Community Spread of Orally Administered Attenuated Poliovirus Vaccine Strains

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A STUDY of orally administered attenuated poliovirus vaccine was conducted in a small community in Minnesota in 1958. In that study (*1*), the feeding of virus to only half of the participating families during the first half of the study provided an opportunity to study the spread of these strains of poliovirus to participants who received placebos. Prior to this study, intrafamily (*2–4*) and intrainstitutional (*5*) spread of attenuated poliomyelitis vaccine viruses had been reported.

This study presents quantitative data on the community spread of vaccine strains of poliovirus. The design of the study, the vaccine strains used, the characteristics of the study population, the illnesses observed during the study, and the method of surveillance used to detect such illnesses were described in the earlier report (*1*).

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The poliovirus vaccine strains used were developed by Dr. Herald R. Cox, director of viral and rickettsial research, Lederle Laboratories Division, American Cyanamid Co. In the report of the 1958 study, no harmful effects were attributed to the use of these strains. Since natural human passage might be expected to produce changes in some properties of these vaccine strains the need for intensive study of these passage strains is indicated. One important source of information on changes in vaccine strains is the medical histories of persons receiving these strains by natural spread. The medical records of these individuals are reviewed. If after several natural passages in humans the strains do not show a persistent and progressive increase in virulence for monkeys, their spread could have definite value. Not only would some immunity be acquired by individuals not fed the vaccine strains, but also the intermittent presence of these strains in a community could provide booster stimulation of previously vaccinated persons. The magnitude of interfamily or community spread of these strains can indicate the extent of added benefit that can be anticipated.

Materials and Methods

Participants in the study were married University of Minnesota students and their children. These families lived in Como Village, a crowded university housing development in Minneapolis. All 371 families in the village were invited to participate in the study and 149 families, 40 percent, volunteered.

The volunteers were divided into two groups of 74 and 75 families on a random basis. Family numbers were assigned alphabetically. Placebo was assigned to the first half of the families encountered in a random search of the random number tables. Thus members of 20 percent of the households in the village were fed vaccine (group B), and stool specimens were available from an additional 20 percent as controls for measuring the community spread of the vaccine strains. A map showing the distribution of vaccine and placebo fed households has been published (*6*). There were 545 persons in the 149 study families; 266 in group B, the vaccine-fed group, and 279 in group A, the placebo-fed, or control, group. Group B included 147 adults, 109 children, and 23 infants (under 1 year of age); group A, 141 adults, 95 children, and 30 infants.

During the study the identity of the two groups was known only to one member of the team. He made the random division and distributed the vaccine and the placebo capsules in envelopes labeled for each family. The sources of the blood serum and stool specimens were not known to the laboratory personnel.

The chronology and sequence of the feeding and collection of stool specimens are shown in the chart. Each participant submitted six stool specimens. The first specimens were collected prior to the feeding of vaccine to either group. The second, third, and fourth specimens were collected after type 2 virus had been fed to group B and before it was fed to group A; the third, fourth, and fifth specimens, after type 1 had been fed to group B and before it was fed to group A; and the fourth, fifth, and sixth specimens after type 3 had been fed to group B and before it was fed to group A. Thus three stool specimens were available to measure the community spread of each type of poliovirus, and this spread was measured for a period of about 8 weeks for each type.

