	14	43	31	9	2	1	-	-	6	4	1	1	-	-	-
4 & 8	48	25	19	2	1	1	-	73	13	49	7	4	-	-	21	1	13	6	-	-	1
16	19	1	3	12	2	1	-	20	1	4	13	1	1	-	71	2	7	48	11	1	2
64	14	3	-	3	6	1	1	3	-	1	1	-	1	-	26	-	2	10	11	1	2
256	16	1	-	-	4	8	3	4	-	-	-	2	2	-	8	-	-	-	1	4	3
1024	20	2	-	-	-	6	12	4	-	-	-	1	1	2	4	-	-	1	1	-	2
Total	1,425	1,248	67	31	24	25	30	147	45	63	23	9	5	2	136	7	23	66	24	6	10
Type III																					
Vaccinated																					
<4	169	145	12	5	5	1	1	5	2	1	1	-	1	-	2	1	-	-	-	-	1
4 & 8	280	171	86	13	6	1	3	11	3	5	2	1	-	-	8	6	2	-	-	-	-
16	494	122	202	134	17	8	11	35	4	7	20	2	1	1	24	-	5	13	2	2	2
64	365	30	103	148	66	13	5	25	-	3	11	8	1	2	21	-	3	3	13	2	-
256	136	2	15	43	52	20	4	39	-	1	1	19	16	2	66	-	1	5	18	35	7
1024	100	-	4	8	19	21	48	57	-	-	-	3	16	38	154	2	-	4	8	38	102
Total	1,544	470	422	351	165	64	72	172	9	17	35	33	35	43	275	9	11	25	41	77	112
Placebo																					
<4	1,457	1,347	35	7	20	26	22	28	23	3	1	-	-	1	17	14	2	-	1	-	-
4 & 8	42	13	23	5	1	-	-	74	13	45	12	-	3	1	23	-	12	11	-	-	-
16	30	2	9	12	6	1	-	27	-	10	14	2	1	-	147	1	13	107	25	-	1
64	33	4	2	3	17	6	1	5	-	-	2	3	-	-	36	-	1	15	16	4	-
256	16	2	-	1	4	7	2	3	-	-	-	1	2	-	8	-	1	1	3	1	2
1024	4	1	-	-	-	-	3	2	-	-	1	-	-	1	5	-	-	2	2	-	1
Total	1,582	1,369	69	28	48	40	28	139	36	58	30	6	6	3	236	15	29	136	47	5	4

(Continued on next page.)

* First, second, and third specimens tested simultaneously.

Table 82 Continued

SECOND BY THIRD SERUM TITERS BY VACCINATION STATUS AND VIRUS TYPE FOR PERSONS WHOSE FIRST SERUM TITERS WERE 64, 256 AND 1024 PLACEBO AREAS*

Antibody Levels	First Serum 64 to Specified Type							First Serum 256 to Specified Type							First Serum 1024 to Specified Type						
	Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers					
		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024
Type I																					
Vaccinated																					
<4	4	4	-	-	-	-	-	7	6	-	-	-	-	1	6	4	-	1	-	-	1
4 & 8	-	-	-	-	-	-	-	2	-	1	-	-	1	-	1	-	1	-	-	-	-
16	12	-	3	4	1	4	-	4	1	1	1	-	1	-	6	-	3	3	-	-	-
64	51	-	2	13	30	5	1	13	-	-	4	4	3	2	5	1	-	4	-	-	-
256	55	-	1	2	17	28	7	66	-	-	1	8	44	13	9	-	-	-	-	4	5
1024	137	-	-	-	5	49	83	207	1	-	-	4	48	154	281	1	-	2	2	18	258
Total	259	4	6	19	53	86	91	299	8	2	6	16	97	170	308	6	4	10	2	22	264
Placebo																					
4	19	15	-	2	-	1	1	18	17	-	-	1	-	-	10	8	-	1	-	-	1
4 & 8	1	-	-	-	1	-	-	1	-	1	-	-	-	-	3	-	3	-	-	-	-
16	40	2	3	17	12	4	2	6	-	-	2	3	-	1	2	1	-	-	1	-	-
64	127	-	4	14	86	21	2	64	-	-	5	29	25	5	9	1	-	1	4	2	1
256	54	-	-	3	24	20	7	156	-	-	3	29	99	25	39	-	-	-	2	17	20
1024	15	-	-	-	5	2	8	66	-	-	-	5	27	34	192	-	1	1	3	30	157
Total	256	17	7	36	128	48	20	311	17	1	10	67	151	65	255	10	4	3	10	49	179
Type II																					
Vaccinated																					
<4	-	-	-	-	-	-	-	3	2	1	-	-	-	-	-	-	-	-	-	-	-
4 & 8	4	1	2	1	-	-	-	2	1	1	-	-	-	-	1	-	-	1	-	-	-
16	10	3	2	2	2	-	1	4	-	2	2	-	-	-	5	1	2	2	-	-	-
64	28	-	-	7	12	4	5	13	-	1	3	3	3	3	4	1	-	3	-	-	-
256	56	-	-	3	18	30	5	38	1	1	-	6	24	6	11	-	-	1	1	4	5
1024	138	-	-	-	4	43	91	184	-	-	-	2	31	151	345	-	1	1	5	14	324
Total	236	4	4	13	36	77	102	244	4	6	5	11	58	160	366	2	3	8	6	18	329
Placebo																					
<4	8	7	-	-	-	-	1	13	10	-	-	-	3	-	20	17	2	1	-	-	-
4 & 8	2	2	-	-	-	-	-	-	-	-	-	-	-	-	1	-	1	-	-	-	-
16	18	1	1	8	8	-	-	5	-	-	-	2	3	-	2	-	1	1	-	-	-
64	128	-	-	14	84	23	7	39	-	-	3	15	17	4	7	-	-	1	-	4	2
256	38	-	-	3	15	14	6	156	-	-	1	22	105	28	40	-	-	1	1	22	16
1024	4	-	-	-	1	-	3	53	-	-	-	2	18	33	283	1	-	2	1	32	247
Total	198	10	1	25	108	37	17	266	10	-	4	41	146	65	353	18	4	6	2	58	265
Type III																					
Vaccinated																					
<4	2	2	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4 & 8	5	2	2	-	1	-	-	1	1	-	-	-	-	-	1	-	1	-	-	-	-
16	9	2	3	3	-	1	-	1	-	1	-	-	-	-	3	2	1	-	-	-	-
64	19	-	2	2	12	1	2	5	1	2	1	1	-	-	1	-	-	1	-	-	-
256	44	-	-	1	15	23	5	34	-	-	-	8	17	9	7	-	1	2	-	3	1
1024	164	1	1	1	1	54	106	148	1	1	-	1	31	114	151	-	-	-	2	10	139
Total	243	7	8	7	29	79	113	189	3	4	1	10	48	123	163	2	3	3	2	13	140
Placebo																					
<4	18	17	-	1	-	-	-	8	7	-	-	1	-	-	8	6	-	1	-	-	1
4 & 8	6	-	2	3	-	-	1	2	-	-	1	-	1	-	-	-	-	-	-	-	-
16	45	-	1	24	16	1	3	4	-	1	1	1	1	-	3	-	-	1	-	1	1
64	142	1	2	24	85	25	5	46	-	-	3	24	16	3	3	-	-	-	2	1	-
256	36	-	-	2	15	15	4	92	-	-	1	20	58	13	21	-	-	1	4	9	7
1024	8	-	-	-	3	3	2	34	1	-	-	4	10	19	92	2	-	1	3	20	86
Total	255	18	5	54	119	44	15	186	8	1	6	50	86	35	127	8	-	4	9	31	75

