Observations on Natural Poliovirus Infections in Immunized Children

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Others than epidemiologists and laboratory researchers in this special field will be helped perhaps by a reminder at the very beginning that this study is concerned with evidences of alimentary tract infections, not with cases of frank or paralytic poliomyelitis. The findings are of immediate moment to all who are concerned with the control of this highly communicable disease.

Poliovirus infection in the immune host is a subject of great current interest. The significance of natural postinfection immunity with respect to the occurrence of disease is hardly open to question in view of the relative sparing of the older and usually immune age groups and the abundant evidence of the effect of immunity induced by experimental infections in animals.[1] Similarly, there is reason to believe that protection from disease may result from passive immunity as induced by inoculation of gamma globulin in both man[2] and animal[3] or as represented by maternally derived antibody in the newborn infant. Finally, the 1954 field trials[4] and the very considerable subsequent experience[5] with the Salk vaccine indicate very clearly that active immunity induced with formalin-killed poliovirus vaccine affords significant although not complete protection against paralytic disease.

However, protection against disease and protection against infection are not necessarily synonymous. In the case of poliomyelitis human infection involves primarily the alimentary tract with serious involvement of the central nervous system (CNS) a secondary and relatively unusual phenomenon.[6,7] In the final analysis polioviruses depend on alimentary infections and not upon CNS infections for their perpetuation in man, the two essentials being: (1) existing sources of infection in the form of intestinally infected persons discharging reasonably abundant virus in their feces; and (2) an adequate number of potential new sources of virus dissemination in the form of persons whose alimentary tracts are still fully susceptible to infection. Hence, although it may obviate the serious consequences of infection, specific immunity will not influence the spread of virus within the human population unless it also influences the occurrence or course of alimentary infections.

The available evidence of the influence of immunity on enteric infections is incomplete. Bodian,[3] working with animals, and Brown and co-workers,[8] studying household associates of patients with clinical poliomyelitis, have shown that passive immunity resulting from the administration of gamma globulin apparently does not influence the occur-

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rence or course of alimentary tract infection. Our own studies of the process of natural immunization [9-11] provide several instances of apparently unmodified alimentary infection in infants in the face of the demonstrated persistence of passive immunity of maternal origin. Similar instances in which infection was induced by attenuated strains of poliovirus have been reported by Koprowski and associates.[12]

Conversely, active immunity derived from previous homotypic infection appears to influence alimentary infection materially. In individuals with such immunity both experimental oral challenge and challenge resulting from natural intrahousehold exposure result either in no demonstrated infection or in infection associated with relatively brief periods of virus excretion in the feces. This has been demonstrated experimentally in chimpanzees challenged with unmodified virus [13, 14] and in man challenged with attenuated virus.[15, 16] Although less thoroughly documented, the same phenomenon has been observed to occur under natural conditions among previously immune persons in households experiencing episodes of infection of sufficient intensity to involve nearly all the nonimmune household members.[9, 11]

The situation with respect to active immunity derived from killed-virus vaccine is less clearly defined. In chimpanzees intensively immunized with formalin-killed vaccine of monkey-cord origin Howe [17] observed that oral challenge resulted in alimentary infection of reduced frequency, duration, and titer of fecal virus. Fragmentary data also are available as to infections after immunization with Salk vaccine. The fairly numerous instances reported of infection associated with disease after vaccination are of little help since there is no certainty in most cases that the individual actually had responded to the vaccine. By the examination of sera collected some 10 months after vaccination Salk [18] has detected marked rises in antibody titer which provide convincing evidence that infection had occurred in 27 children known to have responded to the vaccine, but the fact of alimentary infection could not be established. Lipson, Robbins, and Woods [19] have reported that infection manifested by fecal excretion of virus was found in 13 of 25 vaccinated children and in 21 of 31 unvaccinated children of similar age who were familial contacts of poliomyelitis patients. Finally, Sabin [16] has reported recently on eight volunteers given two doses of Salk vaccine and challenged by oral administration of attenuated Type 1 poliovirus. Frequency and duration of virus excretion in this group were no different from that observed in a parallel group of 11 nonimmune volunteers. Further data obviously are necessary to determine with certainty the influence of immunity induced by killed-virus vaccine upon both the occurrence and the course of natural infections of the alimentary tract.

Efforts to accumulate such data were initiated in January, 1956, when a primary course of immunization with commercially produced Salk vaccine (two inoculations one month apart) was administered to all incompletely immune members of 118 southern Louisiana households which, since 1953, had been under continuous observation in our study of the process of natural immunization. This paper constitutes a preliminary report based on information collected as to serologic response to two inoculations of vaccine and as to the occurrence of poliovirus infections in these households during the first seven months after the second dose of vaccine.

