Does immunization against polio with a killed virus create an immune barrier to virus spread? A study of household infections (1953–1957) produced data which indicate that in persons without natural immunity vaccination did not affect alimentary infection.

THE INFLUENCE OF NATURAL AND ARTIFICIALLY INDUCED IMMUNITY ON ALIMENTARY INFECTIONS WITH POLIOVIRUSES

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I T IS commonly recognized that immunity to an infecting agent may range in degree from absolute resistance to infection down to minimal modification of its morbid consequences. For the individual, distinction between absolute and relative resistance is not of importance provided that the infection permitted shall not result in disease. For the group, the distinction is of practical importance only if the immune but infected individual is capable of serving as a link in the chain of continued dissemination of the agent or if the maintenance of immunity in the individual, and hence, in the herd, depends upon natural restimulation by infection.

Our present interest is in immunity to poliomyelitis. From the characteristic age distribution of clinically evident infections, it appears that immunity initiated by natural infection during childhood ordinarily protects adults from disease. Serosurveys of isolated populations, such as those of certain Alaskan Eskimo communities,[1] afford proof that in many persons seroimmunity may persist indefinitely after infection. However, such studies leave unanswered questions as to the actual proportion of infections that are followed by long persisting immunity, whether or not reinfections are important at all to the maintenance of both individual and herd immunity, and, if reinfections occur, whether the reinfected individual can play a significant role in virus dissemination. Obviously, rather similar questions relate to immunity which is induced artificially. Major interest centers in the possibility that artificially induced immunity, resulting from either killed-virus vaccine or infection with live avirulent strains, may not only prevent disease but also either prevent or so modify alimentary infection that the immune individual can play no effective role in virus transmission. If such were the case, it is clear that extensive but partial immunization of the population might create a significant barrier to virus spread and so afford a measure of protection to those not vaccinated.

Some have suggested that the greatly reduced occurrence of paralytic poliomyelitis in the United States in 1957 is out of proportion to the extent of vaccine application and may indicate that a vaccine-induced immune barrier to virus spread actually has been erected. However, in this connection it should be noted that as recently as 1942 the na-

tional incidence of paralytic disease declined spontaneously so that in the first 39 weeks only 2,832 cases were reported as compared with 4,881 in the equivalent portion of 1957.* In this light, the 1957 decline is no more than the resultant of a naturally occurring depression plus the personal protection afforded those individuals who themselves were vaccinated.

The purpose of this paper is to present in some detail information derived from our own studies and to review other existing information which may help to answer the questions just raised.

Objectives and Methods in the Louisiana Study

Our own contributions stem from a study begun in 1953 which had as its original objective the achievement of more complete understanding of the process of natural immunization against poliomyelitis. During 1953, a total of 157 households, each with a newborn infant to serve as an index child, were recruited from population segments defined on the basis of area of residence, family size, race, and economic status. After collection of base line admission sera from all household members and of pertinent background information, the households were visited regularly every month to obtain interval information concerning the entire family and blood and stool specimens from the index infant. The specimens were examined on a current basis, using now standard tissue culture methods, to detect poliovirus in the feces and new appearance of antibody in the serum. Detection of infection in the index child was followed by an immediate special visit to the house for further specimens from all family members and any indi-

cated extrahousehold contacts. Yearly, blood specimens were obtained from all household members to insure recognition of infection episodes escaped by the index child. This phase of the study terminated in January, 1956, when Salk vaccine was offered to all incompletely immune children of the study group. At this time, 136 households remained after an average observation period of 30 months.

Following a two-dose primary course of vaccine, 118 families agreed to remain under modified observation, the objective of which was to determine what effect vaccination might have on the occurrence and course of enteric poliovirus infections. Since then, stools have been collected twice monthly from all children in each family under age 15 but bleedings have been omitted except in relation to vaccination and episodes of infection. In January of 1957, the third or booster dose of vaccine was given and observations were continued as in 1956. While eight more families withdrew during 1956, seven new ones were added so that 1957 began with 117 households in the study. Detailed accounts of the field and laboratory methods and of the observations in 1953–1955 prior to vaccination have been published only recently [2, 3] and preliminary reports have been made of the information becoming available during 1956 [4] and the first four months of 1957.[5] Preliminary data are now available through August, 1957, and further progress has been made in analyzing previously obtained material.