Table 83

SECOND BY THIRD SERUM TITERS BY VACCINATION STATUS AND VIRUS TYPE FOR PERSONS WHOSE FIRST SERUM TITERS WERE <4, 4 & 8, AND 16 OBSERVED AREAS*

Antibody Levels	First Serum <4 to Specified Type							First Serum 4 & 8 to Specified Type							First Serum 16 to Specified Type						
	Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers					
		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024
Type I																					
Vaccinated																					
<4	462	424	11	5	6	9	7	1	1	-	-	-	-	-	-	-	-	-	-	-	-
4 & 8	175	84	65	11	6	6	3	10	2	6	1	1	-	-	5	-	3	1	-	1	-
16	240	30	89	94	15	5	7	27	-	9	13	3	2	-	26	-	3	19	3	1	-
64	199	5	35	81	64	9	5	33	-	3	8	16	4	2	57	-	2	19	27	6	3
256	89	-	6	18	39	20	6	29	-	-	1	12	10	6	66	-	1	3	19	37	6
1024	27	-	2	2	6	7	10	34	-	-	2	3	12	17	65	-	-	-	3	28	34
Total	1,192	543	208	211	136	56	38	134	3	18	25	35	28	25	219	-	9	42	52	73	43
Controls																					
<4	1,545	1,409	37	25	33	29	12	33	20	9	-	2	1	1	4	2	2	-	-	-	-
4 & 8	46	20	19	5	1	1	-	75	7	51	9	4	2	2	23	-	11	9	1	1	1
16	19	5	5	7	2	-	-	34	1	8	19	5	1	-	201	2	10	153	25	8	3
64	14	7	1	2	3	-	1	9	-	-	3	4	1	1	70	1	1	26	34	4	4
256	12	1	1	-	2	6	2	1	-	1	-	-	-	-	13	-	-	-	4	7	2
1024	6	1	-	-	1	2	2	8	-	-	-	2	1	5	7	-	1	1	1	1	3
Total	1,642	1,443	63	39	42	38	17	160	28	69	31	17	6	9	318	5	25	189	65	21	13
Type II																					
Vaccinated																					
<4	223	180	11	10	8	8	6	1	1	-	-	-	-	-	-	-	-	-	-	-	-
4 & 8	144	57	62	12	9	3	1	13	2	8	2	1	-	-	2	1	-	1	-	-	-
16	339	27	118	148	25	11	10	39	1	12	19	5	-	2	9	-	2	5	1	-	1
64	351	4	43	164	115	19	6	42	-	1	16	21	4	-	39	-	1	11	22	3	2
256	171	2	7	28	76	49	9	55	-	1	3	23	22	6	28	-	-	-	11	15	2
1024	58	2	1	2	9	30	14	30	-	-	1	4	12	13	81	-	-	1	8	25	47
Total	1,286	272	242	364	242	120	46	180	4	22	41	54	38	21	159	1	3	18	42	43	52
Controls																					
<4	1,615	1,406	56	35	30	61	27	52	30	18	2	-	1	1	4	-	2	-	-	1	1
4 & 8	78	29	34	3	1	8	3	104	12	76	6	4	1	5	18	1	9	3	1	2	2
16	23	4	5	13	1	-	-	28	2	9	14	2	1	-	157	-	14	109	27	4	3
64	27	4	3	3	8	5	4	5	-	-	2	1	2	-	64	-	2	23	27	8	4
256	17	2	-	2	3	9	1	5	-	-	-	2	2	1	9	-	-	1	1	5	2
1024	6	2	-	1	-	-	3	2	-	-	-	-	2	-	9	1	-	1	1	1	5
Total	1,766	1,447	98	57	43	83	38	196	44	103	24	9	9	7	261	2	27	137	57	21	17
Type III																					
Vaccinated																					
<4	230	207	6	4	3	7	3	1	-	1	-	-	-	-	2	-	2	-	-	-	-
4 & 8	178	96	61	6	2	8	5	16	4	9	1	1	-	1	3	-	1	2	-	-	-
16	362	73	138	125	10	8	8	37	3	10	17	4	1	2	16	1	1	7	4	2	1
64	276	31	60	121	38	13	13	26	-	6	9	9	1	1	32	-	1	6	24	1	-
256	117	2	14	32	41	20	8	45	-	1	5	15	21	3	73	-	1	-	29	33	10
1024	53	1	3	5	6	17	21	75	-	2	2	5	24	42	171	-	-	1	12	39	119
Total	1,216	410	282	293	100	73	58	200	7	29	34	34	47	49	297	1	6	16	69	75	130
Controls																					
<4	1,666	1,505	30	28	40	36	27	32	22	5	2	1	2	-	6	-	2	3	1	-	-
4 & 8	60	24	21	7	3	3	2	112	9	77	18	3	3	2	39	1	12	20	2	2	2
16	28	6	1	14	1	4	2	36	-	10	22	3	1	-	291	-	21	204	49	12	5
64	16	4	1	3	6	1	1	7	-	-	4	2	1	-	96	-	5	27	59	4	1
256	5	2	-	-	2	1	-	7	-	-	-	4	3	-	11	-	-	2	5	4	-
1024	6	2	-	-	1	1	2	3	-	-	-	1	-	2	9	1	-	1	3	2	2
Total	1,781	1,543	53	52	53	46	34	197	31	92	46	14	10	4	452	2	40	257	119	24	10

(Continued on next page.)

* First, second, and third specimens tested simultaneously.

Table 83 Continued

SECOND BY THIRD SERUM TITERS BY VACCINATION STATUS AND VIRUS TYPE FOR PERSONS WHOSE FIRST SERUM TITERS WERE 64, 256 AND 1024 OBSERVED AREAS*