Over-All Plan and Methods

The nature and composition of the study group and the general methods of observation in both the field and the

laboratory are described elsewhere in some detail.[9, 10] Briefly, 157 households, each containing a newborn index child and chosen to be representative with respect to race, economic status, and family size were recruited in 1953 in nearly equal numbers from three study areas in southern Louisiana: urban New Orleans, urban Baton Rouge, and four semirural parishes designated as the Evangeline area. These households were followed routinely at monthly intervals with collection of interval information concerning the entire household and blood and stool specimens from the original index child and, in numerous instances, from subsequently born siblings. As infection of the index child was detected, special visits were made to collect added information and blood and stool specimens from all household and indicated extrahousehold contacts. This phase of the study was terminated in January, 1956, when commercially produced Salk vaccine (all of a single lot) was offered to all incompletely immune members of the 136 households still under observation.

The study was then reoriented to emphasize detection of alimentary infection in the vaccinated group. The new plan called for collection of stool specimens twice monthly from all children under age 15 rather than once monthly from the index children only, and for blood specimens from all household members in relation to vaccination, i.e., just before and one month after each inoculation, and at semiannual intervals thereafter. Periodic visits to the households were continued as were special visits with extra collections of blood specimens on the occasion of detected infection in a household. The primary course of vaccine, consisting of 1 ml given subcutaneously in January and again in February, was administered to all children six months of age or older, and to some adults, who were not naturally immune to all three types of poliovirus. As younger infants have reached the age of six months they also have been vaccinated. A third booster inoculation of vaccine was scheduled for December, 1956. This reorientation of the study with the associated increase in collection of stools resulted in the withdrawal of 18 families, leaving a starting group of 118 households, all of which remained under observation through August of 1956.

The laboratory methods have remained unchanged. All efforts to isolate virus from feces and to measure the presence of neutralizing antibody in the sera have utilized tube tissue cultures containing primary monolayer outgrowths of epithelial cells derived from trypsinized kidney tissues of healthy monkeys as described elsewhere.[10] It should be pointed out, however, that insufficient time has elapsed in many instances to permit the careful reexamination, heretofore carried out, of particularly important stool specimens from which virus was not isolated in the routine examination. As this is done in the future, some increase in the number of virus isolations may be expected.

Serologic Response to Vaccination

Some 300 children in the study were lacking in immunity to one or more types of poliovirus and received a primary course of Salk vaccine. Only the sera collected just before and one month after vaccination were examined. Tests for rise in titer of those types of neutralizing antibody present prior to vaccination have not been completed, but those done have revealed the commonly observed booster effect. Chief present interest is in the development of those types of antibody which were lacking, the data for which are presented in Table 1 by titer of type-specific antibody after vaccination and the qualitative status of prevaccination seroimmunity. These data, incidentally, are

Table 1—Relation of de novo Appearance of Type-Specific Antibody One Month after a Primary Course of Two Inoculations of Salk Vaccine to Seroimmune Status Prior to Vaccination

Prevaccination Immunity to Poliovirus	No. of Persons	Per cent with Postvaccination Titers of 1:x Against Virus														
		Type 1					Type 2					Type 3				
		0	2–5	10–20	40–80	160+	0	2–5	10–20	40–80	160+	0	2–5	10–20	40–80	160+
None	118	* 36	30	28	5	1	26 **	21	41	* 10	2	* 60 **	23	13	* 3	2
Type 1	27	.. **	..	..	..	..	15	4	33	26	22	19 **	26	37	15	4
Type 2	31	10 *	10	39	26	16	.. ***	..	..	.. *	..	29	39	16	6	10
Type 3	44	11	30	45	14	0	9	18	41	23	9	.. *	..	..	.. *	..
Types 1 and 2	36	.. *	..	..	..	..	..	..	..	..	..	8	31	50	6	6
Types 2 and 3	22	9	23	36	23	9	..	..	..	.. *	..	..	..	..	..	..
Types 1 and 3	26	..	..	..	..	..	0	19	42	27	12	..	..	..	..	..

* Indicates one child whose heel-puncture specimen was negative in 1:10 dilution and could not be tested in lower dilution; or one serum with antibody present through a 1:40 dilution but not yet tested in higher dilution.

based on observation of cytopathic effects rather than of phenol red color changes, a matter which will be discussed later.