Household Episodes of Infection by Year and Virus Type

From the inception of the study in 1953 through August, 1957, a total of 177 household episodes of infection with polioviruses have been detected. These are summarized by year and virus type in Table 1. In 11 instances, of which ten occurred prior to 1956 when only

Table 1—Episodes of Household Infection in Southern Louisiana by Virus Type and Year Before Vaccination (1953–1955), After a Primary Course (1956) and After a Booster Dose (8 Months of 1957) of Salk Vaccine

Virus Type	Number[x] of Episodes in Year Indicated					
	1953 (6 mos.)	1954	1955	1956	1957 (8 mos.)	1953–1957
1	3	8	25(26)	28(29)	3	67(69)
2	1(2)	20(22)	15(17)	4	0	40(45)
3	5(6)	29(31)	8(9)	14	3	59(63)
All	9(11)	57(61)	48(52)	46(47)	6	166(177)

x—Numbers in parentheses include episodes revealed only retrospectively by examination of the annual sera.

the index child was under systematic observation, the episodes were revealed only retrospectively by examination of the sera collected annually from all household members. Such episodes cannot be dated more precisely than the year of occurrence and consequently are lacking in much desirable documentation as to attending circumstances. However, it is of interest that as a group they tended to be abortive in that they not only failed to involve the index children but also failed to involve one or more additional nonimmune members of the affected households. Relative distribution by virus type, as noted elsewhere,[2] varied from year to year in apparent relation to deficiencies in type-specific immunity among the younger children. Over-all, type 1 was most frequent (69 episodes) and type 2 least (45 episodes). Annual variation is of special current interest, the 47 episodes in 1956 actually representing a slightly greater relative frequency of episodes than in the years prior to vaccination. In 1956 we used this fact to support the idea that vaccination did not influence the frequency of infection episodes. The data for 1957, with only six episodes in an eight-month period, appear to reflect a truly reduced frequency although a final statement must await ultimate analysis of the 1957 status of the households with respect to infection-induced immunity. Great in-

terest obviously pertains to determining what part, if any, vaccination may have played in this reduction.

Serologic Response to Salk Vaccine

Before considering the infection episodes in the periods before and after vaccination, it may be helpful to observe the effect of vaccine as measured by seroresponse. Interest naturally centers on the development of antibody of types not present prior to vaccination. The available data are shown in Table 2 for children triply negative and for those with one or two heterologous types of antibody before the primary course. All primary courses were from a single unselected lot of commercially prepared Salk vaccine whereas the booster doses were from a lot specially chosen by Dr. Murray of the Division of Biologic Standards for its high potency. The initial response of children with prior heterologous immunity was quite good to antigens of all three types and that to the booster was excellent with titers of types one and two antibody equalling or surpassing 1:160 in over 80 per cent of cases. However, in the case of the important group of triple-negative children, the results were much less satisfactory with many completely failing to respond to the primary course, especially to type 3 antigen. Administration of the booster dose revealed that, except in the

Table 2—Summary of Antibody Developing Solely in Response to Salk Vaccine One Month After the Primary Course and One Month After the Booster Dose[x]

Doses of Vaccine	Pre-Vaccination Immunity Status	Number of Persons	Per cent of Persons with Antibody to Virus Type Indicated in Titers of 1:x One Month After Primary or Booster																	
			Type 1						Type 2						Type 3					
			0‡	2–5	10–20	40–80	160–320	640+	0‡	2–5	10–20	40–80	160–320	640+	0‡	2–5	10–20	40–80	160–320	640+
2	none only	118	36	30	28	6——→△			26	21	41	12——→			60	23	13	5——→		
	heterol.	97, 97, 94	10	22	41	27——→			8	14	39	38——→			18	32	35	15——→		
3	none only	62	23	5	10	18	27	16	0	0	3	8	55	34	50	6	13	18	8	5
	heterol.	50, 61, 53	0	0	8	4	36	52	0	0	5	15	49	31	4	6	17	25	32	17

x—Not shown in the table are data for rises in antibody of types present prior to vaccination. Further, the post-booster data are only for those children residing in households which escaped episodes of infection in the 11-month interval between the primary and booster doses.

‡—Titer of 0 includes both those negative when tested in 1:2 final dilution (the majority except in the postbooster group) and those negative in heel-blood specimens which could not be tested in final dilution below 1:10.