Antibody Levels	First Serum 64 to Specified Type							First Serum 256 to Specified Type							First Serum 1024 to Specified Type						
	Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers						Second Serum Titers	Third Serum Titers					
		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024		<4	4 & 8	16	64	256	1024
Type 1																					
Vaccinated																					
<4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4 & 8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	1
16	5	-	-	2	3	-	-	3	-	1	1	-	-	1	1	-	-	-	-	1	-
64	45	-	-	5	26	10	4	12	-	-	-	4	4	4	2	-	-	-	-	1	1
256	109	-	-	4	25	68	12	97	-	-	-	10	65	22	21	-	-	-	3	8	10
1024	186	1	-	3	10	69	103	256	1	-	-	-	70	185	185	-	-	1	4	18	162
Total	345	1	-	14	64	147	119	368	1	1	1	14	139	212	210	-	-	1	7	28	174
Controls																					
<4	4	2	-	-	1	1	-	1	-	-	-	-	1	-	3	2	-	-	-	1	-
4 & 8	6	-	-	2	4	-	-	2	-	-	-	1	1	-	-	-	-	-	-	-	-
16	64	1	1	26	27	6	3	2	-	-	1	-	-	1	2	-	-	-	1	-	1
64	314	-	3	31	210	59	11	103	1	-	1	53	39	9	4	-	-	-	1	1	2
256	98	-	-	1	35	52	10	297	1	1	-	49	193	53	90	-	-	-	6	35	49
1024	17	-	-	-	3	8	6	66	1	-	-	4	27	34	186	1	-	-	4	33	148
Total	503	3	4	60	280	126	30	471	3	1	2	107	261	97	285	3	-	-	12	70	200
Type II																					
Vaccinated																					
<4	2	-	-	1	-	-	1	3	2	-	1	-	-	-	-	-	-	-	-	-	-
4 & 8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16	7	-	2	-	1	2	2	-	-	-	-	-	-	-	1	-	-	-	-	-	1
64	29	-	-	2	19	6	2	7	-	-	-	3	2	2	1	-	-	-	-	1	-
256	68	-	-	2	20	36	10	48	-	-	1	3	32	12	10	1	-	-	1	4	4
1024	145	-	-	2	5	41	97	254	1	-	-	7	46	200	268	-	-	-	4	21	243
Total	251	-	2	7	45	85	112	312	3	-	2	13	80	214	280	1	-	-	5	26	248
Controls																					
<4	3	1	-	-	2	-	-	3	2	-	-	-	1	-	-	-	-	-	-	-	-
4 & 8	-	-	-	-	-	-	-	2	-	1	-	-	1	-	-	-	-	-	-	-	-
16	43	-	4	15	19	3	2	4	-	-	1	2	-	1	-	-	-	-	-	-	-
64	233	1	1	21	159	37	14	67	-	1	3	31	25	7	5	-	-	1	1	2	1
256	88	-	1	2	28	48	9	271	3	-	9	44	178	37	70	-	-	-	3	32	35
1024	15	-	-	-	2	8	5	76	-	-	-	3	32	41	276	1	-	-	3	41	231
Total	382	2	6	38	210	96	30	423	5	2	13	80	237	86	351	1	-	1	7	75	267
Type III																					
Vaccinated																					
<4	2	1	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
4 & 8	1	-	-	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16	5	-	1	1	1	1	1	-	-	-	-	-	-	-	1	-	-	-	-	-	1
64	31	-	-	4	16	10	1	6	1	-	1	-	1	3	2	-	-	-	-	-	2
256	94	1	-	1	28	47	17	49	-	-	-	9	29	11	10	-	-	2	2	3	3
1024	235	1	1	3	8	58	164	197	-	-	-	7	43	147	122	-	-	-	2	8	112
Total	368	3	2	11	53	116	183	252	1	-	1	16	73	161	135	-	-	2	4	11	118
Controls																					
<4	4	2	-	1	-	1	-	2	-	1	-	-	1	-	-	-	-	-	-	-	-
4 & 8	7	-	1	4	1	1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
16	64	-	1	31	27	3	2	3	-	-	2	1	-	-	1	-	-	1	-	-	-
64	304	-	3	27	221	39	14	66	-	2	1	40	17	6	12	-	-	-	3	4	5
256	75	1	-	4	28	34	8	178	3	1	4	31	119	20	40	-	-	1	7	17	15
1024	21	-	-	-	5	8	8	44	-	-	-	2	22	20	128	-	-	1	4	18	105
Total	475	3	5	67	282	86	32	293	3	4	7	74	159	46	181	-	-	3	14	39	125

Among the 1,042, when antibody titer was at a level of 16 or greater early after vaccination, it was subsequently reported to be negative in only 13 instances. The variations encountered in the ranges of less than 4 to 8 in this group may well be technicalities. In fact, among placebo controls who were reported positive at any antibody level in the first blood and negative in the second, 85 percent were also reported negative on the third blood indicating a probable error in reading of the first specimens; they also constitute the bulk of declines noted among controls who had antibody in the first blood. These variations in persons with previously reported antibodies are more numerous among the placebo group than among the vaccinated, indicating that vaccine has moved all but a small minority from these low levels to higher levels and thus has provided a stabilizing effect upon the titers of the group.

The patterns of titer changes to Types I and II are similar to those of Type III, but among persons without antibody originally there appears to be a greater stability of titers to these types after vaccination than to Type III; it is best with Type II. Considering only those reported to be without antibody to a given type in the pre-inoculation sample, the changes in the percentages subsequently reported to be without antibody are seen in Tables 82 and 83. It is again apparent in these results that while the controls tend to be acquiring antibody between second and third bleedings, the vaccinated are regressing with resultant additions to the titer ranks of less than 4.

Because of this shifting out of and in to the the less than 4 category attention was directed to its composition at the time of the third bleedings. For this purpose consideration was limited to those without antibody to the specific type in the first specimen since the majority was known to derive from those groups. For example, among the vaccinated of placebo areas there were 392 who were reported to have negative titers to Type I in all three specimens. There were, in addition, out of 1000 vaccinated persons who had no antibody to Type I originally but exhibited

SECOND AND THIRD SERA LESS THAN 4 AS PERCENT OF TOTAL FIRST SERA LESS THAN 4 TO SPECIFIED TYPE, BY VACCINATION STATUS AND VIRUS TYPE PLACEBO AND OBSERVED AREAS

Poliomyelitis Virus Type	Vaccinated			Controls		
	<4 to Specified Type in 1st Serum			<4 to Specified Type in 1st Serum		
	Total Number	% <4 2nd Serum	% <4 3rd Serum	Total Number	% <4 2nd Serum	% <4 3rd Serum
Placebo Areas						
Type I	1,438	30	40	1,439	92	87
Type II	1,416	10	16	1,425	92	88
Type III	1,544	11	30	1,582	92	87
Observed Areas						
Type I	1,192	39	46	1,642	94	88
Type II	1,286	17	21	1,766	91	82
Type III	1,216	19	34	1,781	94	87

Source: Tables 82 and 83.

STABILITY OF ANTIBODY TITERS

Sources of 3rd Serum Negatives Placebo Areas	Type I		Type II		Type III	
	Number	Percent	Number	Percent	Number	Percent
Vaccinated						
<4 in 1st specimen - Total	1,438	100	1,416	100	1,544	100
<4 in 3rd specimen - Total	581	40	222	16	470	30
<4 in all 3 specimens	392	27	124	9	145	9
<4 in 1st, 4 or > in 2nd, <4 in 3rd	189	13	98	7	325	21
Placebo						
<4 in 1st specimen - Total	1,439	100	1,425	100	1,582	100
<4 in 3rd specimen - Total	1,258	87	1,248	88	1,369	87
<4 in all 3 specimens	1,231	86	1,216	85	1,347	85
<4 in 1st, 4 or > in 2nd, <4 in 3rd	27	2	32	2	22	1

titers of 4 or greater in the second (two-weeks post-vaccination) specimen, 189 who were reported to have returned to negative status in the third specimen.

The relative proportions which each of these components represents of the group less than 4 in the third specimen are shown for vaccinated and placebo controls by virus type in the above summary. In the controls, almost the entire contribution to the group less than 4 in the third specimen came from those reported as less than 4 in all three specimens. In contrast, among the vaccinated whose third titer was negative, 33, 44, and 69 percent of the Type I, II, and III components, respectively, were persons who had shown antibody response in the second serum and subsequently declined. Based on the total persons in the different groups, a gross measure of the stability of acquired antibody, all levels combined, is shown by the percentage declining from positive to negative between the second and third specimens: 7 percent for Type II, 13 percent for Type I, and 21 percent for Type III.

A more suitable measure of stability is presented in the following summary. Only those originally negative who showed an antibody response in the second serum are considered. Here it is seen that the percentages becoming negative again in the third specimen were 8, 19, and 24 for Types II, I, and III, respectively. These data emphasize that the stability of vaccine induced Type I antibody

Stability of Vaccine Induced Antibody - Placebo Areas	Vaccinated			Placebo Controls		
	Type I	Type II	Type III	Type I	Type II	Type III
<4 in 1st, 4 or > in 2nd - Total	1,000	1,268	1,375	110	117	125
<4 in 1st, 4 or > in 2nd, <4 in 3rd						
Number	189	98	325	27	32	22
Percent	19	8	24	25	27	18

Source: Table 82.

was much better than that to Type III if a response had occurred. The response to Type II was the most frequent and the most persistent in this period of observation.