Two points stand out after study of the table. First, on an over-all basis without reference to prior immunity the three antigenic components of the vaccine were not equally effective; the Type 2 component was the most antigenic while Type 3 was much the least. Second, the de novo response to each antigen was clearly greater in persons possessing one or more heterologous types of antibody prior to vaccination than in those who were totally devoid of antibody to polioviruses. Response to Types 1 and 2 antigen was enhanced almost equally by the prior presence of either or both heterologous types of antibody. In the case of Type 3 antigen, however, prior Type 1 antibody appears to have exerted a greater influence than did Type 2 antibody. Complement-fixation studies are not reported here in detail, but it may be stated that, in general, vaccination stimulated clear-cut CF response chiefly to those virus types for which antibody existed prior to vaccination.

Episodes of Household Infection

In the seven months following vaccination, February through August, 38 episodes involving one or more instances of primary infection occurred in 34 of the 118 households under observation, four households experiencing two episodes each. All but two followed the second inoculation of vaccine by one month or more. Two additional episodes occurred in which a single previously immune child was reinfected but no nonimmune persons became primarily infected. Thus, there was a total of 40 household episodes. The occurrence of all 40 episodes with respect to month, study area, and virus type is indicated in Table 2. The three study areas were unequally involved with respect to both total episodes and distribution of infections by virus type. The Evangeline area experienced by far the most with 25 episodes while New Orleans, with only six, had the fewest. Type 1 virus predominated in the Evangeline area with Type 3 not appearing until June. Type 2 virus was found only in Baton Rouge where it shared the lead with

Type 3. In New Orleans there were no episodes until June and, of the six detected, four were with Type 3 virus. Over-all, the year began with a continuation of the Type 1 infections which had predominated in 1955, but in the period June through August, Type 3 infections increased sharply. Comparison of the over-all total of 38 episodes involving primary infections among 118 households during only seven months of 1956 with the total of 52 episodes among about 140 households in 12 months of 1955 [10] suggests that vaccination did not act to reduce the frequency of household infections.

Information relating to virus spread within the 38 households with primary infections is summarized in Table 3. These 38 episodes involved 129 exposures of children under 15 years of age from whom stool specimens were collected routinely twice monthly and 79 exposures of older persons from whom only single stool specimens were collected when infection was recognized in a younger household member. It should be stressed that the data presented in Table 3 are preliminary in that many pertinent stools found negative on routine examination have not yet been reexamined. Even with this limitation it is evident that most individuals who were not naturally homologously immune prior to vaccination became infected when virus was introduced into the household. Of 86 children and seven adults in this category, only nine children and four adults escaped infection. Possible reasons for these escapes, aside from limited exposure because of age (four adults and two very young infants), include absence from the home during the episode in one instance and possible interference between two types of poliovirus in another episode. Also,

Table 2—Distribution of Episodes of Household Infections with Poliovirus in 1956 by Virus Type, Month, and Study Area

Study Area	Virus Type	No. of Household Infections in Month Indicated							
		Feb.	Mar.	Apr.	May	June	July	Aug.	Total
Evangeline	1	2	1	2	4	3	3	4	19
	2								0
	3					1	4	1	6
	All	2	1	2	4	4	7	5	25
Baton Rouge	1		1						1
	2			1	1	2			4
	3			1		2	1		4
	All		1	2	1	4	1		9
New Orleans	1					1		1	2
	2								0
	3					2		2	4
	All					3		3	6
All areas	1	2	2	2	4	4	3	5	22
	2			1	1	2			4
	3			1		5	5	3	14
	All	2	2	4	5	11	8	8	40

it should be stated that two of the episodes, involving four escaping children, did not result in the infection of the original index child. By the methods used prior to 1956 these would not have been detected until examination of the annual sera. In the previous 30 months of study, 10 such abortive episodes were recognized and in these many nonimmunes other than the index child also escaped infection.[11] The relation of infection to detected serologic response to vaccination is not shown in the table. Actually, among 29 children who did not respond to vaccination with antibody homologous to the infecting virus type or (in three cases) who were not vaccinated, two escapes occurred while, of 54 who did respond, seven escaped. The difference is obviously not significant. Hence, the over-all impression seems justified that vaccination did not reduce the susceptibility of children to alimentary tract infection following intrahousehold exposure.