△—Sera collected after the primary course were not titrated beyond the 1:40 dilution.

case of the type 2 antigen, failure to respond detectably to the primary course was commonly associated with failure to condition the recipient to the booster inoculum. The final result was that antibody to types 1 and 3 viruses failed to develop in 23 and 50 per cent of the children, respectively.

Intrahousehold Spread of Infection

In Table 3 an effort has been made to indicate, with reference to age and to homologous immunity prior to the episode, the extent of infection among all members of the 124 households which experienced episodes of infection in the period 1953–1955 prior to vaccination. The figures presented now differ somewhat from those previously published [3] because of the inclusion of the index children as well as their household associates and also of persons involved in the episodes discovered only retrospectively. Because of this expansion, the

Table 3—Observations as to Infection Among All Members of 124 Households (Index Children Included) Experiencing Episodes of Infection in the Period 1953–1955 Prior to Vaccination

Homologous Immunity Prior to Episode	Age Group (Years)	Number of Persons		Virus Excretion Ratio[x]	Proved Infections	
		Total	With Sero-response		Number‡	Per cent
None	15 plus	23	15	3/7	15	65
	under 15	284	260	153/214	262	92
	all	307	275	160/221	277	90
Yes	15 plus	207	25	3/131	28	14
	under 15	101	37	4/77	38	38
	all	308	62	7/208	66	21

x—Ratio of persons found excreting virus to those whose stools were tested. It should be noted that, except for the index children, only single stool specimens were tested. Also, in a number of instances including persons associated with the episodes discovered only in retrospect, no specimens were examined.

‡—The number of proved infections is slightly greater in certain instances than the number of persons with seroresponse because of a few viral isolations from persons failing to manifest a clear-cut rise in antibody.

Table 4—Observation During 1956 and 1957 as to Infection Among Members of Vaccinated Households † Experiencing Episodes of Infection After Only a Primary Course of Salk Vaccine (45^x Households) and After the Booster Dose (5‡ Households)

Vaccination Status of Household and Year†	Homologous Immunity of Individual Prior to Household Vaccination	Age Group (Years)	No. of Persons		Virus Excretion Ratio△	Proved Infections	
			Total	With Sero-response		No.*	Per cent
Primary course only	none	15 plus	6	2	1/6	2	33
		<15	100	86	88/100	91	91
		all	106	88	89/106	93	88
1956	yes	15 plus	87	9	3/53	9	10
		<15	53	8	13/49	15	28
		all	140	17	16/99	24	17
Primary plus booster	none	15 plus	1	1	..	1	..
		<15	12	5	10/12	10	83
		all	13	6	10/12	11	85
1957 (8 months)	yes	15 plus	8	1	0/1	1	13
		<15	5	0	0/5	0	0
		all	13	1	0/6	1	8

†—Children naturally immune to all three virus types and many adults, without regard to their natural immune state, did not receive vaccine.

x—Forty-five households in 1956 exclude two episodes in which single infected persons were undergoing reinfection and failed to infect a total of 12 other members (only one nonimmune).

‡—For only five of the 1957 episodes are the data complete; the sixth was so recent that conclusions as to extent of infection are not yet permissible.

△—Ratio as in Table 3. In this case, it should be noted that in 1956 and 1957 stools were collected twice each month from children under 15 years old whereas only single specimens related to known episodes were obtained from older persons.

*—As in Table 3.

data presented in Table 3 are now more nearly comparable with the corresponding data shown in Table 4 for episodes occurring after vaccination. Turning first in both tables to those with no natural immunity, it is apparent that infection spread among children under age 15 to a nearly equal extent whether unvaccinated (92 per cent), recipients of the primary course only (91 per cent), or of the booster dose in addition (83 per cent). The small numbers of older persons in the same categories make the comparisons less meaningful, the corresponding figures being 65, 33, and (on the basis of a single person) 100 per cent, respectively. Turning now to those with prior homologous natural immunity, it is evident that the primary vaccination did little to reduce their susceptibility to reinfection when exposed to an intrahousehold source, the percentages being 14 and 38 before and 10 and 28 after vaccination for the adults and children, respectively. The data for reinfections after the booster dose are scant and indicate certain reinfection of only one adult out of nine adults and five children. In evaluating the data in Table 4, it is important to note a further reason for failing to attribute significance to the minor declines noted in intrahousehold spread after vaccination. This is the increased difficulty of purely serologic detection of infection encountered when preinfection antibody titers are high, a point to be more fully discussed shortly. Over-all, the data sug-

gest that, while prior homologous natural immunity results in measurable resistance to reinfection, vaccination with Salk vaccine, even when reinforced by a booster dose, results in no significant development of resistance to alimentary infection by persons nonimmune prior to vaccination and in little or no increase in resistance to reinfection by those previously naturally immune.