The data from controls are of interest again in pointing out that if antibody was not detected in the first serum but was detected in the second, the great majority of tests, 77 percent, indicated antibody present in the third specimen. Again, error in titration of the first sera must be invoked since in a goodly number of instances the second titers were high, and it seems unlikely that this number of natural infections would have occurred during the period of May 1 to early June. Most of the declines in both vaccinated and controls were in persons with low titers in the second serum.

Stability by Lots as Measured in the Three Simultaneous Tests

The detailed tabulations from which Tables 82 and 83 were prepared also yielded data on first by second by third serum titers for each vaccine lot or lot combination. Tables 84 and 85 present data showing the lot-type response and return-to-negative status among persons who had no type-specific antibody to start with. For Type I the proportion of first-serum-negatives which became second-serum-positives range with different lots from 11 percent to 100 percent; 18 out of 23 lots or lot combinations had 50 percent or more, and 10 of 23 showed 70 percent or greater change from negative in the first serum to positive in the second serum. For Types II and III the proportions which changed from negative to positive status ranged from 21 to 100 percent and 31 to 100 percent, respectively. However, only two lots induced less than 50 percent change to Type II, and only one lot induced less than 50 percent change to Type III. The average change in reported status of control children who were bled was in the range of 6 to 9 percent, again suggesting that range as an indication of technical variation in the laboratory results.

The average regression in titers as reflected by the proportions of vaccinated children who were negative in the beginning, positive in the second serum, and again reported to be negative in the third serum was 8 to 9 percent for Type II, 16 to 19 percent for Type I, and 21 to 24 percent for Type III. This follows the pattern of greatest decline in Type III discussed earlier.

Figures 13, 14, and 15, prepared from Tables 84 and 85, show the relationship between initial response and return-to-negative status among vaccinated children. Each individual lot is plotted and labelled in order that it can be readily compared with other lots.

For Type I the slope of the line of best fit does not differ significantly from zero at the 5 percent level of confidence although a positive correlation coefficient ($r = .374$) was demonstrated between change from negative to positive status and later return to negative status. For Type II (Figure 14) a highly significant negative correlation ($r = -.885$) was shown between the attainment of demonstrable titers and later return to negative status. The grouping of lots at intersections of high response proportions and low decline proportions is quite marked for Type II, and those lots with high return proportions for Type II had low response proportions. This is also true of some of the lots for Type I, particularly Lots 508, 308, and 304. For Type III (Figure 15) a relatively high negative correlation ($r = -.680$) was demonstrated, and the trend was highly significant. The over-all return to negative status was relatively greater for Type III than for either Type I or Type II.

To summarize, in most of the vaccine lots Types II and III antigens were more effective in producing demonstrable antibody than Type I; Type II was more stable than either Type I or III in maintaining demonstrable antibody once attained; to the extent that Type I stimulus was achieved, the regression to negative status was less than that for Type III.

Tables 86 and 87, prepared from the same tabulations as Tables 84 and 85, show the proportions of matched sera which were reported to be less than 4 at each bleeding for each virus type. For most of the lots 100 sera were available for simultaneous testing.

Table 84

FIRST SERA <4 TO SPECIFIED TYPE WITH REPORTED TITERS OF 4 OR > IN SECOND SERUM AND <4 IN THIRD SERUM BY VACCINATION STATUS, VIRUS TYPE, AND VACCINE LOT
PLACEBO AREAS

Vaccine Lot by Virus Type		Vaccinated <4 to Specified Type in 1st Serum and 4 or > in 2nd Serum				Control <4 to Specified Type in 1st Serum and 4 or > in 2nd Serum			
		Total		<4 to Specified Type in 3rd Serum		Total		<4 to Specified Type in 3rd Serum	
Lot	Type	No.	%*	No.	%	No.	%*	No.	%
Total	I	1,000	70	189	19	110	8	27	25
	II	1,268	90	98	8	117	8	32	27
	III	1,375	89	325	24	125	8	22	18
302	I	36	36	8	22	7	6	2	29
	II	50	53	8	16	9	6	6	67
	III	113	91	16	14	12	9	2	17
304	I	111	95	10	9	6	5	-	-
	II	149	97	5	3	10	8	2	20
	III	166	98	24	14	10	8	1	10
306	I	175	84	28	16	15	7	10	67
	II	153	93	16	10	11	6	6	55
	III	197	90	32	16	12	5	5	42
308	I	97	80	4	4	10	8	2	20
	II	103	90	2	2	10	10	1	10
	III	90	80	11	12	13	11	2	15
503	I	5	17	-	-	3	10	3	100
	II	6	21	2	33	3	10	3	100
	III	15	58	3	20	3	9	1	33
505	I	219	69	49	22	15	5	2	13
	II	278	91	34	12	15	5	4	27
	III	276	89	75	27	13	4	1	8
512	I	188	65	41	22	47	14	6	13
	II	283	95	20	7	46	14	7	15
	III	256	88	71	28	51	15	7	14
514	I	169	66	49	29	7	4	2	29
	II	246	95	11	4	13	6	3	23
	III	262	91	93	35	11	5	3	27

* Percent of total <4 to specified type in first serum; all three specimens tested simultaneously.

Table 85

FIRST SERA <4 TO SPECIFIED TYPE WITH REPORTED TITERS OF 4 OR > IN SECOND SERUM AND <4 IN THIRD SERUM BY VACCINATION STATUS, VIRUS TYPE, AND VACCINE LOT
OBSERVED AREAS

Vaccine Lot by Virus Type		Vaccinated <4 to Specified Type in 1st Serum and 4 or > in 2nd Serum				Control <4 to Specified Type in 1st Serum and 4 or > in 2nd Serum			
		Total		<4 to Specified Type in 3rd Serum		Total		<4 to Specified Type in 3rd Serum	
Lot	Type	No.	%*	No.	%	No.	%*	No.	%
Total	I	730	61	119	16	97	6	34	35
	II	1,063	83	92	9	151	9	41	27
	III	986	81	203	21	115	6	38	33
303-303-307	I	6	100	1	17	1	8	-	-
	II	7	100	-	-	-	-	-	-
	III	7	100	1	14	-	-	-	-
303	I	43	84	10	23	8	10	4	50
	II	59	91	2	3	10	10	3	30
	III	46	85	6	13	7	8	3	43
305-305-307	I	72	84	13	18	16	15	5	31
	II	95	96	8	8	20	14	5	25
	III	72	90	16	22	13	10	4	31
305	I	127	72	15	12	16	9	6	38
	II	142	93	11	8	28	15	12	43
	III	162	96	25	15	19	10	8	42
307	I	1	50	-	-	-	-	-	-
	II	2	100	-	-	-	-	-	-
	III	2	67	1	50	-	-	-	-
502-502-307	I	36	46	6	17	5	3	3	60
	II	60	85	12	20	7	4	-	-
	III	72	84	17	24	3	2	1	33
502-502-309	I	29	58	6	21	4	6	2	50
	II	60	86	9	15	3	4	-	-
	III	43	75	14	33	4	5	1	25
506-506-307	I	112	66	29	26	14	5	4	29
	II	188	94	5	3	28	9	10	36
	III	162	90	27	17	20	7	2	10
506-506-309	I	22	92	3	14	-	-	-	-
	II	21	100	-	-	-	-	-	-
	III	20	95	2	10	-	-	-	-

* Percent of total <4 to specified type in first serum; all three specimens tested simultaneously.