It also is evident from Table 3 that intrahousehold exposure again resulted in reinfection of persons already naturally immune. Assuming a greater than fourfold rise in antibody titer as indicative of reinfection and combining the available information as to serologic response and virus isolation, it can be seen that 11 of the 43 naturally immune children (about 26 per cent) became reinfected as did five (about 7 per cent) of the 72 adults. Although these proportions of reinfections are somewhat lower than those observed (37 and 12 per cent, respectively) in the 1953–1955 period prior to vaccination, they suggest two ideas of interest. First, infection among the vaccinated but not naturally immune children apparently constituted nearly as effective exposure for the immune members of the households as did previous episodes involving unvaccinated children. And second, the 11 reinfections of children occurred in spite of the presumed reinforcement of

Table 3—Virus Excretion and Serologic Response to Infection Among Members of Households Undergoing Episodes of Poliovirus Infection

Age Group (Years)	Homologous Prevaccination Immunity	Serologic Response to Infection Episode	No. of Persons	
			Total	Excreting Virus *
Under 15	None	None	11	2
		Rise †	75	72
	Positive	None	35	3
		Rise	8	6
15 and over	None	None	(4) ‡	0
		Rise	(3)	1
	Positive	None	67(43)	0
		Rise	5(3)	2

* For persons under 15 years of age data as to excretion of virus are based on examination of stool specimens collected routinely twice a month; for persons 15 and over, they are based on examination of the single specimen collected as soon as possible after infection had been recognized in a younger person.

† Rise means either de novo appearance of antibody or a greater than fourfold increase over the level observed in the nearest preceding specimen. In the case of vaccinated individuals the reference serum was that collected one month after the second inoculation of vaccine.

‡ Figures in parentheses indicate the number of persons from whom the single stool specimen obtained was collected within one month from the date of collection of the first specimen indicating the presence of infection in the household.

Table 4—The Duration of Fecal Excretion of Virus by Children Infected Following Vaccination

Homologous Seroimmunity Prior to Vaccination	Homologous Serologic Response to Vaccine	Number of Children Excreting Virus	Days Duration of Virus Excretion		
			Observed		Estimated True Mean
			Range	Mean	
No	Yes	45	1–79	21.6	36.6
	No	28	1–63	24.4	39.4
	Total *	73	1–79	22.7	37.7
Yes	Not tested	11	1–29	3.4	..

* One infected child who had not been vaccinated has not been included.

their natural immunity resulting from vaccination.

The data as to virus excretion among the adults, both those experiencing primary infection and those being reinfected, are of relatively little significance since only single stool specimens were examined. The data for the children, however, whose stools were examined twice monthly as a matter of routine, are of considerable interest. It is evident from Table 3 that all except three children known to be undergoing primary infection were found to be excreting virus on at least one occasion as were nine children who were experiencing reinfection. Data as to duration of virus excretion in these children are summarized in Table 4. Of 13 children undergoing reinfection (including two from the atypical episodes and not included in the table) virus was recovered from only two on more than one occasion, whereas many of the children experiencing primary infection were found to be shedding virus on two or more occasions. Interestingly, the duration of virus excretion was the same whether or not homologous serologic response to vaccination had been detected. Taking the group with primary infection as a whole, the observed range was one to 79 days with a mean of 22.7 days and, based on an average interval of 15 days between specimens, the estimated true mean period of viral excretion was 37.7 days. In 1953–1955 among unvaccinated children undergoing primary infection the observed range was one to 114 days with a mean of 24 days, which figures are rather close to those mentioned above. However, because of the longer average interval between specimens, the estimated true mean period of virus excretion was 51 days. Nonetheless, in view of the lack of relation between duration of excretion and detected response to vaccine, it seems unlikely that vaccination materially influenced the duration of virus excretion.

Table 5—Infectivity Titers of Representative Stool Specimens Collected from Unvaccinated and Vaccinated Children Undergoing Primary Infection with Polioviruses

Vaccination Prior to Infection *	No. of Specimens Tested †	Log Titer ‡	
		Range	Median
No	15	$<$2.0–6.5	5.0
Yes	15	3.5–6.5	5.5

* Infections in persons not vaccinated occurred in 1955; those in vaccinated children were in 1956.

† Each specimen chosen was the first specimen found to contain virus from an individual undergoing a known episode of infection.

‡ Log titer expresses TCD_{50} of virus per gram of stool estimated by testing serial tenfold dilutions, two culture tubes per dilution.

A final question may be asked concerning the amount of virus excreted. Infectivity titrations were carried out on representative stools collected in 1955 from unvaccinated index children experiencing primary infections and on stools collected in 1956 from children experiencing primary infection after a primary course of vaccination. The data, as summarized in Table 5, fail to indicate that vaccination exerted any influence on the quantity of virus excreted in the feces.