In Tables 3 and 4 the immunity status prior to exposure has been considered only qualitatively. In Table 5 the same data are presented again but broken down by titer of homologous antibody prior to the infection episode. As might have been anticipated in view of the failure of vaccination to reduce susceptibility to infection, there is no significant correlation between the titer of antibody due solely to vaccination and the per cent of infections. Contrariwise, among persons with prior natural immunity, whether or not reinforced by vaccination, the proportion of proved reinfections decreases significantly with increasing preinfection titer of homologous antibody. Unfortunately, any correlation evident in Table 5 between infection and prior antibody titer may have little meaning. As we pointed out elsewhere,[3] demonstration of a significant rise in antibody becomes increasingly difficult with increasing titer of preinfection antibody. This demonstration, of course, is the most important criterion for detecting infection among adults from whom stool specimens were collected only after knowledge of the existence of an infection episode and it

Table 5—Relation of Infection to Titer of Homologous Antibody Prior to Episode of Household Infection Among Persons Immune Because of Vaccination or of Prior Natural Homologous Infection

| Origin of Immunity† | Antibody Titer (1:x) Prior to Episode△ | No. of Persons | | Virus Excretion Ratio^x | Proved Infections | |
		Total	With Sero-response		No.‡	Per cent
Only Salk vaccine	<10	55	52	52/55	53	96
	10–20	37	32	30/37	32	87
	40–80	10	5	7/10	7	70
	160+	10	2	8/10	8	80
	Total	112	91	97/112	100	89
Only infection	2–5	28	14	3/21	14	50
	10–20	70	17	2/52	18	26
	40–80	120	30	2/90	32	27
	160–320	135	16	5/95	18	13
	640–1280	48	2	2/34	3	6
	2560+	24	0	0/19	0	0
	Total	425	79	14/311	85	20
Infection plus vaccine	<40	0				
	40–320	12	2	4/11	4	33
	640+	24	0	4/24	4	17
	Total	36	2	8/35	8	22

x, ‡—As in Tables 3 and 4.
△—Titer of homologous antibody in the serum specimen taken most recently prior to the infection episode.
†—The careful reader may have noted that, on the basis of figures in Tables 3 and 4, the total numbers in the categories by origin of immunity should have been 119, 308, and 153, respectively, for those only with vaccine, only with infection and with both. The differences, very considerable in two instances, derive from the fact that assignment in Table 4 was based on vaccination status of the household as a whole, whereas in the present table it is based on the individual. As explained in a footnote to Table 4, many household members (epecially adults) were not vaccinated.

Table 6—Homologous Reinfections Among Naturally Immune Persons Exposed
During Household Episodes of Infection by Virus Type and Without
Regard to Possible Reinforcement of Immunity by Vaccination

| Episode Virus Type | Age Group (Years) | No. of Persons | | Virus Excretion Ratio^x | Proved Infections | |
		Total	With Sero-response		No.‡	Per cent
1	15 plus	123	11	1/83	12	10
	under 15	58	12	8/53	17	29
	all	181	23	9/134	29	16
2	15 plus	71	7	2/49	9	10
	under 15	42	17	3/37	18	43
	all	113	24	5/85	27	24
3	15 plus	108	16	2/73	16	15
	under 15	59	18	6/51	21	31
	all	167	34	8/123	37	22
Any	15 plus	302	34	5/201	37	12
	under 15	159	47	17/141	56	35
	all	461	81	22/346	93	20

x, ‡—As in Tables 3 and 4.

remains as an important adjunct in the case of those children who may excrete virus only briefly. This consideration is particularly important in relation to those whose immunity derived only from infection, since many of these were adults, but it also is of importance in the group of vaccine-immune children with antibody titers of 1:40 or higher. Among the 15 "proved infections" in this group, eight failed to manifest a significant antibody rise and were detected solely on the basis of virus isolation. These 15 infections, incidentally, include seven of the 11 infections in triply vaccinated persons which are shown in Table 4.