Table 85 Continued

Lot	Type	No.	%*	No.	%	No.	%*	No.	%
506	I	82	57	11	13	7	3	3	43
	II	131	96	15	11	14	6	2	14
	III	127	98	22	17	11	4	6	55
507-507-307	I	30	48	6	20	1	2	1	100
	II	56	89	5	9	2	4	-	-
	III	62	91	17	27	4	8	2	50
507-507-309	I	29	52	5	17	4	6	1	25
	II	52	71	8	15	2	3	1	50
	III	27	50	12	44	3	4	-	-
507	I	14	11	2	14	3	2	-	-
	II	46	26	14	30	11	5	2	18
	III	48	31	20	42	7	3	2	29
508-508-309	I	72	91	11	15	1	1	-	-
	II	75	99	1	1	7	8	3	43
	III	80	93	11	14	9	9	6	67
508	I	55	72	1	2	17	19	5	29
	II	69	92	2	3	19	21	3	16
	III	56	86	12	21	15	14	3	20

Data on placebo controls and uninoculated controls again provide a measure of technical variation in the laboratory procedure. Such variation was considerably reduced by the procedure of simultaneous testing of all three sera, thus giving support to the view that most of the change depicted in the vaccinated is real. From data presented earlier, the variation between first and second serum titers in the control group has ranged from 6 to 9 percent which may be compared with the range of 1 to 3 percent variation in total results shown in Tables 86 and 87.

For all placebo area lots the response to initial stimulus as measured by the reduction in proportions without demonstrable antibody was approximately the same for Types II and III, 89 percent and 88 percent, respectively. There was a 67 percent reduction in the number without demonstrable antibody to Type I virus. For observed areas the percentage reduction in the proportion without demonstrable antibody was 82 percent, 81 percent, and 61 percent for Types II, III, and I, respectively. The individual lots showed considerable variation but the pattern of higher initial response to Types II and III observed earlier was well maintained, and the least proportionate return to negative status in the third sera among those who were positive in the second sera was demonstrated for Types II, I, and III, in that order.

Antibody Levels One Year Later and Response to "Booster" Vaccine

Additional data relating to the stability and duration of vaccine induced antibodies were provided in a follow-up study of 128 Michigan children who participated in the 1954 Field Trial and were given booster vaccine one year later. Each of the selected children received a complete series of three inoculations of vaccine during the 1954 Field Trial, and each of them was included in the pre- and post-vaccination bleedings: a first pre-vaccination blood, a two-weeks-post-vaccination blood, and a third blood five months post-vaccination.

Table 86

PERCENT DISTRIBUTION <4 TO SPECIFIED TYPE IN FIRST, SECOND, AND THIRD SERA TESTED SIMULTANEOUSLY, BY LOT AND VACCINATION STATUS
PLACEBO AREAS

Vaccine Lot by Bleeding		Vaccinated				Placebo			
		Total Sera	% <4 to Specified Type			Total Sera	% <4 to Specified Type		
Lot	Bleeding		I	II	III		I	II	III
All Lots	1st	2,586	55.6	54.8	59.7	2,525	57.0	56.4	62.7
	2nd		18.2	6.1	6.9		56.0	55.4	60.8
	3rd		24.1	9.3	19.3		53.0	53.0	57.6
302	1st	219	45.2	42.9	56.6	246	45.9	57.7	54.9
	2nd		28.8	21.0	5.5		45.9	58.1	51.6
	3rd		31.1	23.7	11.4		40.7	54.1	41.9
304	1st	262	44.7	58.8	64.9	208	52.9	58.2	57.2
	2nd		2.7	1.9	1.9		52.9	58.2	56.7
	3rd		5.7	3.1	11.1		47.1	54.8	51.4
306	1st	363	57.3	45.2	60.6	365	62.2	51.5	67.1
	2nd		11.3	3.3	7.2		61.4	51.2	65.8
	3rd		19.0	8.0	17.4		61.4	49.6	63.3
308	1st	224	54.5	50.9	50.0	209	61.2	48.8	56.5
	2nd		12.1	5.4	9.8		56.5	45.0	51.2
	3rd		10.3	3.6	10.7		51.7	41.1	48.8
503	1st	63	46.0	46.0	41.3	72	41.7	40.3	47.2
	2nd		38.1	38.1	17.5		37.5	36.1	44.4
	3rd		38.1	38.1	20.6		43.1	41.7	43.1
505	1st	559	56.9	54.4	55.6	541	58.6	56.7	63.4
	2nd		18.4	5.0	6.4		58.0	56.0	62.7
	3rd		25.9	10.9	20.4		55.3	52.9	60.1
512	1st	469	61.8	63.8	62.3	507	64.7	64.5	68.0
	2nd		25.4	3.8	8.3		64.1	64.1	66.3
	3rd		31.3	8.1	24.3		59.8	62.7	65.1
514	1st	427	59.7	60.4	67.7	377	49.3	55.4	64.5
	2nd		20.1	2.8	6.3		48.0	52.8	62.9
	3rd		31.1	4.9	27.6		46.4	51.5	59.7

Table 87

PERCENT DISTRIBUTION <4 TO SPECIFIED TYPE IN FIRST, SECOND, AND THIRD SERA TESTED SIMULTANEOUSLY, BY LOT AND VACCINATION STATUS
OBSERVED AREAS

Vaccine Lot by Bleeding		Vaccinated				Control			
		Total	% <4 to Specified Type			Total	% <4 to Specified Type		
Lot	Bleeding	Sera	I	II	III	Sera	I	II	III
All Lots	1st	2,468	48.3	52.1	49.3	3,379	48.6	52.3	52.7
	2nd		18.8	9.3	9.5		47.1	49.6	50.6
	3rd		22.2	11.4	17.1		43.9	44.4	46.8
303-303-307	1st	19	31.6	36.8	36.8	36	33.3	33.3	47.2
	2nd		-	-	-		30.6	36.1	47.2
	3rd		5.3	-	5.3		30.6	33.3	47.2
303	1st	115	44.3	56.5	47.0	173	46.8	56.1	50.3
	2nd		7.0	5.2	7.0		43.9	52.0	48.0
	3rd		14.8	6.1	12.2		41.6	46.2	48.0
305-305-307	1st	178	48.3	55.6	44.9	241	45.2	59.3	51.5
	2nd		7.9	3.4	5.6		42.3	53.5	49.0
	3rd		13.5	6.2	13.5		36.1	41.9	45.2
305	1st	373	47.2	41.0	45.0	463	39.7	41.5	42.5
	2nd		13.1	2.9	1.6		38.7	38.2	39.1
	3rd		15.8	5.4	8.3		35.2	36.1	35.6
307	1st	6	33.3	33.3	50.0	11	63.6	45.5	54.5
	2nd		16.7	-	33.3		63.6	45.5	54.5
	3rd		16.7	-	33.3		63.6	27.3	54.5
502-502-307	1st	127	62.2	55.9	67.7	263	71.5	66.2	67.7
	2nd		33.9	8.7	11.0		70.0	63.5	66.9
	3rd		38.6	15.7	24.4		69.2	55.1	63.1
502-502-309	1st	127	39.4	55.1	44.9	174	38.5	40.8	44.3
	2nd		16.5	7.9	11.0		36.2	40.8	43.1
	3rd		18.1	12.6	22.0		34.5	36.2	38.5
506-506-307	1st	335	50.4	60.0	53.7	520	51.0	59.2	58.5
	2nd		17.0	3.9	5.4		49.0	55.8	55.8
	3rd		24.5	4.8	12.2		47.1	51.9	50.4
506-506-309	1st	39	61.5	53.8	53.8	7	85.7	71.4	71.4
	2nd		5.1	-	2.6		100.0	71.4	71.4
	3rd		10.3	-	5.1		71.4	57.1	71.4

(Continued on next page.)