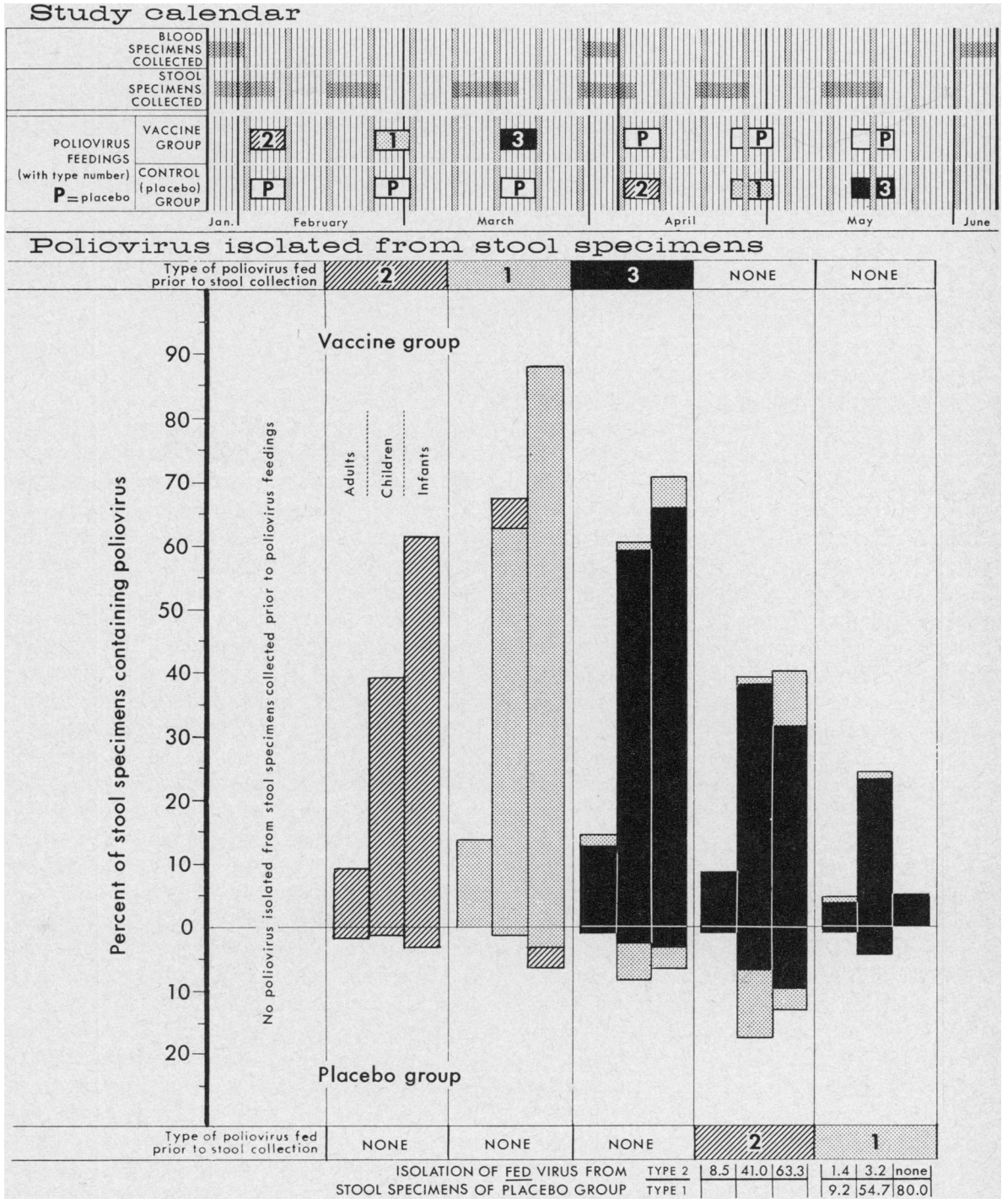
The collection of stool specimens was scheduled for about 14 days after the feeding of virus. The elapsed time between feeding virus and collection of stool specimens was calculated from the Wednesday of the week the virus was fed. The median day of receipt of the second stool specimens was 14 days, of the third specimen 13 days, and of the fourth specimen 14 days, after each immediately preceding virus feeding. More than 93 percent of the specimens were received within 3 days prior to and 6 days following the median day of receipt. There was some overlap between the days for stool collection and the days for feeding virus (chart); however, no family was fed either the vaccine or the placebo until stool specimens had been submitted. The specimens were, in effect, the "ticket" for the vaccine or the placebo capsules. A few individuals who were away from home at the time scheduled for collection of stool specimens were continued in the study. Only 16 stool specimen results were missing; 15 expected stool specimens were not received and 1 specimen was unsatisfactory for isolation of virus.

Stool specimens were stored frozen (−20° C.) prior to processing. For isolation, 20 percent emulsions were prepared in distilled water by shaking for 5 minutes, centrifuging for 10 minutes at 1,500 rpm (International Equipment Co. No. 2) and 30 minutes at 13,000 rpm (Servall). A portion of the supernatant was diluted 1:2 with double strength Hanks' balanced salt solution (BSS) containing 600 units of penicillin and 600 μg. of streptomycin per milliliter. Supernates of processed stool specimens were stored frozen and were thawed prior to inoculation, when 0.1 ml. of each processed specimen was inoculated into each of two HeLa cell tissue culture (TC) tubes. The procedure for preparation of the HeLa cell TC tubes was published in the earlier report (*1*).

Inoculated TC tubes were examined after 1, 3, 5, and 7 days of incubation at 37° C. When characteristic cytopathogenicity was observed after at least one transfer, the isolated virus was typed in the conventional manner. Cytopathogenic agents other than poliovirus were isolated from 16 specimens. These proved to be adenovirus type 1 or type 2. One hundred and forty-three selected stool specimens from which poliovirus had not been isolated on HeLa TC tubes were inoculated into monkey kidney TC tubes. No strains of ECHO virus were isolated.

Stool specimens from control group individuals from which types 1, 2, or 3 poliovirus had been isolated prior to the feeding of each respective type to those individuals were sent to

Chronology of specimen collection and vaccine feeding, January 27–June 7, 1958, and percentages of poliovirus isolated from six stool specimens from vaccine and placebo groups.