Another question with respect to susceptibility to reinfections is that of a possible relation to virus type. Sabin[6] has reported that homologous natural immunity is more effective in preventing infection after a constant oral dose of attenuated live poliovirus in the case of types 1 and 2 viruses (infection ratios of 1/11 and 3/11, respectively) than with type 3 virus (6/12 infection ratio). Our own data, based on the unmeasured

challenge resulting from intrahousehold exposure of 461 persons, are show in Table 6, distributed by episode virus type and by broad age group. The differences observed are small and no meaningful pattern emerges; while type 3 virus caused the greatest proportion of reinfections among adults (15 per cent as compared with 10 for types 1 and 2), the same position among children belongs to type 2 virus (43 per cent as compared with 29 and 31 for types 1 and 3). The available evidence does not permit us to choose betwen various possible explanations for the discrepancy between Sabin's data and our own.

Susceptibility to infection is but one phenomenon related to viral spread which may be influenced by immunity. In so far as susceptibility permits infection, interest turns to the capacity of the immune but infected individual to serve as a source of infection for others. Our own studies provide some information pertinent to this question, especially since the beginning of 1956. The examination of twice-monthly stool specimens from all children under 15, begun at

this time, often enabled us to single out the person initially infected in a household. We already have shown, during 1956 and 1957, that the administration of a primary course and even of the booster dose of Salk vaccine does not result in decreased virus spread within a household. Since children were usually the first ones infected and all of them had been vaccinated, it follows necessarily that vaccinated children were effective sources of intrafamilial spread. In Table 7 the record of one type 1 episode in 1957 is presented to illustrate this point and also because it bears on the current interest in possible pharyngeal spread. In this family of six, only the mother was naturally immune to type 1 virus and only the three older siblings had been vaccinated (primary plus booster) when the episode occurred. Examination of stool and serum specimens collected late in December, 1956, when the booster dose was given revealed no evidence of infection. By January 30, 1957, when the next specimens were collected, the five- and four-year-old siblings had become infected as evidenced both by marked rise in antibody (to which vaccine also

could have contributed) and by recovery of virus from the stool specimens. While the four-year-old, rather inexplicably, was not found to excrete virus again until April 6, the five-year-old excreted continuously through April 17. Presumably from one of these initial sources, three others became infected, namely, the father whose serum collected on March 25 contained newly appearing antibody and the two other siblings both of whose stool specimens became positive in April. Although no tests for pharyngeal virus were made, its presence is generally believed to be too brief to explain the long delayed spread (three to four months) to the other two siblings. With respect to spread from the reinfected naturally immune person our data are still very scant, and relate only to two episodes of 1956, previously reported,[4] in which the first and only infected members were undergoing reinfection and failed to transmit virus to a total of 11 immune and one non-immune other household associates.

If one assumes that fecal virus is the chief source of virus spread, data as to duration and amount of virus excretion in the feces become important. Among

Table 7—Family Record of Household No. 115 Relating to an Episode of Type 1 Poliovirus Infection in 1957 and Illustrating Apparent Spread of Infection from Vaccinated Children (Primary Plus Booster^x)

		Titer of Type 1 Antibody			Isolation of Type 1 Virus on Date Indicated							
Family Member	Prevac †	After Primary	After Booster△	After Episode ‡	1/30	2/25	3/13	3/25	4/6	4/17	5/7	5/20
Father — 39 y	0	N.V.*	N.V.	80	N.S.°	N.S.	—	N.S.	—	N.S.	N.S.	N.S.
Mother — 33 y	160	N.V.	N.V.	320	N.S.	N.S.	—	N.S.	—	N.S.	N.S.	N.S.
Sib — 6 y	0	160	640	320	—	—	—	—	—	+	+	—
" -- 5 y	0	5	640	640	+	+	+	+	+	+	—	—
" -- 4 y	0	0	1,280	1,280	+	—	—	—	+	—	—	—
" -- <6 mo.	0	N.V.	N.V.	320	—	—	—	—	+	+	+	—

x—Booster dose administered to three older siblings 12/27/57; parents were not vaccinated and youngest sibling (born in November, 1956) was not vaccinated until after episode.

†—Dates of bleedings shown as prevaccination for parents were 1/12/57 and 12/27/56 for father and mother, respectively, and for the youngest sibling, 4/2/57, or just prior to first virus isolation.

