THE DETECTION OF POLIOMYELITIS VIRUS IN SO CALLED ABORTIVE TYPES OF THE DISEASE

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PLATE 19

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In another publication dealing with certain clinical and epidemiological aspects of poliomyelitis (1), we have discussed the rôle which so called abortive cases may play in the spread of this disease and have pointed out that discussions dealing with so called abortive poliomyelitis demand a definition of this rather loose term. Definitive statements are necessary because there is little unanimity of opinion as to what constitutes abortive poliomyelitis, although popular and practical usage today tends to designate those cases as abortive, in which signs pointing to meningitic or myelitic involvement exist, but in which no paralysis develops. In other words this concept rests upon the tenet that one cannot diagnose clinical poliomyelitis in the absence of signs pointing to meningitic or myelitic involvement. This is quite different from the view originally proposed by Wickman (2). He felt that the abortive types of poliomyelitis might be manifest by such minor symptoms as fever of short duration, sore throat, headache, and vomiting, and that these symptoms might be the only manifestations of the disease. In his experience the abortive types were one-third as frequent as the frank cases, but he quoted certain estimates, made during epidemics, in which abortive cases outnumbered the frank cases. Draper reflects this same concept intimating that the first phase of the "dromedary" form of clinical poliomyelitis which is often characterized merely by headache, fever, sore throat, and listlessness, may be the only recognizable phase of the disease in 50 to 80 per cent of all cases of poliomyelitis (3). The obvious difficulty of subjecting this situation to analysis is that such nondescript symptoms as those just mentioned do not furnish a clinical picture

which can be readily identified, and probably this is the reason why most physicians are unwilling to make a diagnosis of either poliomyelitis, or abortive poliomyelitis, in the absence of tangible specific signs; namely, signs pointing to meningitic or myelitic involvement. In any event the question of uncertainty has excluded such cases from statistics on poliomyelitis (4, 5), although it is needless to point out, that, if the disease is thus limited, such a concept will enormously influence views not only on its epidemiology but also on its fundamental nature.[1] Unfortunately the problem of definition of abortive poliomyelitis is far from settled, and the uncertainty which has clouded Wickman's original contentions, and Draper's subsequent concepts is that the clinical entities they embrace are vague, and their relation to poliomyelitis is based essentially on circumstantial evidence. Furthermore, although many have suspected that it is through the abortive cases that the mass immunization of most adult populations to poliomyelitis occurs, this contention has apparently resisted recent experimental proof (6).

In our own studies on these problems (1), which were made in New Haven during the summer of 1931, we were immediately confronted with the numerical importance of possible mild and fleeting attacks of the disease and the problems which they offered in the field of practical clinical medicine and epidemiology. It seemed to us that common usage of the term abortive poliomyelitis had in the past proved so ambiguous, that, to define the issues in this disease, we would employ instead the term *characteristic minor illness*, in association with poliomyelitis, so that ground might be cleared for a de-

[1] Almost 20 years ago Frost discussed this question in the following terms.

"The inclusion of definite abortive cases more than doubles the secondary attack rate. The inclusion of suspected abortive cases more than quadruples it, giving to poliomyelitis an apparent contagiousness comparable to that of scarlet fever and diphtheria, diseases which are generally considered highly contagious. It is evident, therefore, as stated before, that the question of contagiousness of poliomyelitis as determined by epidemiologic studies, hinges largely upon the question of which are and which are not cases of poliomyelitis. To omit from epidemiologic studies cases without paralysis, to use a somewhat exaggerated simile, is like undertaking to study the epidemiology of typhoid fever by considering only cases of hemorrhage. The inclusion of cases without paralysis is, on the other hand, open to the very reasonable objection that the epidemiology of the disease may thereby be confused by the consideration of cases in no way related to the disease in question" (5).

finitive study. Essentially these *characteristic minor illnesses* owe their identity merely to the fact that they appear during an epidemic of poliomyelitis. We have reviewed the clinical symptomatology of a series of 136 examples of these illnesses in another publication (1). This analysis revealed little whereby they might be identified clinically, although, as Draper has pointed out, there is a close similarity between their symptomatology and that of the first phase of the "dromedary" form of clinical poliomyelitis. Our estimates (1) of their relative frequency showed that (*a*) in a large series of families these characteristic minor illnesses developed in about 40 per cent of children under 5 with familial exposure to poliomyelitis, as opposed to a 4 per cent incidence of secondary familial cases of frank poliomyelitis in the same group of families; or, in other words, in this selected group the former were about ten times as frequent as the latter; and (*b*) in each of three communities in which estimates were made during the epidemic period, these examples of minor illness were six times as frequent as the frank cases of poliomyelitis. However, the most significant observation of this study was the detection of the virus of poliomyelitis in the nasopharynx of two children suffering from these characteristic minor illnesses and in the present communication details of its detection and isolation will be given. We believe that this finding furnishes more than circumstantial evidence that there is a common causal relationship between frank poliomyelitis and illnesses corresponding to Wickman's abortive types.

In order that the experiments to be described may be compared with previous studies dealing with the isolation of the virus of poliomyelitis from the human nasopharynx, the literature on this subject will first be reviewed.

Review of the Literature on the Isolation of the Virus from the Throat

(*a*) *Frank Cases.*—Shortly after the earliest successful experiments upon the transmission of poliomyelitis to monkeys and with the development of strains of the virus which were highly potent for monkeys, Flexner and Lewis (7) succeeded in 1910 in isolating the virus from Berkefeld filtrates of extracts of the nasal mucous membrane excised from monkeys suffering with the experimental disease. The corollary to this experiment or the isolation of the virus from human tonsillar tissue and pharyngeal mucosa obtained from a fatal case of poliomyelitis, was soon supplied by Landsteiner, Levaditi, and Pastia (8). At about the same time

Flexner and Clark (9) reported several similar human isolation experiments of this type, drawing attention to the fact that when they injected filtrates of the tonsillar and nasal tissues, they were unable to recover the virus; but when the same unfiltered material was rendered bacteria-free with 0.5 per cent phenol, the virus could be recovered. Subsequently it has become a well established fact that poliomyelitis virus may be detected in washings from the throats of acute cases of frank poliomyelitis, but rarely from human throats under other conditions.[2] Lucas and Osgood (11) have isolated it from the throat of a child, 4 months after the acute stage of a second attack of poliomyelitis, but as far as we know this is the only example of the human convalescent carrier in this disease.

(*b*) *Healthy Carriers.*—To our knowledge there are but two examples of the detection of the virus in nasopharyngeal washings taken from healthy familial contacts (12, 13). In the observation of this type reported by Flexner, Clark, and Fraser (12) definite success was obtained in one instance, which will be described in some detail.

Pooled saline washings (about 150 cc.) were obtained from both parents of a child who had recently had poliomyelitis. These washings were taken on the 16th day after the onset of their child's case. The fluid was shaken and passed through a Berkefeld filter and 1.5 cc. was injected the same day into the sheath of each sciatic nerve and 140 cc. into the peritoneal cavity of a monkey who subsequently developed poliomyelitis. The virus thus isolated was passed to subsequent monkeys. The authors concluded that the parents of a known case of poliomyelitis, neither of whom showed any symptoms of illness, harbored the virus in the nasopharynx.

A year later Kling and Pettersson (13) reported a single instance of the successful isolation of the virus from pooled washings taken from four healthy members of a family in which one member had recently died of poliomyelitis. The washings were obtained on the 5th day from the onset of the fatal case and were injected into a monkey intracerebrally and intraperitoneally 15 days later. The investigators used large quantities of washings amounting to 1 liter of fluid, which they subsequently filtered through a Berkefeld candle after concentrating the material to 75 cc. by vacuum distillation at 35–38°C. The experimental disease was induced in the monkey inoculated with this material and the virus was successfully passed to a second monkey.