Stool specimens collected: *Vaccine group*—147 from adults, 109 from children, 23 from infants; only 3 specimens missing, no more than 1 from any age group. *Placebo group*—141 from adults, 95 from children, 30 from infants; only 13 specimens missing, maximum of 4 from adults, 2 from children, 1 from an infant.

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Dr. Cox for study of neurovirulence in monkeys. Intracerebral tests in monkeys showed no increase in paralytic ratio for any of the three poliovirus types when compared to virus-containing stools from vaccine fed individuals (*7*).

Evidence of community spread of vaccine strains to group A, the control group, was also shown by a significant rise (two tube, sixteenfold) in antibody titer of the second blood specimen, collected at the middle of the study period, compared with the first blood specimen. Type 3 virus was fed to group B, the study group, from March 17 to 22, and second blood specimens were collected from March 31 to April 5. The elapsed time between feeding type 3 virus and collection of second blood specimens was, comparatively, much shorter than the elapsed time between feeding types 2 and 1 virus and the collection of blood specimens. For this reason virus spread, as measured by antibody response in group A, the control group, was not as fully measured for type 3 as for types 2 and 1.

It is also possible that the capacity for type 3 virus to spread to group A participants was not completely measured because the spread may have been reduced by feeding type 2 and type 1 vaccines to this group during the period of potential spread of type 3 vaccine (chart). The spread of type 3 vaccine strains may have been reduced by the feeding of type 2 and type 1 vaccines, which interfered with the spread of type 3, or the spread of type 3 may have occurred but was not measured if the fed vaccine strain replaced the naturally acquired type 3 virus.

During the study 16 infants were born, 5 to group A families and 11 to group B families. These newborns received the same vaccine or placebo capsules as their families were receiving even though they had missed earlier feedings. Forty-six stool specimens were received from the newborns, the number per infant varying from 0 to 5. Poliovirus was isolated from 11 specimens (type 2 from 1, type 1 from 5, and type 3 from 5), all collected after feeding of the virus. Results on the specimens from these newborns are not included in this paper.

Criteria used in evaluating the illnesses observed in group A, the placebo-fed individuals who acquired the vaccine strains by natural passage, are presented with "Results." The medical followup was continuous and included numerous house visits (*1*).

The climate in Minneapolis is the humid continental type with a general tendency toward extremes. During the study period (January 27–June 6, 1958) maximum, minimum, and mean monthly temperatures were slightly higher than average, except in February, when they were slightly lower. Temperatures varied from −15° F. on February 16 to 88° F. on May 29. The climate was unusually dry, with normal precipitation only in April (*8*).

Results

The polioviruses isolated from stool specimens of group B, the vaccine-fed group, provide a rough measure of the viruses available for spread to group A, the control group. The percentage of isolations from each of the six stool specimen sets received from the vaccine-fed group is shown in the chart.

Poliovirus was not isolated from the first stool specimens collected prior to feeding vaccine. The second stool specimen, submitted approximately 2 weeks after type 2 virus had been fed, yielded type 2 virus in 8.8 percent of the adults, 38.5 percent of the children, and 60.9 percent of the infants. The third stool specimen, submitted after the feeding of type 1 virus, yielded type 1 virus in 12.9 percent of the adults, 61.5 percent of the children, and 87.0 percent of infants. Thus type 1 virus appears to have replaced type 2 in the intestinal tract of many of the recipients. However, five children were still excreting type 2 virus in the third stool specimen.

Three of these five children lacked detectable antibodies to all three types of poliovirus prior to receiving vaccine and developed antibodies against type 1 virus to a titer of 1:1,024 or greater following vaccine feeding. Two of the three children developed antibodies to type 2 virus, and one failed to develop antibodies against type 2 virus even though type 2 had been isolated from the third stool specimen. The remaining two children had antibodies to both types 1 and 2 virus prior to receiving

vaccine, and the titer rose sixteenfold or more to both types following feeding of vaccine.

The fourth stool specimen, submitted after feeding type 3 virus, yielded type 3 in 12.2 percent of the adults, 58.7 percent of the children, and 65.2 percent of the infants. Type 3 virus appears to have replaced type 1 in the intestinal tract of many vaccine recipients, but two adults, one child, and one infant were still excreting type 1 virus in the fourth stool specimen. One adult had type 3 antibodies in dilution 1:1,024 or greater prior to receiving vaccine, which may account for the suppression of the type 3 virus. The other adult was triple negative prior to receiving vaccine, and during the study responded serologically only to type 2 virus even though type 1 was also isolated from a stool specimen. The 13-month-old child was triple negative prior to vaccine and responded serologically to type 1 and weakly (titer 1:4) to type 3 vaccine but not to type 2. The 6-month-old infant was double negative with low titer (1:4) antibodies to type 2 virus and developed both type 1 and type 3 antibodies following vaccine even though only type 3 virus was isolated.

