STUDIES OF THE DISTRIBUTION OF POLIOMYELITIS VIRUS

V. The Virus in Familial Associates of Cases*

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During the past decade much attention has been directed toward the recovery of poliomyelitis virus from the intestinal tract of individuals afflicted with the disease. In addition, various workers have reported the isolation of virus from apparently healthy persons who were associated, in different degrees of intimacy, with actual cases (1–14). The results of these studies are presented in Table I where it will be seen that of 494 so called contacts, 116, or 23 per cent were excreting virus in their intestinal discharges *at the time of testing.* It must be emphasized that most of the above attempts at isolation were made from single specimens obtained from the individuals several days to several weeks following exposure to a case. The number of individuals positive for virus might have been greater because stool specimens in three of the studies were pooled for testing and more than one individual in some pools might have been carrying virus. Some of the individuals whose stools contained virus suffered minor illnesses which may have been abortive attacks of the disease. Of the associates studied, 277 were identified as either children or adults. Among the children, 69 of 228 (30 per cent) were positive and 8 of 49 (16 per cent) of the adults harbored virus in their intestinal contents.

Lépine and his coworkers (15) reported the successful isolation of virus from the child of a father afflicted with the disease, 41, 74, and 123 days after a mild affection which may have been abortive poliomyelitis. Ward and Sabin (7) found virus in the stool of one sibling at 4 weeks but not at 9 and 13 weeks after a brother's illness; and in the stool of another sibling at 4 and 9 weeks but not at 12 weeks. They considered the possibility that "these siblings might have been the carriers which served as sources of infection." Wenner and Casey (16) reported positive stools collected from a child 2 and 6 weeks following a poorly defined illness but not after 11 weeks. In studies of familial associates of frank cases in Fort Worth, Texas, single specimens were found positive as late as 7 weeks after the onset of the diagnosed cases (10).

The above examples are representative of the few studies in which repeated sampling of associates has been attempted. If the rôle of the familial associate

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as a healthy carrier or a possible source of infection is to be evaluated specimens should be obtained at frequent and regular intervals beginning as soon as possible from the onset of illness in the family. The present report describes the results of such a study.

TABLE I

Recovery of Poliomyelitis Virus from Stools of Associates

	Number positive	Numbernegative
1. Kramer, Gilliam, and Molner (1939)	6	17
2. Trask, Paul, and Vignec (1940)	0	36
3. Kessel, Moore, Stimpert, and Fisk (1941)	1	18
4. Piszczek, Shaughnessy, Zichis, and Levinson (1941)	8	32
5. McClure and Langmuir (1942)	20	7
6. Howitt, Buss, and Shaffrath (1942)	6	25
7. Ward and Sabin (1944)	2	6
8. Brown, Francis, and Pearson (1945)	5	1
9. Gear, Yeo, and Mundel (1945)	2	5
10. Pearson, Brown, Rendtorff, Ridenour, and Francis (1945)	14*	93
11. Melnick, Horstmann, and Ward (1946)	3*	72
12. Gear and Mundel (1946)	7	9
13. Gordon, Schabel, Casey, Fishbein, and Abendroth (1947)	26	22
14. Pearson, Brown, and Rendtorff (unpublished)	16*	35
Total	116	378
Positive, *per cent*	23	

* Specimens pooled—may be greater number positive.

Collection of Materials

Four families residing in Detroit or its environs were selected for study in Sept., 1946. Two criteria were required: first, that the family include at least two children other than the case; and second, that collections could be started within 3 days of onset of illness in a member of the family.[1]

Family I consisted of the parents, both 38 years old, and three children, 3, 7, and 12 years. There was nothing unusual in the activity of the family except for a motor trip through Canada to Connecticut and back, from July 27 to Aug. 11. The child of 7 developed headache and fever on Sept. 4, was diagnosed as having bulbar poliomyelitis on admission to the hospital the next day, and died Sept. 7. It is of interest that an abscessed molar tooth had been extracted 5 days prior to onset. The youngest brother, 3, had been feverish on Sept. 2; otherwise the family had been and were, in good health.

[1] The original information concerning the date of onset of symptoms and diagnosis was made available through the kind assistance of Dr. Franklin Top, Medical Director, and Dr. C. G. Jennings, both of Herman Kiefer Hospital, Detroit, Michigan.

Pharyngeal washings of gargled distilled water from the parents and the oldest boy and pharyngeal swabs from the younger child were obtained on Sept. 6, 9, 13, 20, 27, Oct. 4 and 25, and Nov. 29.[2]

Stool specimens were collected Sept. 8, 13, 20, 27, Oct. 4 and 25, and Nov. 29. No recognizable illness occurred in this family during the period of study.

Family II consisted of the parents, 39 and 36 years old, and four children, 15, 12, 11, and 6 years. The boy, 11, had headache and sore neck but no fever on Sept. 11. The next day nausea and vomiting occurred and on Sept. 13 typical signs of mild bulbar poliomyelitis were noted. He remained at the hospital during the time of the study. The father had a cold and headache on Sept. 11 as did the brother, 15, 3 days later. A sister, 6, had a cold and "sore stomach" on Oct. 4, 20 days after this last incident. No other illness was observed during the period of observation.