Knowledge concerning the healthy human carrier of the virus of poliomyelitis rests largely upon the results of these two observations both of which were obtained with pooled washings. The number of similar attempts to isolate the virus

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[2] We have recently gone over the well known work of Kling, Pettersson, and Wernstedt (10), who reported the detection of poliomyelitis virus from a rather high percentage of examples of minor illnesses and from healthy contacts. The criteria which these authors used for the detection of the virus are so different from those in use today that it is difficult to evaluate their results.

from healthy contacts is not known, but it is probable that failures greatly outnumber positive results. It is evident, of course, that the significance of our own attempts (subsequently described in this paper) to demonstrate the virus in minor illnesses contemporary with familial or community cases of poliomyelitis could be best evaluated if we knew the healthy carrier rate, but unfortunately this information is still lacking.

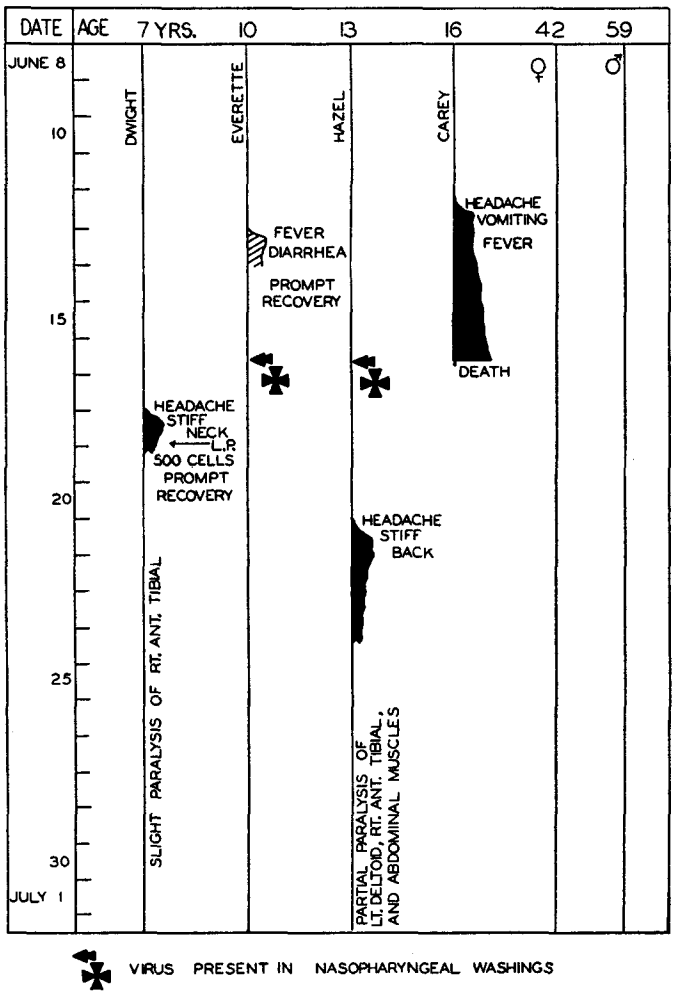
(*c*) *Abortive Cases.*—The literature affords few examples of the isolation of the virus of poliomyelitis from so called abortive cases. The claims of the Swedish investigators (10) were that from seven examples of minor illnesses occurring in association with poliomyelitis, the virus was isolated in two instances, but a careful analysis of their results would lead us to believe that a single questionably positive result was obtained from this group.

On the other hand there is a single noteworthy example of the successful isolation of the virus by Taylor and Amoss (14) from the throats of two members of a poliomyelitis family including (*a*) a case of minor illness or abortive poliomyelitis, and (*b*) a child, 5 days prior to the development of a mild case of frank poliomyelitis. In their family study the clinical events were so similar to many of those in our recent experiences that they will be transcribed from their paper in some detail.

The family which lived in the village of Waitsfield, Vermont, consisted of the parents and four children (see Text-fig. 1). On June 12, 1917, the oldest boy, Carey, developed poliomyelitis with initial symptoms at first thought to be those of a gastrointestinal upset. Extensive paralysis was present on the 4th day of the disease and death occurred on this date. On June 13 the next boy, Everette, developed what was probably a characteristic minor illness, marked by fever and diarrhea. He recovered quickly and, subsequently on minute examination, showed no muscular weakness. The youngest child, Dwight, became ill on June 18, and the girl, Hazel, on June 21. Both of these illnesses proved to be mild attacks of poliomyelitis, although, if it had not been for the fact that particular attention had been attracted to this family by the presence of a fatal case of poliomyelitis in the oldest member, it seems questionable whether the other cases would have been readily diagnosed. In other words it is conceivable that they could have passed as examples of "summer grippe," etc., had not careful examinations been done in both instances.

Nasopharyngeal irrigations were obtained from two of the children,—Everette and Hazel, — on June 16; *i.e.*, 4 days after the former had developed symptoms of a minor illness, and 5 days before the latter developed symptoms of a mild attack of poliomyelitis. The material obtained was treated in the following manner. Distilled water was used as the irrigating medium, 60 cc. for Everette, and 100 cc. for Hazel. To the sample washings 10 per cent of ether was added; they were then shaken with glass beads for 2½ hours, and centrifuged at high speed for 2½ minutes. The supernatant fluid was passed through a Berkefeld N candle and concentrated to 2 cc. *in vacuo* at 35°C. This amount was injected intracerebrally into two *rhesus* monkeys (A—Everette, and B—Hazel) within 6 hours after the collection of the specimens.

Both monkeys developed paralyses. Monkey A recovered, its sera was subsequently shown to be capable of neutralizing poliomyelitis virus, and the animal itself was resistant to the reinoculation of a large dose of virus. Monkey B was sacrificed on the 9th day after inoculation. The histological picture of the spinal cord and medulla was that of poliomyelitis, and emulsions of these organs were capable of inducing the disease in another monkey.



TEXT-FIG. 1. Schematic diagram of a family study reported by Taylor and Amoss (14). The vertical lines represent individual members of the family; their respective ages appear at the top. The solid areas roughly indicate the clinical course of an attack of poliomyelitis; the shaded area, the course of a minor illness.

The observations quoted above are of great importance. Here again the number of times that attempts of this kind have been repeated, and the number of unsuccessful attempts to isolate the virus from cases with mild or abortive poliomyelitis either by these or other workers is unknown, but the reported successes are sufficiently small to suggest that its isolation from such cases is not easy.

Methods

Prompted by the results of Taylor and Amoss (14) we followed somewhat the same procedure in our own attempts to isolate the virus from examples of characteristic minor illnesses occurring coincidentally either within a family, or within a small community in which poliomyelitis was present. In general the following procedure was employed.

Preparation of Material for Inoculation.—The patient was instructed to gargle the throat with 25 to 125 cc. of sterile distilled water, or it was washed through the nasopharynx by means of a syringe inserted into the nares. The washings thus obtained were transferred to a flask containing glass beads, 10 per cent of ether was added, and the flask was shaken for 15 minutes. The material was then usually concentrated by vacuum distillation at 37°C. for a period of from 4 to 7 hours,—by this procedure we were seldom able to reduce the washings to less than a fourth of their original volume. To the concentrated washings phenol was added to make a concentration of 0.5 per cent and the material was allowed to stand for ½ hour. This step in the procedure was employed in preference to filtration because of the experiences previously reported by Flexner and Clark (9); it has also been subsequently shown that the virus may remain active in this concentration of phenol for many months (15).

All inoculations were done under ether anesthesia. One monkey was employed for each of the tests, which were done by the intracerebral route, using between 0.8 to 1.2 cc. of the concentrated, phenolized washings as the amount of inoculum. Bidaily temperature readings covering a period of 3 weeks were taken on all monkeys thus inoculated. Of the twenty monkeys employed for the experiment, sixteen were *Macacus rhesus*, four were of other varieties listed in Table I. One monkey inoculated with material from a healthy contact succumbed on the 6th day from a brain abscess and has not been included in the table.