Type 3 virus was isolated from 60 of the fifth and 31 of the sixth stool specimens from group B individuals. The excretion of type 3 virus continued longest and thus was the largest source of virus "supply" for spread to the control group compared with the supply available for types 2 and 1.

Forty-five isolations of poliovirus were obtained from specimens from 29 individuals in group A, the placebo-fed control group. The percentages of isolations from each of the six collections of stool specimens from this group are shown in the chart. Isolations due to community spread are shown as bars; isolations of types 2 and 1 from specimens submitted after these types of poliovirus had been fed to this group are shown as a tabulation at the bottom of the chart.

Poliovirus type 2 was isolated from the stools of two children and two adults in three group A families (table 1). The stool specimens were collected 12 to 15 days after the group B participants were fed type 2 virus. Two of the four persons were children in the same family (Nos. 4–3 and 4–4). Neither child had antibodies to type 2 virus detectable in the first blood specimen, but both showed a significant antibody response in the second blood specimen. Both adults had antibody titers to type 2 in the first blood specimen, and neither showed an increase in titer in the second blood specimen. Both adults had received Salk vaccine.

Four of the other five members of these three families had type 2 antibodies. In the fifth, a child of No. 105–2, no type 2 antibodies were detectable in serum dilution 1:4. There was no evidence that any of these five individuals had picked up type 2 poliovirus.

Poliovirus type 1 was isolated from 12 children in 7 group A families (table 2). Type 1 poliovirus was isolated from three children in family No. 29. The virus was first isolated

Table 1. Isolation of type 2 poliovirus and type 2 antibody results on four placebo-fed study participants

Family and person Nos.	Sex	Age	Number Salk vaccine inoculations	Stool specimens		Type 2 poliovirus antibody titer		
				Order No.	Number days[1] since virus feeding	First	Second	Third
4–3	Female	34 mo	2	2d	14	<4	256	256
4–4	Female	4 mo	0	2d	13	<4	16	64
				3d	36			
12–1	Male	32 yr	1	2d	15	16	16	64
105–2	Female	20 yr	3	2d	12	64	64	1,024

[1] Virus fed to vaccine group families Feb. 3–8, 1958. Number of days between feeding virus and collecting stool specimens, calculated from Feb. 5.

from the third stool specimen submitted from the 3-year-old (No. 29–3), and later from her and her two younger brothers. Type 1 poliovirus was isolated from four individuals in family No. 165. The virus was isolated earliest from the 8-month-old infant (No. 165–6), and later from her and her three older brothers. The remaining five type 1 isolations share several characteristics: they were all from children aged 2–5 years who had been fed type 2 virus; they were late isolations, being found only in the fifth stool specimens; they were collected within a 5-day period; types 1 and 2 poliovirus were isolated from all five specimens. None of these five children showed an antibody response to type 1 virus in the second blood specimen, which had been collected prior to the receipt of the fifth stool specimen.

In addition to the 12 children who picked up type 1 virus there were 18 other members in these 7 families. Eleven had type 1 antibodies and only one, No. 47–1, the father of No. 47–4, showed an antibody response to type 1 in the second blood specimen. The other seven had no antibodies in dilution 1:4 against type 1 virus and showed no serologic response in the second blood specimen.

Poliovirus type 3 was isolated from 12 children and 1 adult in 8 group A families (table 3). Type 3 poliovirus was isolated from the fourth stool specimens of the adult (No. 157–1) and three children (Nos. 87–3, 144–3, 144–4), but only one of these four individuals (144–3) showed an antibody response in the second blood specimen. Type 3 poliovirus was first isolated from the fifth or sixth stool specimens from the remaining nine children; no antibody response was observed in the second blood specimens, which had been collected from these children prior to the time when they were shown to be excreting type 3 virus.

Besides the 13 persons who picked up type 3

Table 2. Isolation of type 1 poliovirus and type 1 antibody results on 12 placebo-fed individuals

Family and person Nos.	Sex	Age (years)	Number[1] Salk vaccine inoculations	Stool specimens		Type 1 poliovirus antibody titer		
				Order No.	Number days[1] since virus feeding	First	Second	Third
29–3	Female	3	3	3d	6	<4	16	64
				4th	26			
				5th	49			
29–4	Male	2	3	4th	26	<4	64	256
				5th	49			
29–5	Male	1	3	4th	26	<4	4	256
				5th	49			
165–3	Male	5½	3	4th	25	4	4	64
				5th[2]	44			
165–4	Male	4	3	4th	26	4	16	256
165–5	Male	2	3	4th	23	<4	256	1, 024
				5th	44			
165–6	Female	8 mo.	3	3d	9	<4	4	256
				4th	23			
				5th[2]	44			
27–3	Male	4	2	5th[3]	49	<4	<4	256
47–4	Male	2	2	5th[3]	53	<4	<4	1, 024
63–3	Female	5	3	5th[3]	50	<4	<4	<4
67–3	Female	2	3	5th[3]	50	<4	<4	16
103–3	Male	2	3	5th[3]	50	<4	<4	1, 024