Garglings were obtained on Sept. 14, 16, 20, 27, Oct. 4, 11, 25, and Nov. 29. Stools were collected Sept. 16, 20, 27, Oct. 4, 11, 25, and Nov. 29.

Family III consisted of parents, 30 and 27 years, children 8 and 6 years, and their uncle, 22. The father, 30, complained of headache, nausea and vomiting, and had an oral temperature of 101° on Sept. 13. He was hospitalized on Sept. 15 at which time both legs were paralyzed. Ascending paralysis involving the diaphragm, intercostal muscles, and right arm necessitated his being placed in a respirator on Sept. 17 where he remained throughout the period of study. The only other illness observed in the family was a severe headache and nausea experienced by the wife, Oct. 11.

Pharyngeal washings were obtained Sept. 16, 18, 20, 27, Oct. 4, 11, 25, and Nov. 29. Stool specimens were dated Sept. 16–17, 20, 27–28, Oct. 4, 11, 25, and Nov. 29

Family IV consisted of parents, 45 and 44 years, and children 14 and 11. The father, 45, experienced nausea and vomiting on Sept. 12, difficulty in swallowing the next day, and on Sept. 14 a change in voice and other signs of bulbar poliomyelitis necessitated hospitalization where the illness progressed rapidly to death on Sept. 15. The daughter, 14, had complained of nausea and diarrhea on Sept. 10, but seemed perfectly well the next day and her symptoms were attributed to the onset of menses. Nausea recurred with vomiting on Sept. 14 and she was confined to bed with symptoms described as "psychological" as a result of extreme affection for her deceased father. During this period she complained of not being able to walk although her physician could detect no muscular weakness. When this condition persisted, she was admitted to the hospital for examination on Oct. 2 at which time spasms of the hamstrings and left side of back, and weakness of left quadriceps and anterior tibialis were demonstrated. She remained in the hospital for 2 weeks and when discharged was emotionally better, even cheerful and happy, and without paralysis.

The mother and the other child, a boy aged 11, had been well and remained so throughout the period of study.

Throat washings and stools were obtained on Sept. 16–18, 20, 27, Oct. 4–5, 11–13, 24–27, and Nov. 29.

Testing of Materials

All specimens were preserved in refrigerators with solid CO_2 until tested. Individual stool specimens were thawed, a portion ground with alundum, and suspended in physiological salt solution to approximately 10 per cent by weight. The material was agitated daily for 30 minutes on a shaking machine with

[2] The results of virus studies on throat washings are not complete and will be published at a later date. Tests with specimens taken at the time of the first stool collection from all subjects have, however, been completed and the results have been uniformly negative.

20 per cent ether for 6 to 7 days, after which it was centrifuged at 3000 R.P.M. for 30 minutes in a horizontal centrifuge. The ether was removed by evaporation under low pressure, and the specimen was again centrifuged at 4500 R.P.M. for 30 minutes. Both aerobic and anaerobic sterility tests were applied to each preparation and if no bacterial growth was observed the specimen was inoculated into a *rhesus* monkey. An initial intracerebral injection of 0.5 cc. into the vicinity of the thalamus was followed every 2 or 3 days by inoculations of 10 to 15 cc. intraperitoneally and 2 cc. intranasally until the specimen was exhausted. Daily temperatures were recorded and the animals observed for symptoms a maximum of 30 days. All monkeys which developed paralysis were subjected to autopsy promptly and autopsy was performed at the end of 30 days on animals which had shown any suspicious signs such as elevated temperature, irritability, or ruffled fur. A diagnosis of poliomyelitis was made if sections of nervous tissue revealed typical changes including perivascular cuffing, leucocytic infiltration, neuronolysis, and neuronophagia.

RESULTS

The results of this study are presented in Table II. It will be seen that virus was isolated from the stools of seven of the nine children but from none of the seven adults, among the familial associates. The virus was present in the stools of five at the time of the first collection and in the remaining two 4 days later; in all instances within 9 days of onset of recognized poliomyelitis in a member of the family. There was no consistent relationship between a history of illness and the presence of virus. In only one was illness clinically suggestive of poliomyelitis. Hence, the majority of those positive can be considered to represent inapparent or carrier infections. In three individuals (C.M., A.T., and M.A.), the presence of virus in the intestinal tract was detected on each of five successive collections, covering periods of 25, 26, and 36 days, respectively. Stools from an associate (K.M. in family I) yielded virus on the first, fourth, and fifth collections but were negative during both the 2nd and 3rd weeks; second preparations were made from the negative stools and tested in new monkeys with the same results. This irregularity in the detection of the carrier state was observed in a member of family III (R.S.) whose stools were positive on the first and third collections but negative on the second. It is of interest that this second or negative specimen was collected only 3 days after the first, positive stool. Again, these specimens were retested by processing the original stools and inoculating into new monkeys, with identical results.