Various alterations were made from time to time in our methods of obtaining and treating the washings prior to their inoculation. These consisted in (*a*) attempts to reduce the volume of the irrigating fluid by washing about 30 to 40 cc. of saline solution through and through the nasopharynx; (*b*) the concentration of the material by ultrafiltration through collodion sacs. In the latter procedure we were guided by the belief that the virus was not diffusible through the collodion mem-

branes we employed. It may suffice to say, however, that the procedure first outlined was the one in which our two positive results were obtained.

Selection of Cases

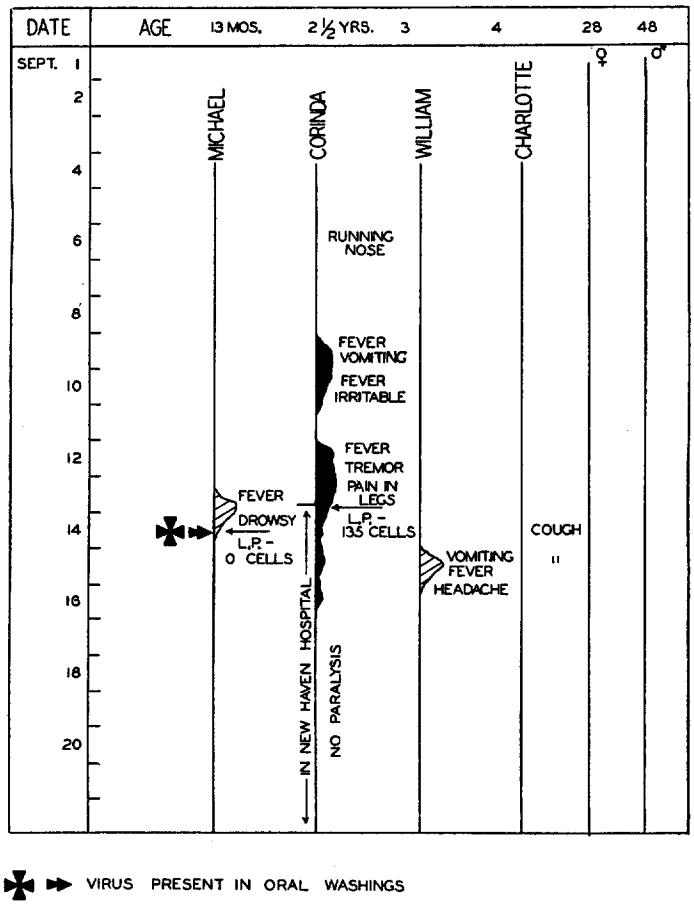
It was our object to select and test oral washings on patients who developed a characteristic minor illness (comparable to one of Wickman's abortive types), under circumstances in which known exposure to a case of poliomyelitis had existed; and to compare the results with findings similarly obtained from known patients with poliomyelitis, and from healthy contacts. Text-figs. 2, 3, and 4 are sample diagrammatic representations of some of the situations under which our washings were obtained.

In Text-fig. 2 is shown a family with four children,—Family Rn. In this family a frank case of poliomyelitis occurred which was followed closely by two cases of characteristic minor illness in two other children. In one of the latter, the most prominent symptoms were fever and drowsiness; in the other, vomiting, fever, and headache. Both of these children were well within 36 hours of the onset of symptoms. In the youngest child (Michael), however, the symptoms were sufficiently suspicious to warrant a diagnostic lumbar puncture which proved negative. At the time the puncture was done nasopharyngeal washings were also obtained.

In Text-fig. 3 is shown another family,—Or. In this family which is composed of six children, there occurred one case of frank poliomyelitis (Irving); one suspected case (Frances); and two examples of characteristic minor illness (Evelyn and Charles). The series of small black arrowheads, which appear as legends in this figure, indicate that on September 16, washings were obtained from the child Irving, supposedly on the 1st day of an attack of poliomyelitis; two children Evelyn and Charles, who were on the 3rd day of a minor illness; and one child Edward, who was presumably a healthy contact.

In Text-fig. 4 a diagram is shown portraying events in one of the communities in which similar studies were made. This community consisted of a summer colony situated on the shore of Long Island Sound in fairly close proximity to New Haven. All of the juvenile members of the group have been portrayed as vertical lines, denoting by their length the period of time in which they were members of the

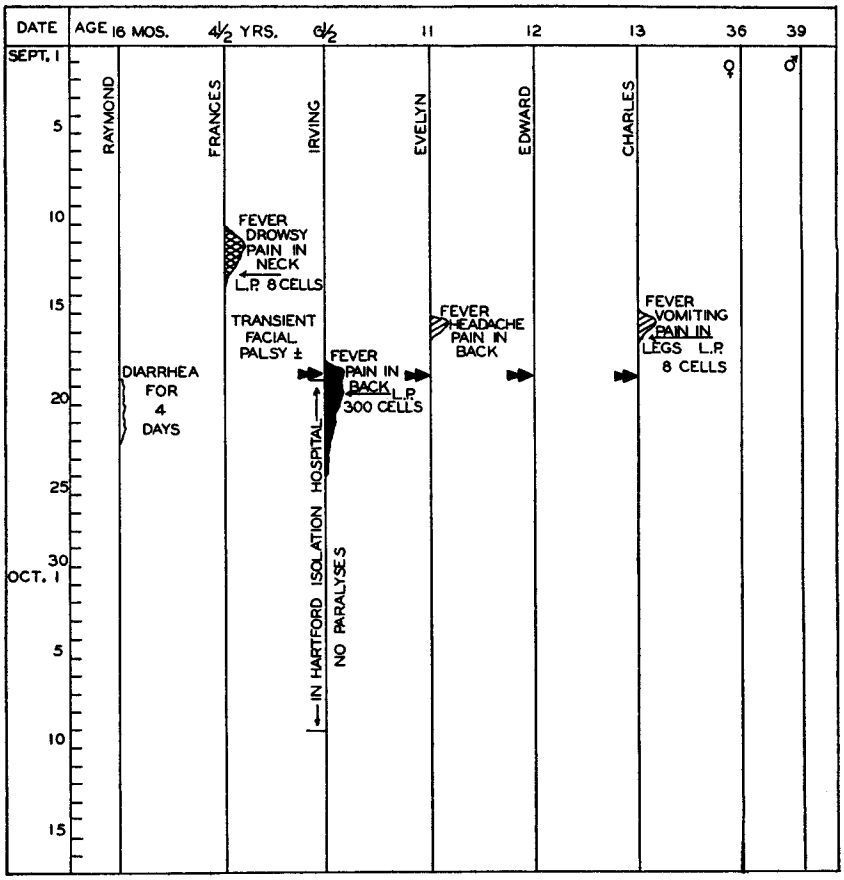
group. Illnesses have been recorded by the legends used in the previous figures. It will be seen that the population was not fixed, in that families were constantly moving in or out. During late July and early August several cases of mild illness, characterized by sore



TEXT-FIG. 2. Diagram of Family Rn. The legends are the same as those in Text-fig. 1.