[1] Type 1 poliovirus fed to vaccine group families February 24–March 1. Number of days between virus feeding and stool specimen collection calculated from February 26.

[2] Type 1 poliovirus also isolated from sixth stool specimen, but type 1 virus had been fed to the placebo group prior to collection of sixth specimen.

[3] Types 1 and 2 poliovirus isolated; type 2 virus fed prior to collection of fifth stool specimen.

Table 3. Isolation of type 3 poliovirus and type 3 antibody results on 13 placebo-fed individuals

Family and person Nos.	Sex	Age (years)	Number Salk vaccine inoculations	Stool specimens		Type 3 poliovirus antibody titer		
				Order No.	Number days [1] since virus feeding	First	Second	Third
41–3	Female	3	3	6th	48	<4	<4	16
41–4	Female	1	2	5th	25	4	<4	1,024
45–5	Male	6 mo.	0	5th	27	<4	<4	<4
69–3	Female	2½	3	5th	29	<4	<4	16
69–4	Male	6 mo.	0	5th	28	<4	<4	64
72–3	Female	3	2	5th 6th	27 48	<4	<4	256
72–4	Female	1½	0	6th	48	<4	<4	64
87–3	Male	3½	2	4th 5th	11 33	<4	<4	4
92–3	Female	5	1	5th	26	<4	<4	64
92–4	Male	3	1	5th 6th	27 53	<4	<4	16
144–3	Male	2½	3	4th 5th	7 26	<4	64	1,024
144–4	Male	11 mo.	2	4th 5th	8 25	<4	<4	1,024
157–1	Male	27	3	4th 5th 6th	9 26 47	<4	<4	16

[1] Type 3 poliovirus had been fed to vaccine group families March 17–22. Number of days between virus feeding and stool specimen collection calculated from March 19.

Table 4. Serologic evidence of spread of poliovirus to control group A individuals, unconfirmed by virus isolation from stool specimens

Poliovirus type	Family and person Nos.	Sex	Age (years)	Number Salk vaccine inoculations	Antibody titer		
					First	Second	Third
2	5–3	Male	3½	3	16	256	1,024
	43–1	Male	25	0	4	256	64
	56–1	Male	31	1	64	1,024	256
	107–1	Male	25	3	16	256	256
1	[1] 47–1	Male	26	2	16	256	256
	[2] 144–1	Male	25	3	16	256	64
3	33–2	Female	26	3	64	1,024	256
	[1] 47–1	Male	26	2	64	1,024	256
	[2] 144–1	Male	25	3	4	64	64

[1] Type 1 poliovirus isolated from 1 child of 47–1.
[2] Type 3 poliovirus isolated from 2 children of 144–1.

poliovirus there were 21 additional persons in these 8 families. Eight had antibodies against type 3 poliovirus, and one of these (No. 144–1) showed an antibody response to type 3 (1:4 to 1:64) in the second blood specimen. The remaining 13 persons had no antibodies against type 3 poliovirus detectable in serum dilution 1:4, and no antibody response was observed in the second blood specimen.

Serologic evidence of community spread of the poliovirus vaccine, unconfirmed by virus isolation, was observed in seven persons. There were nine instances of poliovirus spread indicated by a rise in antibody titer; four for type 2, two for type 1, and three for type 3 (table 4). Types 1 and 3 poliovirus both appear to have been picked up by two male adults (Nos. 47–1 and 144–1). A child of No. 47–1 had also picked up type 1 but not type 3 (table 2), and two children of No. 144–1 had picked up type 3 but not type 1 (table 3).

The community spread of these poliovirus vaccine strains, whether supported by virus isolation, antibody response, or both, is shown in table 5. Among the 266 control group individuals, type 2 poliovirus had spread to 8, type 1 to 14, and type 3 to 16. These 38 instances of spread involved 36 individuals, 13.5 percent of the control group, distributed among 23 of the 74 control group families. Since the spread of two types of virus to one family was observed on only 2 occasions, this represents 11.3 percent of the total potential interfamily spread.