The stool of an associate in family II (R.T.) was negative on the first collection but one collected 4 days later was positive. This was followed by four negative specimens.

The seventh individual shown to be positive (N.A.) was carrying virus at

the time of the first and second collections but four successive specimens thereafter were negative. This girl was probably an actual case of poliomyelitis but it is of interest that the muscle weakness was observed *following* the two positive collections, and her intestinal excreta were negative for virus at the time of hospitalization.

TABLE II

Detection of Poliomyelitis Virus in Stools of Familial Associates

Family	Age	Sept.					Oct.			Nov.
		8	13	16–17	20	27–28	4–5	11–13	25–27	29
	yrs.									
I. R. M. (case)	7	(onset Sept. 4)								
F. M.	38	○	○		○	○	○		○	
M. M.	38	○	○		○	○	○		○	
K. M.	12	●	○, ○		○, ○	●	●		○	○
C. M.	3	●, ●	●		●	●	●		○	○
II. J. T. (case)	11	(onset Sept. 11)								
A. T.	39			○	○	○	○	○	○	
M. T.	36			○	○	○	○	○	○	
R. T.	15			○, ○	●, ○	○	○	○	○	
J. T.	12			○	○	○	○	○	○	
A. T.	6			●	●, ●	●	●, ●	●	○	○
III. C. S. (case)	30	(onset Sept. 13)								
F. S.	27			○	○	○	○	○	○	
E. S.	22			○	○	○			○	
R. S.	8			○, ●	○, ○	●, ○	○	○	○	
L. S.	6			○	○	○	○	○	○	
IV. C. A. (case)	45	(onset Sept. 13)								
E. A.	44			○		○	○	○	○	
N. A.	14			●	●	○	○	○	○	
M. A.	11				●	●	●	●	●	○

When two results are presented they represent separate tests with the original specimen.
○ = negative
● = positive

DISCUSSION

The presence of virus in a large percentage of healthy familial associates confirms observations published elsewhere. The persistence of this carrier state, however, has not been thoroughly demonstrated nor has the regularity with which virus may be isolated from successive weekly stool specimens. Three individuals were excreting virus consistently over a period of approximately a month following the occurrence of poliomyelitis in the family and a

fourth was shown to be positive for the same length of time except for a period of at least one week when virus was not recovered. The fact that some carriers may apparently lose that capacity only to regain it is verified by the results with another individual who was found positive on the first and third collections but negative on the second and from the fourth till the end of the study. This irregularity in the excretion of virus by carriers illustrates the difficulty of establishing the percentage of healthy individuals positive for virus when observations are based on single specimens. It may also explain certain differences in percentages reported by various investigators.

It is of interest that healthy carriers in this study were found to be positive for a period of time considerably longer than in the one probable non-paralytic case (N.A. in family IV), whose stool was negative at the time of onset of muscle weakness. This is in keeping with an impression gained earlier in this laboratory that the well carrier maintains virus more consistently than the frank paralytic case of poliomyelitis. The question arises as to whether this individual developed poliomyelitis as a result of exposure to the healthy carrier in her family or was otherwise exposed simultaneously with her father who succumbed to the infection. Evidence for the actual development of the carrier state from another carrier is suggested in only one instance (R.T. in family II) and even here it is not indicated whether the significant exposure was to the carrier (A.T.), to the frank case in the family, or to a common source to which all three were related. The results as a whole point out the probability of simultaneous infection of the family group, rather than serial transmission, a fact emphasized in other studies from this laboratory.

It should be remarked that although single monkeys were used for most of the specimens, the regularity with which a person was either positive or negative week after week speaks well for the efficacy of this method for detection of virus in stools. This was, moreover, a year in which virus was sharply effective in producing disease of monkeys. The several results which at first cast suspicions on the technique, *i.e.* individuals found positive then negative then positive, were verified by means of reworking the original specimens and inoculating new monkeys. Of ten such specimens which were retested, identical results were obtained with seven and the remaining three probably contained such small amounts of virus that isolation from a given sampling was chance.

If approximately one-fifth of all the familial associates of a case of poliomyelitis are carriers, (23 per cent from Table I), and if each case has from five to ten associates, the number of silent carriers in a given population must be equal to, or at most, twice, the number of cases and not 10 or a 100 times the number as theoretically advanced by some individuals. And since most of these carriers will be found among the familial or close associates (8, 10, 13, and present report) and not among the population at random (10, 16, 17)

it is increasingly evident that measures directed toward the control of infected individuals would be most profitably applied to families in which cases of the disease have been recognized.

SUMMARY AND CONCLUSIONS

The occurrence and duration of the carrier state in familial associates of recognized cases of poliomyelitis was studied by the examination for virus of stool specimens collected from the members of four families at regular intervals for a period of over 2 months. The results indicate that: (1) virus may persist in their stools continuously for 4 to 5 weeks; (2) virus may be encountered intermittently in the stools; (3) in some instances virus may be present for brief periods only; (4) children are more likely to maintain virus than are adults in the same family; (5) infection of a family takes place rapidly, suggesting again simultaneous infection from a common source.

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