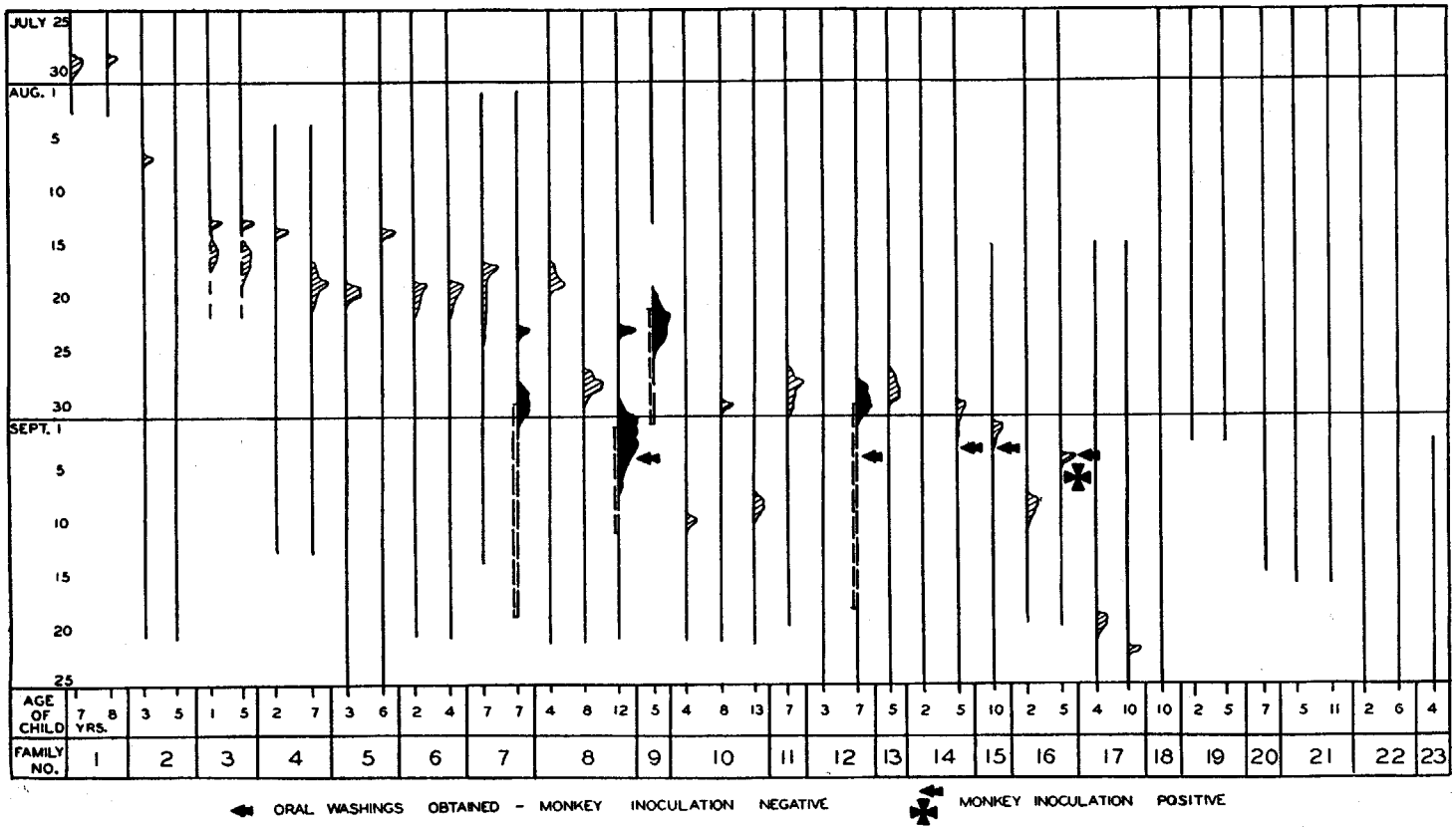
throat, fever, vomiting, and headache appeared among the children, but although there was considerable apprehension by attending physicians and the community itself, as to whether these illnesses might be poliomyelitis, symptoms did not appear at first from which

a definite diagnosis could be made, and for want of a better term they were labelled "summer grippe." However, on August 20 a child from Family 9, who had left the summer colony the week before, developed poliomyelitis, and shortly thereafter three other cases



TEXT-FIG. 3. Diagram of Family Or. The black arrowheads indicate the time at which oral washings were obtained.

appeared among members of the colony in rather rapid succession. Meanwhile the "summer grippe" continued. Three out of seven children who contracted it during September, had arrived in the community subsequent to August 15. In all, therefore, out of 41 children



TEXT-FIG. 4. Diagram of the juvenile members of a community in which an epidemic of poliomyelitis occurred during the summer of 1931. All of the community children under 15 years of age appear as vertical lines, their length designating the period in which they were members of the community. The double set of divided lines indicates hospitalization; otherwise the legends are the same as those used in the previous diagrams.

in the colony there were 29 instances of acute illness between July 30 and September 22. Four of these illnesses were examples of frank poliomyelitis. Many of the others merely consisted of fever, headache, and vomiting lasting for only a day; but some were of several days' duration; others presented two distinct phases, and not a few offered real problems in the differential diagnosis of frank poliomyelitis. It will be seen in Text-fig. 4 that five oral washings were obtained from this group. They include two cases of poliomyelitis (one of which was in the convalescent stage), representing Families 8 and 12 respectively; three children with so called "summer grippe" at various stages of the disease, representing Families 14, 15, and 16; and one healthy contact, a 16 year old nurse girl, who, owing to her age, does not appear on the chart. The virus was detected in one of these washings, namely, the older child from Family 16 whose throat was irrigated within a few hours after he had come down with an attack of fever and vomiting on September 4. He was symptom-free within 24 hours of the onset of his illness.

RESULTS

From a series of twelve attempts to isolate the virus in early and late stages of these characteristic minor illnesses in association with poliomyelitis, we were successful in two instances.

The circumstances under which the washings were obtained have already been given in Text-figs. 4 and 2 respectively. A brief account of the actual clinical events which transpired in these cases was as follows:

Robert We., aged 5, (*cf.* Text-fig. 4) had been exposed during the period of Aug. 20 to Aug. 29 to three cases of poliomyelitis. At noon on Sept. 4 he became ill with fever and vomiting; these were the symptoms which many children in this community had had during the preceding 6 weeks. At 5:00 p.m. on Sept. 4, oral washings were obtained. This material was inoculated into Monkey 22 that same evening. The child was well by the following morning. The monkey developed the experimental disease.

Michael Rn., aged 13 months, (*cf.* Text-fig. 2) had been exposed to his sister Corinda, who was admitted to the New Haven Hospital suffering from poliomyelitis on Sept. 13. She was then in the 6th day of her disease. On the same day Michael became ill with fever and drowsiness and on the evening of the following day he was brought to the New Haven Hospital under the suspicion that he also

might have poliomyelitis. A lumbar puncture was done at this time, which showed no cells and a negative test for globulin by the Pandy test. Oral washings were obtained at this time. The child was well by the following morning,—Sept. 15. The washings were inoculated into Monkey 29, which subsequently developed the experimental disease and will be described later.

Our results have been analyzed in a number of ways. The first analysis appears in Table I. Here are included data which bear on the evidences of exposure to poliomyelitis in the cases studied; the results of lumbar punctures made on the day on which most of the washings were obtained; methods and technique of obtaining and treating the washings; and the immediate or subsequent fate of the monkeys employed. The experiments were run in three sets, in each of which we attempted to include (*a*) cases of characteristic minor illness with exposure to poliomyelitis, (*b*) frank cases of poliomyelitis, (*c*) contacts. Successful results in obtaining the virus were encountered only in the first set, and only with the characteristic minor illnesses. In none of the three cases of frank poliomyelitis did we succeed in isolating the virus, and in none of the contacts.