Table 87 Continued

Vaccine Lot by Bleeding		Vaccinated				Control			
		Total	%<4 to Specified Type			Total	%<4 to Specified Type		
Lot	Bleeding	Sera	I	II	II	Sera	I	II	III
506	1st	309	46.6	44.0	42.1	512	50.0	46.3	49.8
	2nd		20.4	1.6	1.3		50.2	45.1	48.8
	3rd		23.6	6.5	8.4		46.9	42.4	45.9
507-507-307	1st	110	57.3	57.3	61.8	83	57.8	57.8	60.2
	2nd		30.0	7.3	5.5		56.6	55.4	55.4
	3rd		30.9	10.0	21.8		53.0	49.4	53.0
507-507-309	1st	127	44.1	57.5	42.5	127	48.8	60.6	54.3
	2nd		21.3	16.5	21.3		46.5	60.6	54.3
	3rd		23.6	18.1	30.7		42.5	49.6	48.8
507	1st	265	49.4	65.7	59.2	346	52.0	62.4	59.5
	2nd		44.2	49.4	41.5		51.7	60.4	58.7
	3rd		43.0	48.3	46.4		48.0	52.9	53.8
508-508-309	1st	160	49.4	47.5	53.8	190	46.8	47.9	53.2
	2nd		4.4	0.6	3.8		48.4	47.4	50.5
	3rd		11.3	1.3	10.0		45.3	45.3	49.5
508	1st	178	42.7	42.1	36.5	233	37.8	38.6	45.1
	2nd		11.8	3.4	5.1		30.9	33.0	40.8
	3rd		10.7	3.9	11.2		27.0	28.3	34.8

By arrangement with Dr. Gordon C. Brown a fourth blood was drawn just prior to, and a fifth blood was drawn two weeks subsequent to the administration of a single "booster shot" of vaccine in May, 1955. Of the original 128 in this study, complete data on simultaneous tests done in one laboratory on all five bleedings were obtained for 100 children.[8]

Table 88 compares two-weeks-post-vaccination titers with titers ten or more months later (approximately one year after the first inoculation of vaccine).

The reductions in titer, in agreement with the total data compiled five months after vaccination, occurred particularly among those persons with titers of 16 or less two weeks after the third inoculation. The reduction to less than 4 among those persons with second blood titers of 4 or greater was 6 out of 90 for Type I, 4 out of 92 for Type II, and 12 out of 91 for Type III.

Table 89 presents pre-booster titers by post-booster titers for the same 100 children. The response to booster stimulus among these children is quite emphatic. All but one of 14 who were less than 4 to Type I in the pre-booster serum had titers of 4 or greater in the post-booster serum but 6 of them behaved like initial responders; 11 out of 11 and 20 out of 20 responded to Types II and III, respectively, most of them to high levels.

Further study was made of 19 children reported to have no antibody to any virus type prior to the initial vaccination. These 19 were among the 100 children included in Tables 88 and 89. Table 90 presents titer readings at each bleeding for these 19 children. Initial response to Type I was shown for 15 of the 19 children; 16 out of 19 responded initially to Types II and III. At the fourth, or pre-booster

Table 88

TWO-WEEKS POST-VACCINATION TITERS BY ONE-YEAR POST-VACCINATION TITERS BY VIRUS TYPE - 100 SELECTED CHILDREN IN THREE MICHIGAN STUDY AREAS*

Antibody Levels by Virus Type	2 Weeks Post-vaccination Titers	1 Year (approximately) Post-vaccination Titers					
		<4	4 & 8	16	64	256	1024
Type I							
<4	10	8	1	1	-	-	-
4 & 8	5	2	3	-	-	-	-
16	15	2	8	3	1	1	-
64	15	2	4	4	4	1	-
256	13	-	-	-	6	5	2
1024	42	-	-	1	4	14	23
Total	100	14	16	9	15	21	25
Type II							
<4	8	7	-	-	-	1	-
4 & 8	5	2	2	-	1	-	-
16	16	2	6	5	2	1	-
64	28	-	3	14	6	2	3
256	17	-	2	3	9	2	1
1024	26	-	-	-	5	9	12
Total	100	11	13	22	23	15	16
Type III							
<4	9	8	-	1	-	-	-
4 & 8	8	5	3	-	-	-	-
16	20	5	9	4	1	1	-
64	24	2	7	6	6	3	-
256	11	-	-	1	5	5	-
1024	28	-	-	-	3	17	8
Total	100	20	19	12	15	26	8

* All children received complete series of three inoculations of vaccine during the 1954 Field Trial and were in the contingent of children selected for bleedings. All five samples of blood were tested simultaneously.

Table 89

PRE-BOOSTER TITERS BY POST-BOOSTER TITERS BY VIRUS TYPE - 100 SELECTED STUDY CHILDREN IN THREE MICHIGAN STUDY AREAS*

Antibody Levels by Virus Type	Pre-booster Titers	Post-booster Titers					
		<4	4 & 8	16	64	256	1024
Type I							
<4	14	1	5	1	-	-	7
4 & 8	16	-	-	-	2	2	12
16	9	-	-	-	-	2	7
64	15	-	-	-	2	1	12
256	21	-	-	-	-	8	13
1024	25	-	-	-	-	2	23
Total	100	1	5	1	4	15	74
Type II							
<4	11	-	-	4	1	3	3
4 & 8	13	-	-	-	2	3	8
16	22	-	-	-	-	10	12
64	23	-	-	-	2	4	17
256	15	-	-	-	-	6	9
1024	16	-	-	1	-	1	14
Total	100	-	-	5	5	27	63
Type III							
<4	20	-	1	1	9	7	2
4 & 8	19	-	-	2	7	9	1
16	12	-	-	-	2	3	7
64	15	-	-	1	4	5	5
256	26	-	1	-	-	14	11
1024	8	-	-	-	-	1	7
Total	100	-	2	4	22	39	33

* All children received complete series of three inoculations of vaccine during the 1954 Field Trial and were in the contingent of children selected for bleedings. All five samples of blood were tested simultaneously.

Table 90

SECOND, THIRD, FOURTH, AND FIFTH SERUM TITERS OF 19 MICHIGAN CHILDREN WITH NO ANTIBODY TO ANY TYPE PRIOR TO VACCINATION*

Identification Number	Type I				Type II				Type III			
	2nd Blood	3rd Blood	4th Blood	5th Blood	2nd Blood	3rd Blood	4th Blood	5th Blood	2nd Blood	3rd Blood	4th Blood	5th Blood
1	64	T	<4	16	64	64	<4	64	64	1024	8	64
2	16	16	<4	16	64	1024	4	64	64	256	<4	16
3	<4	<4	4	64	<4	<4	<4	8	<4	<4	<4	64
4	16	<4	T	1024	64	16	T	1024	64	<4	T	256
5	8	T	<4	1024	16	T	4	1024	16	T	<4	64
6	8	T	T	1024	16	T	T	1024	16	T	T	64
7	<4	<4	<4	1024	16	<4	<4	1024	4	<4	<4	64
8	8	4	T	1024	16	16	16	1024	16	8	16	256
9	16	<4	<4	1024	256	16	8	1024	64	64	8	256
10	16	T	8	1024	64	64	16	256	16	T	<4	256
11	64	<4	<4	1024	64	8	8	1024	64	<4	<4	64
12	16	16	256	1024	256	64	64	1024	64	16	64	1024
13	16	<4	<4	1024	16	8	4	256	64	8	<4	64
14	14	8	<4	1024	256	16	8	1024	64	8	8	256
15	64	16	8	1024	64	64	16	256	64	256	64	256
16	<4	T	<4	4	<4	T	<4	64	<4	T	<4	16
17	16	4	8	1024	64	8	16	1024	16	<4	4	256
18	16	16	8	1024	64	16	64	1024	8	8	4	64
19	<4	<4	<4	T	<4	<4	<4	16	<4	<4	<4	1024

T = Toxic.