Discussion

The data on serologic response to the currently recommended two-inoculation primary course of Salk vaccine require some comment. While much more extensive information undoubtedly exists, the present observations appear to constitute the first published data on the response of man to vaccine released since the more rigorous procedures of inactivation and safety testing were instituted in June of 1955. As such, they may seem relatively disappointing since a considerable proportion of those vaccinated apparently failed to respond serologically, especially to Type 3 antigen. However, it should be emphasized that our method for detecting neutralizing antibody depends on direct microscopic observation of inhibition of viral cytopathic effect. Sabin [16] has recently suggested that antibody formed early in the response to vaccine and to infection may be of lesser avidity than that developing subsequently and he has demonstrated that such antibody of presumed low avidity is detected much more readily by the metabolic inhibition test [20] than by the cytopathogenic test which we employed. Thus, it is very possible that the course of vaccine elicited a true response in a much greater proportion of instances than we were able to detect. It must be remembered further that we have tested but a single lot of vaccine and also that the picture may be considerably brightened by the administration in December of the third or booster inoculation.

Of somewhat more academic interest is the additional clear evidence of antigenic relationship between all three types of poliovirus provided by analysis of the serologic responses with respect to the types of preexisting antibody which were present. In general our observations parallel very closely similar observations reported by Salk and co-workers,[18, 21] in which prior experience with one or two types of poliovirus antigen materially enhanced the response to the type for which no antibody was present prevaccination. The major peculiarity in our results is that prior Type 1 antibody appeared to exert a greater influence upon Type 3 response than did prior Type 2 antibody. Using the method of complement-fixation, Melnick [22] has obtained very convincing evidence for a closer relation between Types 2 and 3 than between Types 1 and 3 viral antigens.

Some comment may be made regarding the two atypical episodes of household infection, in each of which a single previously immune child was reinfected. First, these instances provide some slight measure of the risk of reinfection as the result of extrahousehold exposure. In so far as reinfections detected because of viral excretion are concerned intrahousehold rather than extrahousehold sources of infection were implicated much more frequently. Second, the reinfected children did not appear to constitute very efficient sources of infection for others in the same households. Not only did the one nonimmune child exposed, a five-month-old infant, escape infection, but also a total of 11 previously immune household members (seven children under nine years of age and four adults) escaped reinfection.

Of greatest interest, of course, is the evidence bearing on the possible influ-

ence of vaccination upon the occurrence and course of alimentary infections with polioviruses. Evaluation of these observations obviously is facilitated by the existence of base line observations of similar nature made in the same group of households during the 30-month period preceding vaccination. Certain limitations to direct comparison, of course, are imposed by the fact that the "reference" observations were not made coincidentally with the "experimental" observations, by the inescapable aging of the individuals under study and by the increasing immunity of the group as a whole with time. It is felt, however, that the possible influence of aging and increasing group immunity are counteracted to some extent by the continual and considerable increase in the group due to births and that the disadvantages associated with noncoincidental periods of observation are largely offset by the near identity of important environmental factors resulting from reuse of the same study group.

Comparison of the 1956 observations as to infections in the study group with those made in the 30-month period prior to vaccination [9, 11] permits some rather firm conclusions in spite of the fact that the 1956 data are incomplete in many respects. First, household episodes involving instances of primary infection actually were relatively more frequent in 1956 than in 1955 (46 per 100 household months in 1956 versus 31 per 100 household months in 1955). Second, intrahousehold spread of infection to persons vaccinated but not naturally homologously immune was essentially as extensive as that to completely nonimmune household members observed in the prevaccination period. Third, failure to become infected upon intrahousehold exposure was not significantly related to failure of homologous serologic response to the vaccine as detectable by our serologic method. Fourth, as judged by the frequency of reinfections, vaccinated children undergoing primary infection afforded nearly as effective sources for challenge of the naturally immune members of the households as did the primarily infected but unvaccinated children previously. Fifth, the excretion of fecal virus during primary infection in vaccinated children, in terms of frequency of demonstration, observed duration, and level of stool infectivity, did not differ materially from that previously observed in unvaccinated children.