A further analysis has been made which concerns the day of the disease on which the washings were obtained. This appears in Table II. Here it will be readily seen that our two successful attempts to isolate the virus from the minor illness cases occurred from material obtained on the 1st and 2nd days of the disease; that a single attempt made on the 1st day was successful, and that one out of four attempts made on the 2nd day was successful; the remaining seven attempts made on subsequent days were all negative. There is, however, a further point, best shown in Text-fig. 5 which may be of some significance; namely, that of the four irrigations done on the 2nd day of the disease, two were obtained while the patient was still having symptoms, and two after symptoms had subsided. One of the two having symptoms on the 2nd day of his minor illness harbored the virus, while from neither of the two whose symptoms had subsided was the virus demonstrated. It is unfortunate that we were unable to isolate the virus from oral washings obtained from the three frank cases of poliomyelitis. In two of them the irrigation was probably done too late in the disease, but in one (see Text-fig. 3) the circumstances should have been satisfactory for its detection.

TABLE

Various Procedures Employed in Obtain

No. of experiment	Patient	Clinical aspects of case				Technique		
		Age	Evidence of exposure to poliomyelitis	Day of illness	No. of cells in spinal fluid	Method of collecting material for inoculation	Amount of washings	M
		yrs.					*cc.*	
Experiment 1, started Sept. 4, 1931	Minor illnesses							
	We.	5	4 nearby cases	1	Not tested	Throat rinsed with water	25	N
	Rn.	1	Case in family	2	0	Throat and nose irrigated with water	100	V
	Bt.	7	4 nearby cases	2	Not tested	Throat rinsed with water	150	
	Pn.	10	4 " "	4	" "	" "	250	
	Ld.	5	4 " "	5	" "	" "	100	
	Ln.	5½	4 " "	13	0	" "	100	
	Poliomyelitis cases							
	Ks.	7		9	38	Throat rinsed with water	125	V
	Gn.	12		13	91	" "	125	
	Contact							
	L. N.	16	Taking care of case		Not tested	" "	150	
Experiment 2, started Sept. 20, 1931	Minor illnesses							
	Ev. O.	11	2 cases in family	4	Not tested	Throat rinsed with saline	70	U
	C. O.	13	" "	4	8	" "	50	
	Poliomyelitis							
	I. O.	6½		1	300	Throat rinsed with saline	50	U
	Contact							
	E. O.	12	2 cases in family		Not tested	" "	100	
Experiment 3, started Oct. 3, 1931	Minor illnesses							
	R. B.	6	In New Haven, fall, 1931	3	4	Throat and nose rinsed repeatedly with saline	20	N
	P. L.	7	" "	2	4	" "	20	
	E. M.	6	" "	2	3	" "	100	
	E. W.	11	In Westport, Conn., fall, 1931	3	5	" "	40	
	Contact							
	Sister of P. L.	10	In New Haven, fall, 1931		Not tested	" "	20	
	Brother of E. W.	7	In Westport, Conn., fall, 1931		" "	" "	40	

* This monkey together with several others of the same species was probably suffering from some

inoculation			Result of monkey inoculation		
thod of concentrating washings	Final volume of washings	Interval between collection of washings and inoculation	No. of monkey inoculated and species	Symptomatology of monkey	Autopsy	Susceptibility to subsequent inoculation with poliomyelitis virus
	cc.	*hrs.*				
concentration	25	4½	22, *Macacus rhesus*	Fever 13th day; paralysis 16th day	Typical poliomyelitis	
cuum distillation	20	17	29, " "	Fever 7th day; paralysis 12th day	" "	
" "	100	11	20, " "	Negative	Negative	
" "	150	10	21, " "	"		Yes
" "	60	10½	24, " "	"		"
" "	20	42	28, " "	"	"	
cuum distillation	100	5	26, *Macacus rhesus*	Negative		Yes
" "	100	5	23, " "	"		"
" "	50	10	25, " "	"		"
ltrafiltration	5	48	30, *Cercocebus lunulatus*	Negative	Negative	
"	4	48	33, *Lasiopyga callitrichus*	"		Yes
ltrafiltration	4	48	31, *Lasiopyga callitrichus*	Negative	Negative	
"	5	48	32, *Erythrocebus patas*	Weak and ill,* no fever	"	
o concentration	20	3	18, *Macacus rhesus*	Negative		Yes
"	20	4	19, " "	"		Not tested
"	100	16	25, " "	"		Yes
"	40	2	43, " "	"		"
"	20	20	16, " "	"		"
"	40	40	42, " "	"		"

ype of dietary deficiency.

Evidences of Poliomyelitis in the Monkey.—It is pertinent to recall at this point that the intracerebral inoculation of human or monkey material containing the virus of poliomyelitis does not invariably produce the disease in the monkey (9, 16), and that the experimental disease induced in monkeys by human strains is considerably milder than that obtained with so called fixed monkey virus. We were, therefore, fortunate in obtaining what appear to be definite results in our two positive monkeys.

TABLE II

Summary of Results of Monkey Inoculations with Oral Washings

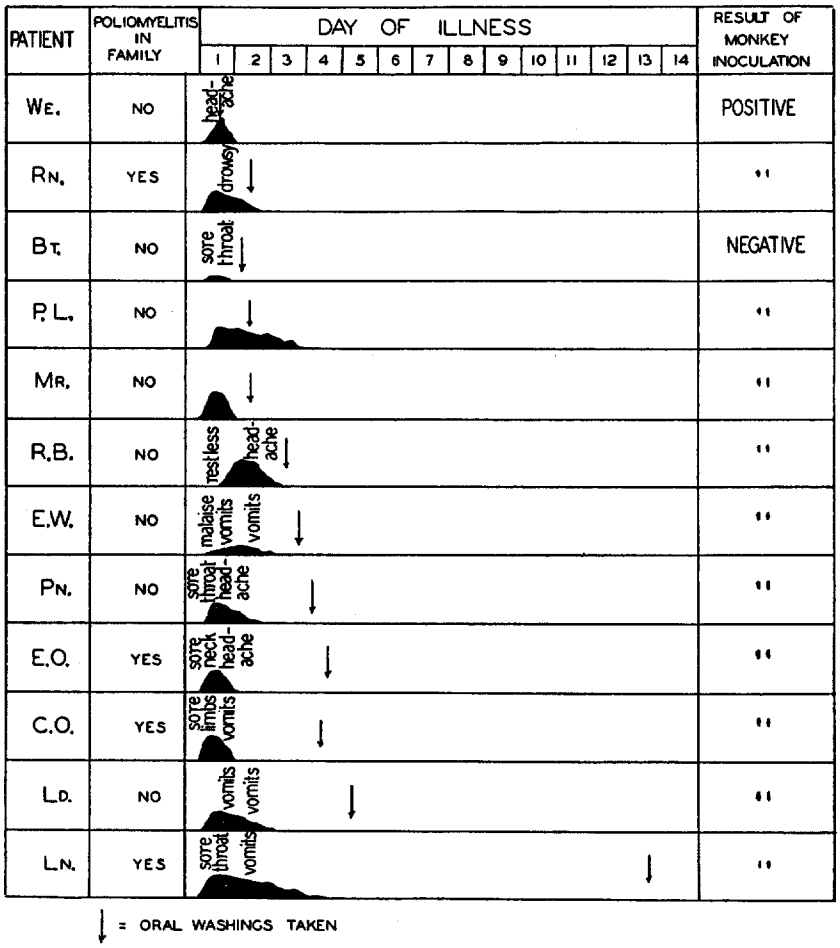
	Day of illness or contact on which washing was done							Total
	1	2	3	4	5	6–10	11–15	
Minor illness								
No. of cases	1	4	2	3	1	1		12
No. of positive results	1	1	0	0	0	0		2
Contacts								
No. of subjects		1*	1*	1*				3
No. of positive results		0	0	0				0
Poliomyelitis								
No. of cases	1					1	1	3
No. of positive results	0					0	0	0
Contacts								
No. of subjects	1*							1
No. of positive results	0							0

* The day of contact represents the day numbered from the onset of the last case to which the subject was intimately exposed.

Four criteria have been used as evidence of poliomyelitis in the inoculated monkeys: (*a*) the temperature curve; (*b*) the development of paralysis; (*c*) the findings at autopsy; and (*d*) the passage of the disease to other monkeys.