Poliovirus was not isolated from any adults or children with antibodies detectable in serum dilution 1:4 unless the individual was known to have received Salk vaccine. Virus isolation rates from stool specimens as a function of antibody status on the initial blood specimen and Salk vaccine experience is shown in table 6. Among the adults the majority, 63 percent or more, had poliomyelitis antibodies detectable in serum dilution 1:4 or greater in the initial specimen, but virus isolation was accomplished from few of these individuals compared with the isolation rates from those without antibodies. Furthermore, virus isolation from adults in the presence of serum antibody was limited to those who had had two or more doses of Salk vaccine, with one exception, and this individual had had one dose of Salk vaccine.

Among the children the majority had no detectable antibodies to types 1 and 3 poliovirus, and over one-third had no detectable antibodies to type 2. Virus isolation rates were high among children without poliomyelitis antibodies, regardless of their Salk vaccine status. These rates from children were significantly lower if poliovirus antibodies were demonstrable than if these antibodies were absent.

Virus isolation rates were high for infants, regardless of the presence of poliovirus antibodies in the initial blood specimen and regardless of their Salk vaccine status. In almost every instance the presence of poliovirus antibodies in the infant's serum appeared to be the result of placental transfer, as judged by the presence of the same type of antibody in the mother's serum and the extrapolated fall in titer as related to the age of the infant.

Evaluation of Symptoms

Study of the occurrence of symptoms of poliomyelitis in individuals to whom the virus had spread during the first half of the study revealed no illnesses which were attributable to the vaccine strains. For individuals to whom spread was proved by isolation of poliovirus the period 2 weeks prior to the collection of the stool specimen from which virus was first isolated and the 2 weeks following, or until type 2 virus was fed to group A, was classified as pertinent. During this pertinent period gastrointestinal disturbances were reported for one child and one adult; no other illnesses or symptoms were reported.

For persons with serologic evidence of spread, the time period for evaluation of occurrence of symptoms was from the date of feeding of the respective type of virus to group B, the vaccine group, to the date of feeding type 2 vaccine to group A. During this time one child and one adult reported gastrointestinal disturbances, one adult reported a respiratory illness, and one adult reported a respiratory illness and later a gastrointestinal disturbance. Additional members of the 23 families to whom the vaccine strains had spread reported essentially the same rates of respiratory illness and gastrointestinal disturbances as were observed in the study group as a whole (*1*).

In individuals with laboratory evidence of

spread, as well as in members of their families, the gastrointestinal disturbances occurred at the same time (March 9–22) as those observed for the entire study group.

Medical records are presented for the two families listed in table 2 in whom considerable intrafamily spread of the virus appears to have followed the entrance of type 1 vaccine strain into the household. The medical records for family No. 165, two adults and four children, show no illnesses during the entire study period. In family No. 29, two adults and three children, both adults had a gastrointestinal disturbance in the middle of March; one child had a nasal discharge in late February and loose stools on 1 day in late March; one child had loose stools for 2 days in late March; the third child was well throughout the entire study period.

Table 5. Total spread of poliovirus vaccine strains to control group, as evidenced by isolation of virus, serologic response, or both

Persons involved	Total	Vaccine strains							
		Type 2		Type 1		Type 3		Total	
		Number	Percent	Number	Percent	Number	Percent	Number	Percent
Families	74	7	9. 5	8	10. 5	10	13. 4	25	[1] 11. 2
Individuals	266	8	3. 0	14	5. 3	16	6. 0	[2] 36	13. 5
Adults	141	5	3. 5	2	1. 4	4	2. 8	[2] 9	6. 4
Children	95	2	2. 1	11	11. 6	9	9. 5	22	23. 2
Infants	30	1	3. 3	1	3. 3	3	10. 0	5	16. 7

[1] To give total interfamily spread, 100 percent = 74 x 3, since each type could spread as a separate entity.
[2] 2 less than apparent total; evidence of spread of types 1 and 3 poliovirus to 2 adults reduces the person total.

Table 6. Virus isolation rates from stool specimens as a function of antibody status and Salk vaccine experience

Salk vaccine experience	Initial titer less than 4						Initial titer 4 or more					
	0–1 dose			2 or more doses			0–1 dose			2 or more doses		
	Number persons[1]	Virus isolations		Number persons[1]	Virus isolations		Number persons[1]	Virus isolations		Number persons[1]	Virus isolations	
		Number[2]	Percent		Number[2]	Percent		Number[2]	Percent		Number[2]	Percent
Adults:												
Type 1	29	12	41. 4	41	13	31. 7	46	0	0	166	8	4. 8
Type 2	32	12	37. 5	25	3	12. 0	43	1	2. 3	182	13	7. 1
Type 3	39	8	20. 5	65	15	23. 1	36	0	0	141	3	2. 1
Children:												
Type 1	16	14	87. 5	119	86	72. 3	1	0	0	65	28	43. 1
Type 2	16	8	50. 0	53	35	66. 0	1	0	0	131	47	35. 9
Type 3	17	7	41. 2	146	72	49. 3	0	0	0	38	3	7. 9
Infants:												
Type 1	35	28	80. 0	5	4	80. 0	11	10	90. 9	3	3	100. 0
Type 2	30	22	73. 3	5	3	60. 0	16	12	75. 0	3	1	33. 3
Type 3	37	12	32. 4	7	1	14. 3	9	5	55. 6	1	0	0
Total	251	123	49. 1	466	232	49. 8	163	28	17. 2	730	106	14. 5