△—All postbooster sera were collected on 1/30/57.

‡—Dates of bleedings shown as after episode were 3/18/57 for all but youngest sibling which was 5/7/57; later specimens have been obtained in all cases but the results are not yet available.

*—N.V.=not vaccinated.

o—N.S.=no specimen.

Table 8—Duration of Fecal Excretion of Virus as Related to Homologous Immunity Prior to Infection

| Prior Natural Immunity | Vaccination Status | Number of Children Excreting Virus | Days Duration of Virus Excretion | | Estimated True Mean[x] |
| | | | Observed | | |
			Range	Mean	
None	None	112	1–114	24	51
	primary	84	1–105	25	42
	booster	11	1–77	24	41
Yes	Yes	16	1–43	9	24

x—Determined by adding the average interval (days) between collection of specimens to the observed mean period of excretion.

children without natural immunity there was little variation in the duration of excretion in relation to vaccination. The observed range and mean, respectively, were as follows: 1–114 and 24 days for 112 unvaccinated children; 1–105 and 25 days for 84 who had received only a primary course of vaccine; and 1–77 and 24 days for a small group of only 11 who also had been given a booster dose. By adding the average interval between collection of specimens to the observed means, the true mean durations were estimated to be 51, 42, and 41 days, respectively. In contrast, among naturally immune children undergoing reinfection, viral excretion was not regularly detected and among 16 who were shown to shed virus the range was 1–43 days with an observed mean of nine days and an estimated true mean of 24 days.

Rather surprisingly, however, tests for the amount of virus present in the first virus-positive specimen revealed nearly as much virus (4.2 mean long infectivity) in stools from children with prior natural immunity as in those, whether vaccinated or not, without natural immunity (4.0 to 4.9 mean log infectivity).

Discussion

The fundamental questions with which we are now concerned are the relation-ship of immunity, however derived, to susceptibility to alimentary infection with polioviruses and to the ability of the immune but infected person to serve as a source for further virus spread. Just a year ago, we presented a preliminary report[4] on our observations during the first seven months after completion of two-dose course of Salk vaccine. At that time, no evidence could be found that primary vaccination had influenced either the occurrence or course of alimentary infections in any way, whereas it was already clear that immunity resulting from natural infection did exert a significantly limiting effect. We also predicted that this lack of influence would prevail following booster reinforcement of vaccine-induced immunity. Now we have been able to present a more complete picture for the year following primary vaccination which differs in no significant way from the preliminary sketch presented and we also have preliminary data for an eight-month period following the booster dose.

In one important respect, the 1957 data do not appear to have fulfilled our predictions. Whereas by August 31, 1956, we had observed 40 infection episodes among some 118 observed households, during the same period in 1957 we have detected only six epi-

sodes among almost the same number of households. While depletion of susceptibles (meaning persons not naturally immune) undoubtedly occurred to an extent not yet measured, our data in their present form suggest that, in 1957 after booster vaccination, infection episodes have been relatively much less frequent than in previous years. Rather obviously, this parallels the nation-wide reduction in clinical poliomyelitis which some believe to be greater than can be explained by the direct protection afforded by vaccination. While natural variation in dissemination of virus, due to causes as yet unknown, seems to us to be a more probable explanation for the reduction in disease, a possible alternative could be reduction in virus spread mediated by increased herd immunity due to vaccination.

How this might be brought about then becomes a major question. Our own data for 1956 and the data of others are in agreement that a primary course of Salk vaccine does not alter susceptibility to or the course of lower alimentary tract infection either with wild viruses [7, 8] or with attenuated strains.[6, 9, 10, 11] Our own rather scanty 1957 data indicate that, once infection enters the household, vaccination reinforced by a booster also does not appear to reduce susceptibility to infection nor to influence fecal virus excretion. Only in chimpanzees has vaccination been reported to result in reduced fecal excretion of virus.[12] Thus it would appear that, if Salk vaccination is to be credited with a limiting influence on viral spread, it hardly can be by modifying either susceptibility to or the course of infections of the lower alimentary tract. This has led to renewed consideration of the possibility that pharyngeal virus is more important than fecal virus and that vaccination may influence upper alimentary or pharyngeal infection even though it has no effect on the process at a lower level. The available data do not seem to support this idea. In the first place, our data indicate that vaccination does not interfere with the mechanism mediating intrahousehold virus spread, whatever its nature. Second, the example of spread in household No. 115 which was delayed for at least three months in the case of two children seems incompatible with spread from a pharyngeal source. Third, even in the chimpanzee the influence of vaccination appears to have been relatively slight on pharyngeal virus in contrast to its marked effect on fecal virus.[12] And finally, there are the crucial observations of Horstmann and co-workers [10] with Sabin's attenuated type 1 virus. They recovered virus from the pharyngeal washings of six out of seven vaccine-immune volunteers who were fed virus in fluid form and demonstrated its continued presence for ten days in one "representative" case. Our feeling, thus, is that the reduction in viral spread, reflected in our experience and postulated to explain in some part the nation-wide reduction in disease, cannot be attributed to the use of Salk vaccine.