The differences in estimated true mean duration of virus excretion (37.7 days after vaccination and 51 days before) are of uncertain significance. Factors of possible importance in addition to vaccination include variations in the properties of the strains of infecting virus and such host-related variables as age and prior infections with heterotypic polioviruses. Analysis of the data with respect to age revealed no correlation at all. Analysis with respect to prior experience with heterotypic viruses yielded contradictory results: in 1955 observed excretion among 37 immunologically inexperienced index children averaged 16 days, whereas, among 20 with prior heterotypic experience, the average was 28 days; in 1956 the positions were reversed with 37 inexperienced but vaccinated children averaging 27 days observed excretion as compared with 17 days for 35 children with prior experience. In any event, vaccination itself is not believed to have been a factor since virus excretion within the vaccinated group did not differ as between those who did and those who did not manifest homologous response to the vaccine, again as detectable by the cytopathic method which we employed. All told, therefore, it does not appear that primary vaccination demonstrably influenced either the occurrence or course of alimentary infections.

Some may argue that this lack of influence is to be attributed to the rela-

tively poor quality of the lot of vaccine employed. To them we may answer that homologous antibody of presumably high avidity and resulting from vaccination was present in more than two-thirds of the infected children and that the presence or absence of such antibody could be related neither to escape from infection nor to fecal excretion of virus. Others, accepting these observations, may predict nonetheless that the immunity resulting from the booster inoculum will exert a suppressive effect on alimentary infections. During 1957 we hope to provide a definitive answer to this question. Meanwhile, however, we are inclined to predict that, in spite of the anticipated booster effect of the third inoculum, vaccine-induced immunity again will be found to exert no great influence on alimentary infection. The basis for this, in large part, is the observation herein reported that reinforcement of natural immunity by vaccine failed to reduce greatly the frequency of alimentary reinfection following intrahousehold exposure.

Obvious implications of the findings predicted above, if substantiated, are that widespread use of killed-virus vaccine will not interfere seriously with virus spread through the population and that, as a corollary, in many situations the process of natural immunization can be relied upon to reinforce and maintain immunity initiated artificially by such vaccine. Rather clearly, there is little justification for the hope that the phenomenon of gradual elimination of the viral agent, which has occurred in the case of smallpox, will be repeated for polioviruses with extended use of Salk vaccine.

Finally, there are certain theoretic questions as to the nature of the relative immunity of the alimentary tract which clearly follows actual infection. As judged from the continuing susceptibility of the alimentary tract in the presence of circulating antibody of passive origin [3, 8] or as actively induced by killed-virus vaccine, the immunity observed following infection must be to some extent local in nature and in any case dependent upon actual prior infection of the alimentary sites of primary virus localization. In some ways, the situation seems analogous to the local immunity of mice and monkeys recovered from intracerebral infection with 17D yellow fever virus.[23] Such animals resisted intracerebral challenge with neurotropic yellow fever virus which was lethal for animals possessing much higher titers of circulating antibody as the result of immunization by extraneural routes. In the case of the mice it was possible to show that animals recovered from cerebral infection had much higher titers of antibody in the cerebral tissue than did those hyperimmunized by intraperitoneal inoculations. Morgan [24] has reported rather similar observations with polioviruses in neurally infected and extraneurally vaccinated monkeys, emphasizing the critical importance for resistance to CNS challenge of adequate levels of CNS antibody. In the present instance of local resistance of the alimentary tract, however, it is a little harder to conceive of an explanation based on relatively high local concentration of antibody in the tissues. Perhaps some cellular mechanism is operating which involves those cells serving as the primary sites of virus multiplication, possibly anamnestic in the immunologic sense, or possibly dependent on residual latent viral infection.

Summary

Some 300 incompletely immune members of 118 Louisiana households were given a two-inoculation primary course of Salk vaccine. The serologic response at one month after the second inoculation has been determined by measuring the ability of the sera to inhibit the

cytopathic effect of polioviruses. Overall, the three components of the vaccine were not equally antigenic, the Type 3 component being the least so. The de novo response to a particular type of antigen was enhanced materially by the preexistence of heterotypic antibody.

In the first seven months following vaccination, child members of these households were closely observed for alimentary infections, a total of 40 household episodes having been detected. These 1956 observations (made after vaccination) on the frequency of household episodes of infection, the extent of intrahousehold spread of virus, and the frequency, duration, and amount of virus excretion in the feces have been compared with similar observations made in the same study group in the period prior to vaccination. This comparison has led to the conclusion that two doses of Salk vaccine did not materially influence the frequency or duration of alimentary infection or the amount of virus excreted in the feces.

The prediction is made that a third booster inoculation also will fail to influence enteric infection and that, as a corollary, extended use of killed-virus vaccines will not result in the gradual elimination of polioviruses from vaccinated areas.

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