Temperature Curves.—The characteristic temperature curve which is exhibited by monkeys infected with standard strains of poliomyelitis virus has been described by Kramer, Hendrie, and Aycock (17). These authors call attention to the fact that there may be an immediate

brief rise in temperature following inoculation, but this usually does not last beyond the first 24 hours. The incubation period or period



TEXT-FIG. 5. Diagram showing twelve examples of minor illnesses from which oral washings were obtained. The solid areas roughly indicate the course of the disease as reconstructed from temperature readings.

of normal temperature prior to the onset of the true experimental disease generally lasts 4 to 8 days, but at times as long as 18 to 21 days. With the onset of the disease there is an abrupt rise in tem-

perature reaching 104–107°F. Fever may persist from 1 to 3 days before the onset of the usual recognizable symptoms, such as paralysis. With the appearance of these symptoms the temperature is already declining and when paralysis is extensive there may be a pronounced drop to subnormal values.

In Text-fig. 6 are shown the temperature charts of the two monkeys in which the experimental disease was produced. The experimental protocols read as follows:

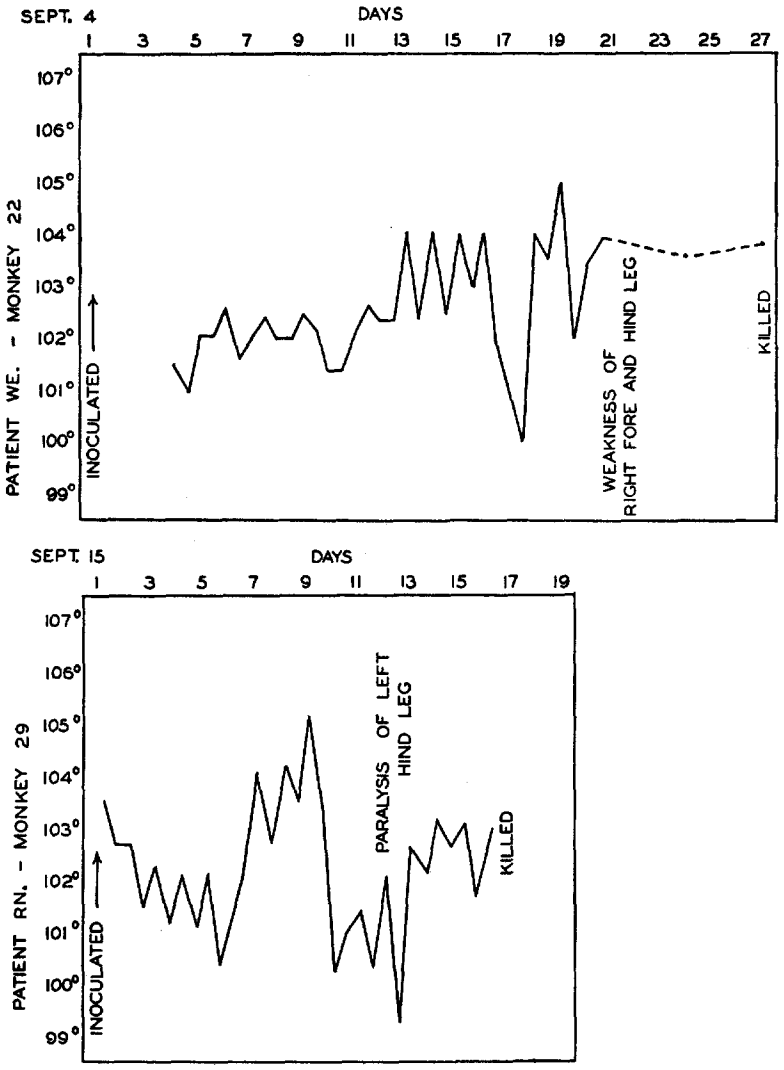
Monkey 22—Patient We. 20 cc. of oral washings were obtained on Sept. 4, 0.5 per cent phenol was added, and 1.2 cc. was inoculated intracerebrally a few hours later on the same day. For 12 days the temperature fluctuated between 101° and 102.6°. On the 13th day it rose to 104° and fluctuated between 102° and 104° for 4 days, falling abruptly to subnormal on the 17th day. It is possible that paralysis may have developed at this time but it was not definitely noted until 3 days later when it became evident the animal was not using the right arm, and that the right leg was weak. The animal was sacrificed on the 27th day. The autopsy revealed typical lesions of poliomyelitis in the spinal cord (*cf.* Fig. 1).

Monkey 29—Patient Rn., 100 cc. of oral washings were obtained at 10:00 p.m. on Sept. 14 to which 10 per cent of ether was added and the material was left in the ice box overnight. On the following day it was concentrated to one-fifth its original volume by vacuum distillation over a period of 5 hours at 37°C.; 0.5 per cent phenol was added; and 1 cc. of the material was inoculated intracerebrally into this monkey at 3:00 p.m. Sept. 15. The monkey's temperature gradually fell over a period of 6 days and then underwent a rapid rise of 3–4°. This febrile period lasted 4 days, to be followed by a sharp drop on the 10th day after inoculation, with an irregular return to normal values. On the 12th day it was first noted that the animal dragged the left hind leg. Subsequent examinations revealed complete paralysis of this limb. The animal was sacrificed on the 17th day. The autopsy revealed typical lesions of poliomyelitis in the spinal cord (*cf.* Fig. 2).

Several of our other monkeys, which failed to show evidences of the experimental disease, were sacrificed and studies of the tissues were made. In none of these did we find evidences of poliomyelitis (*cf.* Table I). Practically all of the remaining, surviving monkeys were subsequently tested and found susceptible to infection with a standard strain of poliomyelitis virus.[3] It seems pertinent to add,

[3] We are indebted to Drs. W. H. Park and E. R. Weyer of the Bureau of Laboratories, Department of Health, City of New York, for this strain of virus. It is a mixed strain derived from several sources.

however, that the latter procedure may not be as satisfactory a test for immunity to poliomyelitis in the monkey as was once believed, for recent work by Australian investigators has shown that wide differences may exist between different strains of the virus (18).



TEXT-FIG. 6. Temperature curves in Monkeys 22 and 29 in which the experimental disease was produced by the inoculation of oral washings from two examples of characteristic minor illness.

Autopsy Findings.—As stated in the preceding protocols, tissues from the spinal cord and brain of Monkeys 22 and 29 revealed lesions characteristic of poliomyelitis. Both animals were sacrificed 5 days after paralysis was first noted. The lesions are shown in Figs. 1 and 2.

Passage Experiments.—Both strains We. and Rn., isolated from oral washings as above described, were subjected to subsequent monkey passage. Here we encountered the usual problems which arise in attempting to establish in the monkey, recently isolated human strains, for the experimental disease so produced is often not easy to detect and may not fulfil all of the usually recognized diagnostic criteria: (*a*) characteristic temperature reactions; (*b*) paralysis; and (*c*) the presence of typical histological lesions in the spinal cord or medulla, that is to say lesions which include the characteristic, perivascular, round cell infiltrations. All of our positive diagnoses have been based upon the last criterion; *i.e.*, histological lesions in the central nervous system.

To facilitate the early passage of these strains recourse was had to the method of double inoculation (9). The results of the early passage experiments appear in Text-fig. 7.