The other type of active immunity to poliovirus is that resulting from infection. We have cited substantial data from our experience indicating that natural immunity materially reduces susceptibility to infection resulting from intrahousehold exposure and also exerts a limiting influence on duration of viral excretion. We also have scant but interesting data compatible with the concept that the reinfected person is not an effective source for viral spread. Sabin [6] and Koprowski [9] have supported the concept of reduced susceptibility by direct challenge of naturally immune persons with attenuated virus. Horstmann and co-workers [10, 11] have confirmed these observations and, in addition, demonstrated the resistance of naturally immune persons to infection resulting from the spread of attenuated virus within an institution. As noted elsewhere,[4] natural infection appears to

result in some form of local immunity of the alimentary tract which is not promoted by vaccination with killed-virus vaccine.

There is an obvious temptation to transfer directly the very desirable attributes of naturally acquired immunity to that which follows oral vaccination with living attenuated polioviruses. Challenge experiments by both Sabin[6] and Koprowski[9] justify this in part by indicating that, in persons deliberately immunized by infection with attenuated strains, resistance to reinfection with these same strains is entirely equivalent to that of naturally immune persons. It would, therefore, seem safe to predict that, when the basic safety of live-virus vaccines is accepted, their widespread use would create the immunologic barrier to virus spread which some now attribute (we think unjustifiably) to use of the Salk vaccine.

Summary

From mid-1953 through August, 1957, we observed 177 episodes of household infections with polioviruses occurring among a study group consisting of between 157 and 118 representative households. Vaccination was begun in January, 1956, with a two-dose course of Salk vaccine and completed in December, 1956, when a booster dose was given. De novo development of antibody induced by the vaccine was excellent in children possessing one or two types of heterologous antibody but among triple negatives nearly a quarter and a half, respectively, developed no antibody after the booster to types 1 and 3 viruses. Infection episodes continued at unreduced frequency in 1956 after the primary course but declined sharply in 1957 after the booster dose. However, analysis of the data as to intrahousehold infections suggests that this decline is not due to the vaccine. Measurable resistance to infection on intrahousehold

exposure and reduced duration of viral excretion when infection did occur were observed among persons with natural homologous immunity. In contrast, among persons without natural immunity, vaccination apparently exerted no influence on susceptibility to or the course of alimentary infection. Resistance to homologous reinfection among the naturally immune was possibly related to homologous antibody titer but did not differ significantly in relation to viral type. Infected but vaccinated children appeared to be just as effective sources for intrahousehold spread of virus as did unvaccinated children, whereas some evidence was obtained that infected but naturally immune children are ineffective sources. A delay of at least three months in viral spread in one episode is believed to be strong evidence against spread from a pharyngeal source. Because of the foregoing evidence and the observations of other workers including challenge experiments with live attenuated polioviruses, it is concluded that widespread use of Salk vaccine should not by any reasonable mechanism influence poliovirus dissemination.

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A graduate fellowship is being offered to a woman physician, either native or foreign, by the Women's Medical Association of New York City. The Mary Putnam Jacobi Fellowship provides a stipend of $2,000, given for medical research, clinical investigation, or postgraduate study in a specialized field of medicine, including public health. The committee is accepting applications between August 1, 1958, and February 1, 1959. The successful candidate will be notified by May 1, 1959.

Mary Putnam, who is honored through the fellowship, was the first woman student in the New York School of Pharmacy where she went because no medical school would accept her. She was the first woman graduate of l'Ecole de Médecine in Paris and the first woman admitted to the New York County Medical Society—in 1870—on motion of her future husband, Abraham Jacobi, M.D.

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