[1] Total persons who had indicated prevaccine antibody titer and Salk vaccine experience.
[2] Persons from whom isolations were accomplished from at least one of the stool specimens.

Discussion

Using a time interval of about 3 weeks between feedings of the three types of poliovirus the number of virus isolations accomplished would seem to indicate that type 1 virus replaced type 2 and type 3 replaced type 1 very well (chart). The presence of one virus is usually expected to interfere with the establishment of another virus. However, since there was a time lapse of about 1 week between collection of the stool specimens and the feeding of another type of virus, replacement of the virus type is not proved but is strongly suggested by the evidence presented, and is a most striking phenomenon.

The continued excretion of type 3 poliovirus by group B individuals, as shown by isolation of virus from the fifth and sixth stool specimens, is in marked contrast to the small amount of continued excretion of types 2 and 1 poliovirus when followed by the feeding of another type. This long period of excretion may be a characteristic of the type 3 vaccine strain, and it is not known whether type 3 would have been well replaced if fed ahead of types 1 or 2. The possibility must also be considered that the long-continued excretion of type 3 was observed because no other virus was fed, and therefore there was less competition for "lebensraum."

The absence of "wild" poliovirus in this community was demonstrated by the absence of poliovirus in the stool specimens collected prior to feeding the vaccine strains and by the sequential appearance of each type of poliovirus only after each specific type had been fed. Since only 16 cytopathogenic agents (adenoviruses types 1 and 2) other than poliovirus were isolated during this study, the possible effect of enteric viruses other than poliovirus in interfering with the establishment of the vaccine strains of poliovirus has not been measured.

The number of isolations shown in the chart for group B, the vaccine-fed individuals, is not an accurate measure of all persons who excreted virus. The specimens were collected about 2 weeks after virus feeding, and it can be assumed that additional group B individuals excreted virus for shorter periods of time. This assumption is supported by the published results (*1*), which indicate that the proportion of individuals showing antibody response for each virus type was larger than the proportion yielding virus in stool specimens collected 2 weeks after feeding virus. The value of the isolation rates shown in the chart is therefore limited to a comparison of the differences in amounts of virus of each type available for community spread rather than as a graphic representation of the total number of excreters in the community.

The difference in the amount of spread observed with the three types of poliovirus is probably related to the number of susceptible persons in the community (*1*). Considering susceptible persons as those without antibody to poliovirus, the smallest number were susceptible to type 2, and type 2 spread the least; the largest number were susceptible to type 3, and type 3 spread the most. As has been pointed out, we have reason to believe that the spread of type 3 was less completely measured in this study than was the spread of types 1 and 2.

The presence of antibodies in the first blood serum specimen does not always indicate protection against establishment of the vaccine strains in the intestinal tract (table 6). Several investigators have established that Salk vaccine is not effective in preventing multiplication of poliovirus in the intestinal tract. It also appears to be true that antibodies induced by Salk vaccine are not effective in preventing multiplication of the vaccine strains of poliovirus used in this study (table 6).

In the absence of detectable poliovirus antibodies, prior Salk experience does not markedly reduce the virus isolation rates in either adults or children. Differences between naturally acquired antibodies and antibodies induced by Salk vaccine cannot be determined, but it is logical to assume that poliovirus antibodies are natural in origin in adults more often than in children. On the basis of this assumption the differences in virus isolation rates observed in adults and children who have detectable antibodies and Salk vaccine experience are explainable (table 6, last column). If the poliovirus antibodies in the majority of the adults were natural in origin, the low rates of virus isolation which were obtained for the various types (2.1 to 7.1 percent) are to be expected; in a

larger proportion of the children showing antibodies these antibodies can be assumed to have been induced by Salk vaccine because the virus isolation rates are higher (7.9 to 43.1 percent).

Recently, Gelfand and co-workers have reported intrafamily (*4*) and community (*9*) spread of the attenuated poliovirus vaccine strains developed by Sabin. Spread of the vaccine strains was not observed when an attempt was made to observe long-continued interfamily spread (*4*). When experimental design maximized known factors which could be expected to facilitate interfamily spread of virus, only 30 percent of the contact children excreted virus (*9*). These results are basically similar to the very limited extent of community spread reported in this study.