With the We. strain the first-passage monkey (No. 67) received two inoculations of a 10 per cent suspension of spinal cord intracerebrally and intraperitoneally. It is probable that the second inoculation was superfluous to establish the infection. There were certain unusual features about this monkey in that the animal had diarrhea, and on the 6th day after inoculation the limbs and face became edematous. Subsequently it became quite ill, weak, and refused to move about. The edema practically disappeared by the 8th day at which time a second inoculation was done. The animal died the next day. Unfortunately, temperature readings were discontinued during the edema period but on the day of death the temperature was found to have fallen to a subnormal value. Extensive lesions typical for poliomyelitis were found in sections of the cord in spite of the fact that the development of actual paralysis during the last few days had not been noted although the animal had been too weak for an adequate examination. The second-passage monkey (No. 35) received a single intracerebral and intraperitoneal inoculation of a 5 per cent suspension and developed the experimental disease with unusual rapidity. Subsequently this strain has been carried on through further monkey passages.

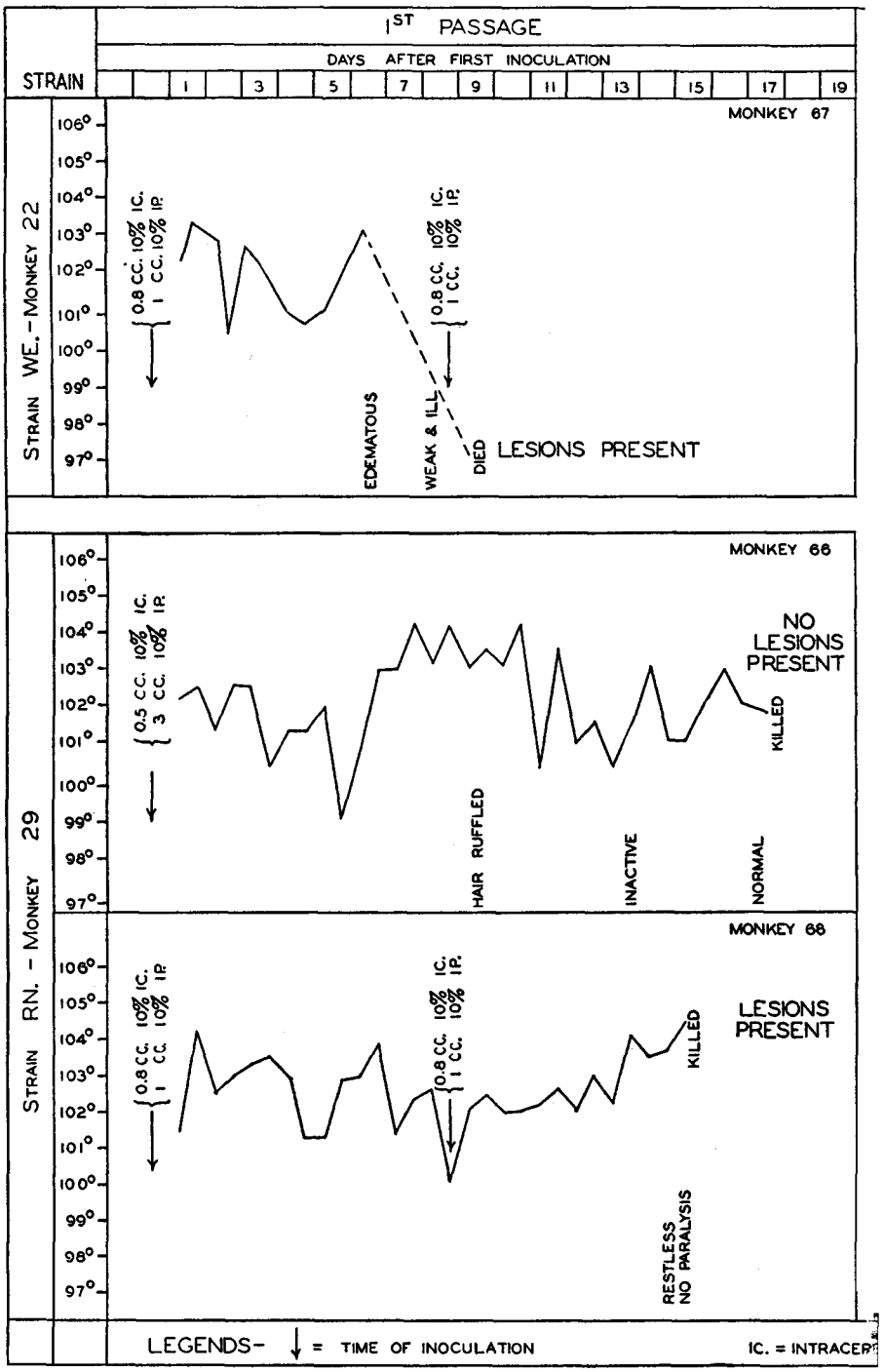
Two first-passage monkeys were inoculated with the Rn. strain. One monkey (No. 66) received only one inoculation, and, starting on the 6th day developed

fever which ran a course comparable to that which we have seen in experimental poliomyelitis. With the fall in temperature no paralysis was detected and subsequently at autopsy the examination of the central nervous system proved negative. The other first-passage monkey showed no elevation of temperature by the 7th day and was then given a second inoculation. The temperature rose 6 days later and the animal was killed. Paralysis had not been observed, but it is possible that it would have developed had the animal been spared a few more days. Typical lesions of poliomyelitis were present in the cord and medulla. In the second-passage monkey which was inoculated with material from Monkey 68, these events were practically reduplicated, only in this animal the experimental disease was allowed to run for a longer period. Fever developed 5 days after the second inoculation, persisted irregularly for 6 days, and subsequently fell with the development of paralysis. Typical lesions of poliomyelitis were found at autopsy.

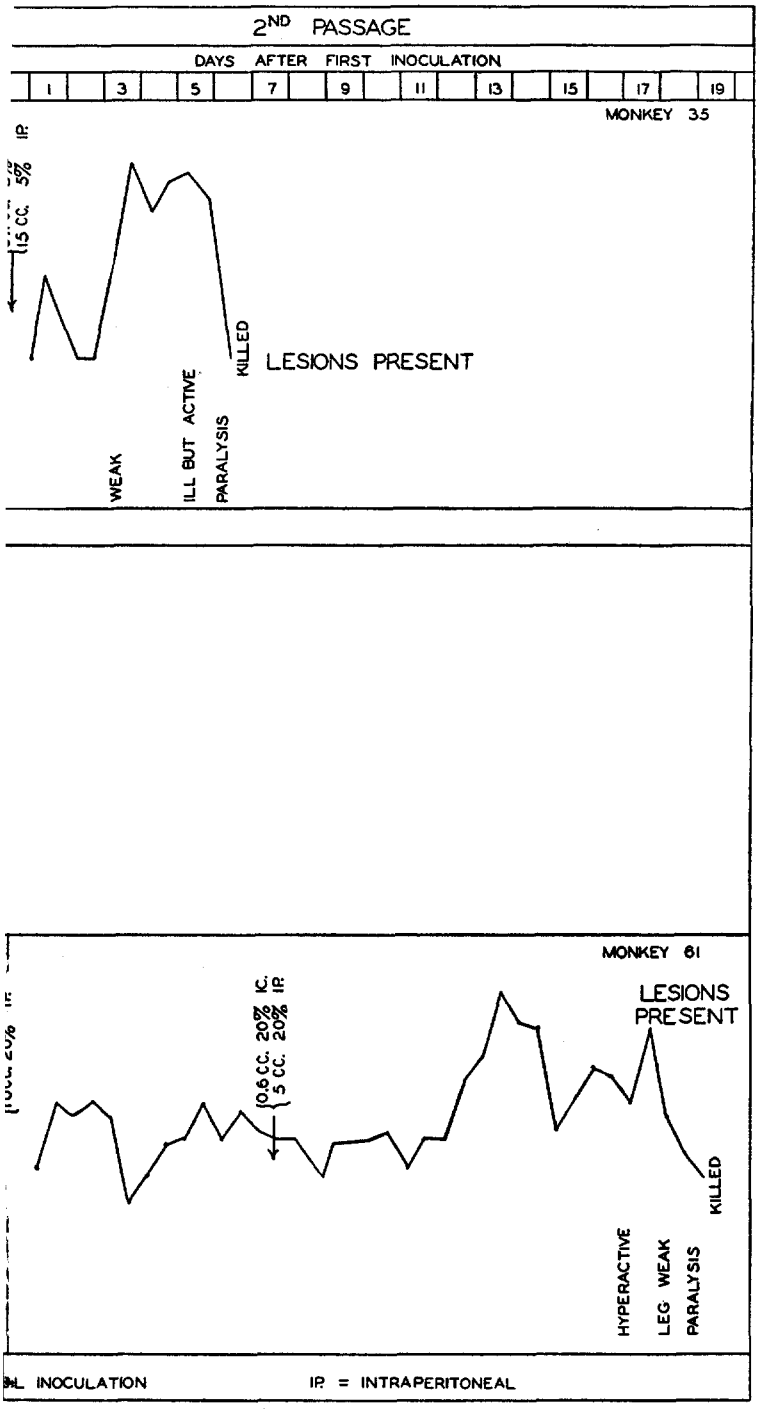
The results show that both strains We. and Rn. could be subjected to monkey passage. We became impressed early in this phase of the work, however, with the differences which exist between the experimental disease produced by strains recently derived from human sources and the experimental disease produced by an established or fixed monkey strain. In the latter so called missed and abortive cases of the experimental disease have been described (16), and we are inclined to believe that these may be more frequent in recently isolated strains and that here examples of actual infection with the poliomyelitis virus without the development of all the usual unequivocal signs, particularly without the development of typical paralysis, may be common. The number of experimental observations which we have at present are insufficient as yet for a statistical analysis of this point.