* All 19 children received complete series of three inoculations of vaccine during the 1954 Field Trial. First, second, and third bloods were drawn routinely during the Field Trial. Fourth and fifth bloods were drawn approximately one year after the 1954 vaccine clinics began, the fourth just prior to and the fifth two weeks subsequent to the administration of a single "booster shot" of vaccine in the spring of 1955. All five specimens of blood were tested simultaneously.

bleeding, 10, 5, and 9 children were reported as less than 4 to Types I, II, and III, respectively. A booster response to each type of virus was demonstrated in the fifth sera of all 19 children. Most of them attained levels of 64 or greater, and a surprising proportion reached the level of 1024 or greater. Subjects 3 and 19 showed no initial response to any type but did respond to the booster stimulus, suggesting that they may have been sensitized by the initial vaccine even though no demonstrable antibodies were present.

Data from this study, though limited in scope and extendability, show that the administration of vaccine approximately one year after the initial vaccine stimulus provided a substantial booster effect on the antibody levels of these 100 children.

Figure 13

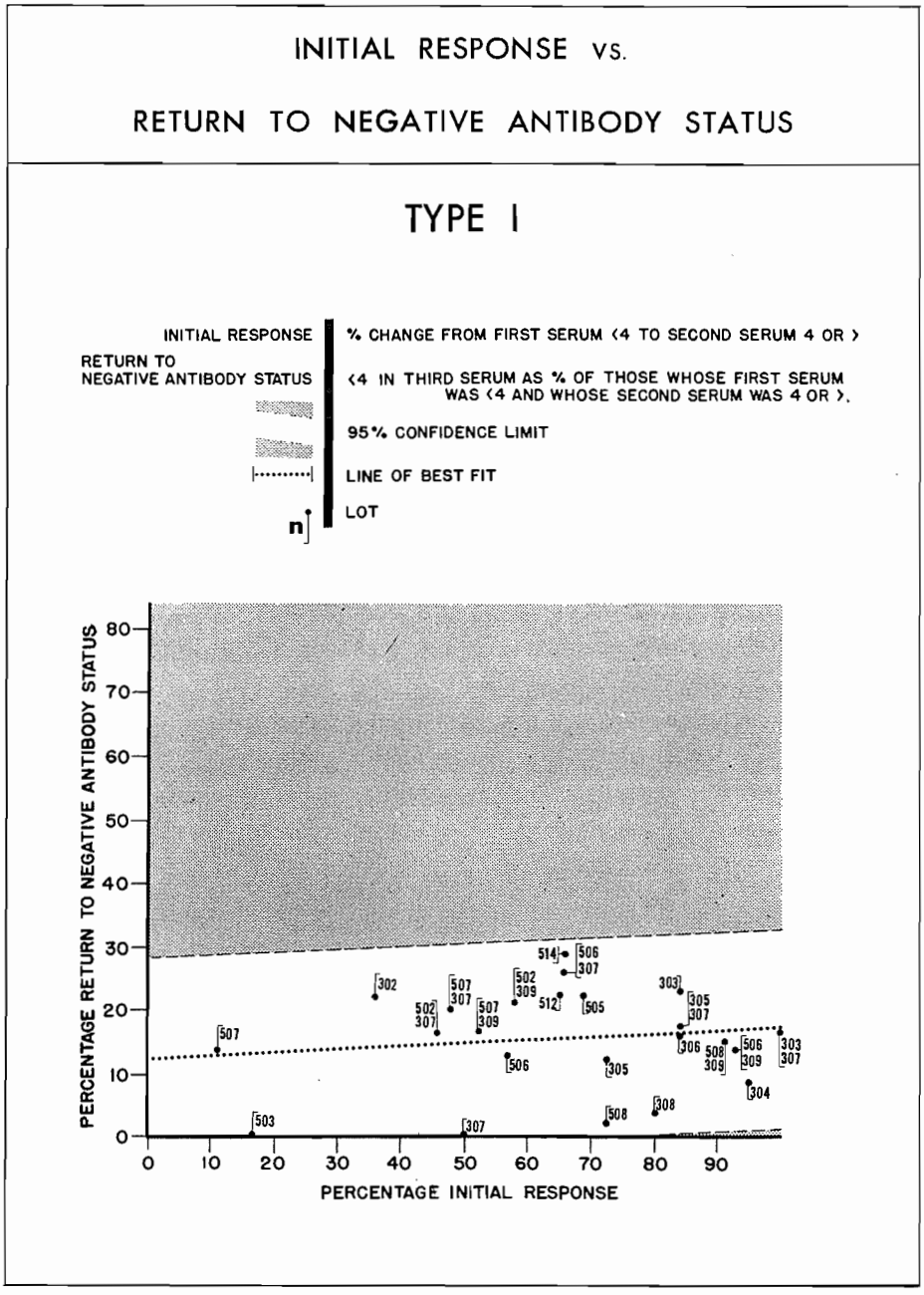

INITIAL RESPONSE vs.
RETURN TO NEGATIVE ANTIBODY STATUS
TYPE I
INITIAL RESPONSE
% CHANGE FROM FIRST SERUM <4 TO SECOND SERUM 4 OR >
RETURN TO NEGATIVE ANTIBODY STATUS
<4 IN THIRD SERUM AS % OF THOSE WHOSE FIRST SERUM WAS <4 AND WHOSE SECOND SERUM WAS 4 OR >.
95% CONFIDENCE LIMIT
LINE OF BEST FIT
n
LOT
PERCENTAGE RETURN TO NEGATIVE ANTIBODY STATUS
PERCENTAGE INITIAL RESPONSE
0
10
20
30
40
50
60
70
80
90