The rate of spread of these vaccine strains of poliovirus can be expected to vary in different communities, and more spread could be expected in this community if a study were conducted during the summer months. There is a need to measure the rate of interfamily spread in a variety of community settings.

The findings reported in this paper suggest that the extent of spread will vary inversely with a community's prior experience with "wild" poliovirus. The immunity-producing potential of live attenuated poliovirus vaccine is such that one can expect that the spread of vaccine strains may also vary inversely with a community's prior experience with live attenuated poliovirus vaccine. It may be practical in the future to maintain immunity to poliomyelitis in a population by administering the oral vaccine to newborn infants and to the family of the infant. Study may later indicate that the feeding of the infants only may be effective in maintaining immune status for a community by the potential the infant has shown as a source of intrafamily spread which would supply booster exposure to the vaccine.

The modest rate of community spread of poliovirus vaccine strains observed in this study indicates that, beyond the households of vaccinees, the benefit of inadvertent immunization against poliomyelitis will be limited.

It is worth repeating that in this study a large proportion of the community participated; members of 20 percent of the households were fed vaccine and an additional 20 percent were studied as contact families.

Summary

The interfamily spread of poliovirus vaccine strains was studied in a community of 371 households. Oral poliovirus vaccine was fed to 279 individuals in 75 families (group B), and placebos were fed to 266 individuals in 74 families (group A). The "supply" of virus available for spread was measured by virus isolations from group B. Spread to the control group (A) was measured by virus isolations and antibody response.

Poliovirus type 2 spread to 8 individuals in 7 families, type 1 to 14 individuals in 8 families, and type 3 to 16 individuals in 10 families. The variation in the rates of spread among the three types of virus appears to be related to the proportion of susceptible individuals rather than to any measurable variation in the potential for spread.

The 38 instances of virus spread involved 9 adults, 22 children and 5 infants, a total of 36 persons, or 13.5 percent of group A.

The 36 individuals were distributed among 23 of the 74 group A families; thus, one or more persons in one-third of the group A families were infected. Each family was usually infected by the natural spread of only one of the three types of virus; therefore, the observed spread represents 11.3 percent of the total potential interfamily or community spread.

These results indicate that the community spread of these poliovirus vaccine strains is markedly less than has been observed for intrafamily spread.

No illnesses attributable to infection with the vaccine strains were observed among the 36 individuals who acquired the poliovirus vaccine strains by natural interfamily spread.

REFERENCES

(*1*) Barr, R. N., et al.: Use of orally administered live attenuated polioviruses as a vaccine in a community setting. J.A.M.A. 170: 893–905, June 20, 1959.

(*2*) Martins da Silva, M., et al.: Studies of orally ad-

ministered attenuated live virus poliomyelitis vaccine in newborns and infants under six months. Univ. Minnesota M. Bull. 29: 133–150, December 1957.

(3) Gard, S., Bottiger, M., and Lagercrantz, R.: Vaccination with attenuated poliovirus type 1, the Chat strain. First International Conference on Live Poliovirus Vaccine, Washington, D.C., June 22–26, 1959. Scientific Publication No. 44. Pan American Sanitary Bureau, Washington, D.C., 1959, pp. 350–354.

(4) Gelfand, H. M., Potash, L., LeBlanc, D. R., and Fox, J. P.: Intrafamilial and interfamilial spread of living vaccine strains of polioviruses. J.A.M.A. 170: 2039–2048, August 22, 1959.

(5) Horstmann, D. M., Niederman, J. C., and Paul, J. R.: Attenuated type 1 poliovirus vaccine; its capacity to infect and to spread from "vaccinees" within an institutional population. J.A.M.A. 170: 1–8, May 2, 1959.

(6) Barr, R. N., et al.: The use of orally administered live attenuated polioviruses as a vaccine in a community setting; a controlled study. First International Conference on Live Poliovirus Vaccine (Washington, D.C., June 22–26, 1959). Scientific Publication No. 44. Pan American Sanitary Bureau, Washington, D.C., 1959, pp. 369–393.

(7) Cabasso, V. J., et al.: Oral poliomyelitis vaccine, Lederle—thirteen years of laboratory and field investigation. An interim review. New England J. Med. 263: 1321–1330, December 1960.

(8) U.S. Weather Bureau: Local climatological data with comparative data, 1958, Minneapolis-St. Paul, Minnesota. U.S. Government Printing Office, Washington, D.C., 1959.

(9) Gelfand, H. M., et al.: The spread of living attenuated strains of polioviruses in two communities in southern Louisiana. Am. J. Pub. Health 50: 767–778, June 1960, pt. 1.

exhibits

SMOKING
Medical Research and Practice

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