COMMENT

In corroboration of the beliefs held by many previous observers, and in confirmation of experimental proof obtained 15 years ago (14), evidence has been brought in this paper to suggest that a common causal relationship exists between certain characteristic minor illnesses and the usually accepted entity of clinical poliomyelitis. This evidence consists in the detection of the virus of poliomyelitis in the throats of two patients during the early or mid stage of a characteristic minor illness, who, although seen by several physicians, were not thought to be suffering from either frank poliomyelitis or the



TEXT-FIG. 7. Temperature curves exhibited by the first- and second-passage monkeys of strains We.) and 29 (Str.



inoculated with material originally obtained from Monkeys 22 (Strain Rm.).

abortive form of the disease in its usually accepted sense. We are aware of the possibility that the presence of the virus in the throats of two children who had been exposed to poliomyelitis, may indicate that they were carriers of the virus and not necessarily suffering from infection with it. The consistency with which we encountered negative findings among contacts and also those who had had these characteristic minor illnesses but were convalescent, would, however, militate against this view.

The question as to whether such characteristic minor illnesses are actually examples of poliomyelitis or not would seem to be one of definition. The answer involves an appreciation of the complex adjustments occurring between host and incitant, which may be expressed by different reactions in the former; such as, severe, mild, or absent clinical manifestations of disease. The elucidation of this problem must rest upon further observation and experiments, particularly upon the nature of immunity in this disease. Nevertheless the evidence at hand is sufficient to suggest that, since these characteristic minor illnesses outnumber by many times examples of frank poliomyelitis, their rôle as far as the spread of the disease is concerned is, indeed, important.

CONCLUSIONS

Experiments are reported which describe the isolation of poliomyelitis virus from the throats of two patients during an attack of so called abortive poliomyelitis (Wickman type), or what we have termed characteristic minor illnesses in association with poliomyelitis.

This finding represents added evidence in favor of the belief, previously held by many observers, that certain types of minor illness, which accompany an epidemic of poliomyelitis, probably represent mild cases of the disease.

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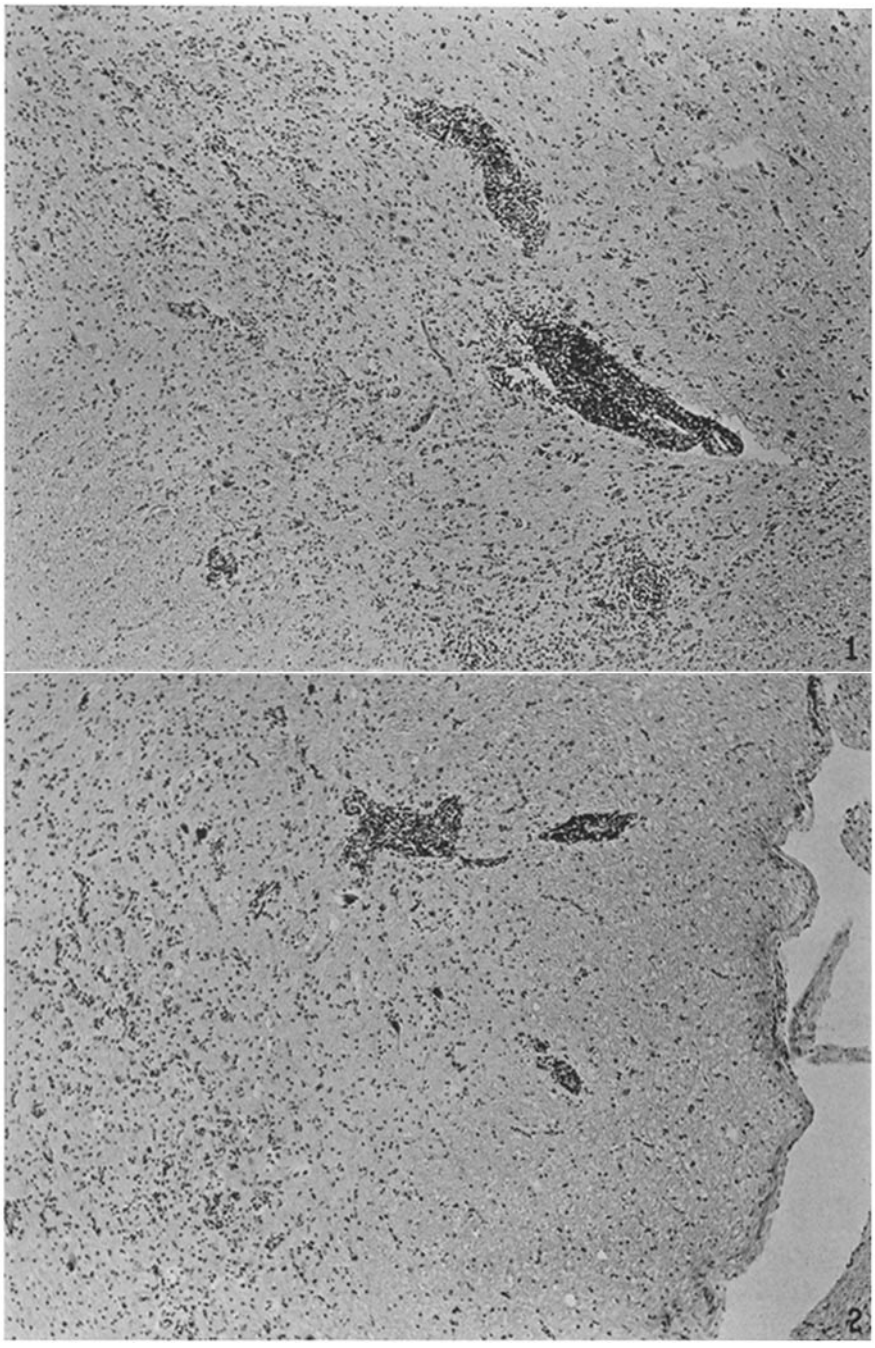
EXPLANATION OF PLATE 19

FIG. 1. A section of spinal cord from Monkey 22. × 75.
FIG. 2. A section of the spinal cord from Monkey 29. × 75.



(Paul and Trask: Poliomyelitis virus in abortive types)