Figure 14

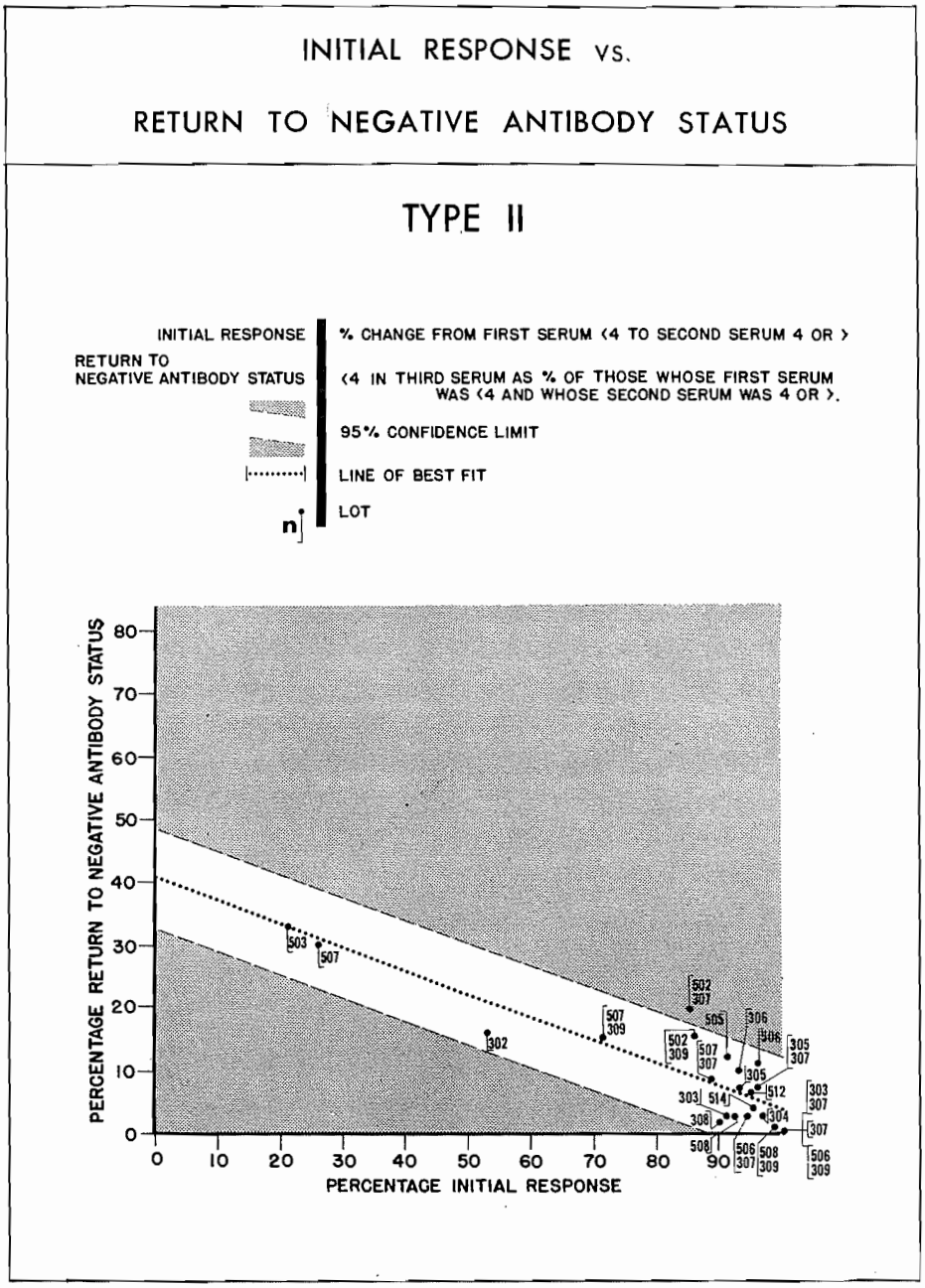
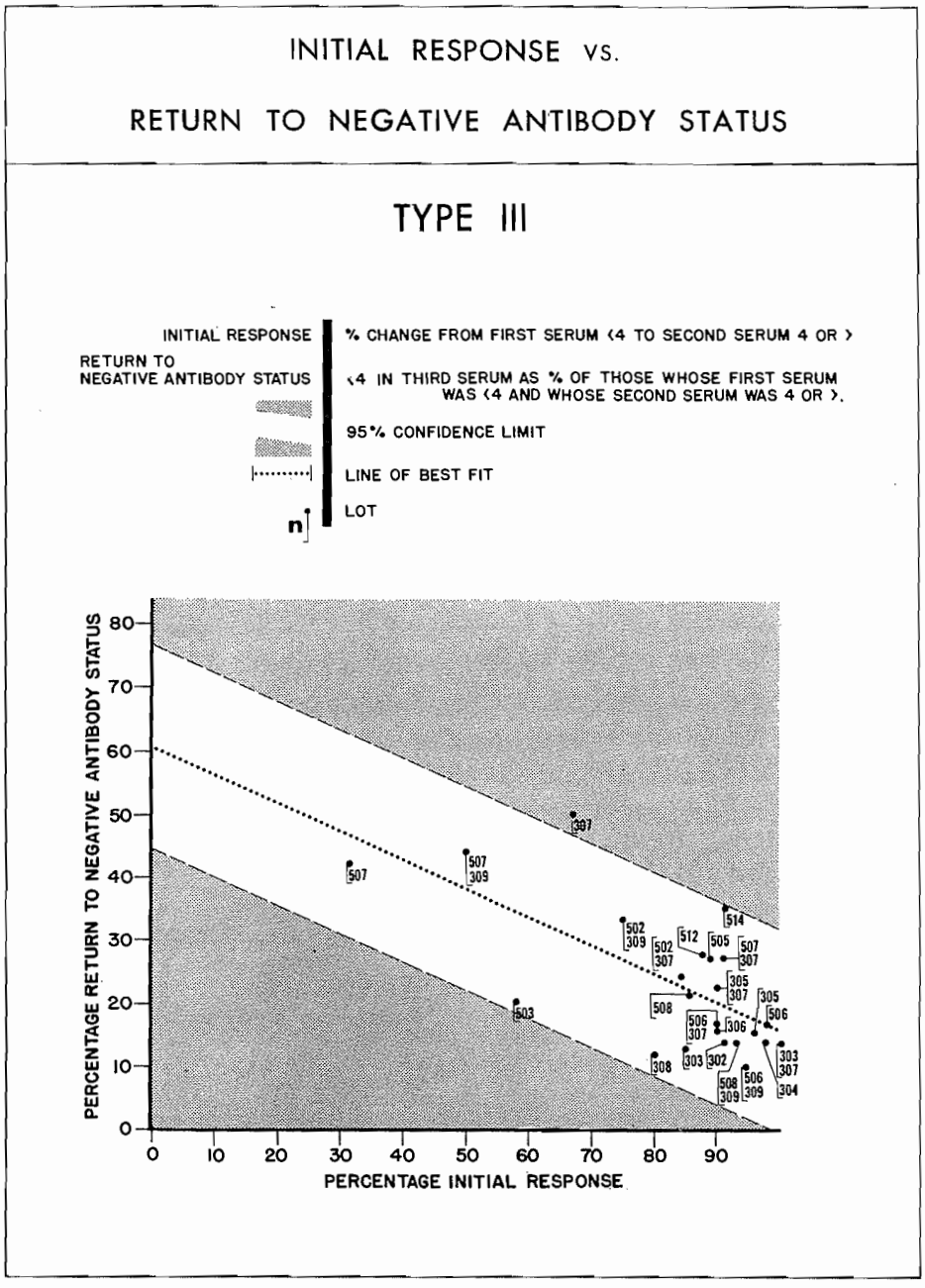

INITIAL RESPONSE vs.
RETURN TO NEGATIVE ANTIBODY STATUS
TYPE II
INITIAL RESPONSE
% CHANGE FROM FIRST SERUM <4 TO SECOND SERUM 4 OR >
RETURN TO NEGATIVE ANTIBODY STATUS
<4 IN THIRD SERUM AS % OF THOSE WHOSE FIRST SERUM WAS <4 AND WHOSE SECOND SERUM WAS 4 OR >.
95% CONFIDENCE LIMIT
LINE OF BEST FIT
n
LOT
PERCENTAGE RETURN TO NEGATIVE ANTIBODY STATUS
PERCENTAGE INITIAL RESPONSE
0
10
20
30
40
50
60
70
80
90
302
303
307
502 307
507 309
505
306
502 309
507 307
305 307
305
303 514
512
303 307
308
304
307
508
506 307
508 309
506 309

Figure 15


INITIAL RESPONSE VS.
RETURN TO NEGATIVE ANTIBODY STATUS
TYPE III
INITIAL RESPONSE
% CHANGE FROM FIRST SERUM <4 TO SECOND SERUM 4 OR >
RETURN TO NEGATIVE ANTIBODY STATUS
<4 IN THIRD SERUM AS % OF THOSE WHOSE FIRST SERUM WAS <4 AND WHOSE SECOND SERUM WAS 4 OR >.
95% CONFIDENCE LIMIT
LINE OF BEST FIT
n
LOT
PERCENTAGE RETURN TO NEGATIVE ANTIBODY STATUS
PERCENTAGE INITIAL RESPONSE
0
10
20
30
40
50
60
70
80
90
397
507
507 309
514
502 309
502 307
512
505
507 307
305 307
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