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Some observations on the outbreak of  
encephalo-meningomyelitis encountered in  
Ehime Syuso area through twenty-eight  
hospitalized patients (1956)

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# Some observations on the outbreak of encephalo-meningomyelitis encountered in Ehime Syuso area through twenty-eight hospitalized patients (1956)\*

Isamu Kitamura

## **Abstract**

An outbreak of encephalomyelitis in Ehime-Syuso area from April to June 1956 was clinico-virologically investigated with the materials obtained from 28 hospitalized cases and their healthy visiting relatives. The major rise in polio type I antibody titer and the positive isolation of 4 strains of type I indicate the epidemic in this area to be the polio type 1. Three undeterminable cytopathogenic agents were concomitantly obtained in the HeLa cultures. The style of this episode was duly compared with the documents already reported.

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**SOME OBSERVATIONS ON THE OUTBREAK OF  
ENCEPHALOMENINGOMYELITIS ENCOUNTERED  
IN EHIME-SYUSO AREA THROUGH TWENTY-EIGHT  
HOSPITALIZED PATIENTS (1956)**

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The transforming features in the manner of outbreaks of the paralytic episodes in Setouchi area have attracted a considerable interest by piloting analysis of Guillain-Barré syndrome<sup>1</sup>. The multiple ideology in these features would be obviated through the view that the analysis of single influencing factor would conform the stepping stone to approach to the problem. Accordingly, the character of the recent outbreak of encephalomyelitis in Ehime-Syuso area in 1956 would replenish the methodology aimed to clarify the situation, since the episodes were determined to be produced by the single polio type I virus. The intrinsic factors in admitting the large extent of paralytic episodes in this area would be described in later paragraphs.

This report deals briefly with the classification of the agents isolated from the materials of 28 hospitalized cases and their clinical observations together with the exploration into the nature of the epidemy encountered.

**MATERIALS AND METHODS**

*Virus* : The HeLa cell adapted polio viruses, Brunhilde, MEFI, and Leon strains were obtained together with the HeLa cell lines through the courtesy of Dr. M. KITAOKA, National Institute of Health of Japan.

*Cell cultures* : HeLa cells were grown in the growth medium containing 20 parts of human serum and 80 parts of Y. L. A.<sup>2</sup> with penicillin 500 units and streptomycin 100  $\mu$ g/ml. on the glass wall in the stationary position. The transfer of cells were made by the method originally described by SCHERER<sup>3,4,5,6</sup>.

*Virus assay* : The tube cultures containing approximately  $10^5$  cells

were washed three times by Hank's BSS solution and replaced with 100 parts of Y. L. A. along with antibiotics. TCID<sub>50</sub> was employed for assay.

*Polioantiserum* : Obtained through the courtesy of Dr. H. A. Wenner, National Foundation for Infantile Paralysis. Standard monkey serum.

*Clinical materials* : 28 patients in the polioward of Tomita Hospital admitted in April-June 1956, Imabari City. The fecal specimens were directly frozen and stored in CO<sub>2</sub> dry ice. 5 ml. of phosphate buffer solution with penicillin 500 U. and streptomycin 50 mg/ml. were added to the thawed materials 0.5g. followed by centrifugation 2500 r. p. m. for 30 minutes. at room temperature. Supernatant after centrifugation were further centrifuged at 10,000 r. p. m. for 30 minutes at 4°C, and 0.1 ml. of final supernatant was employed for inoculant into tube cultures. Cytopathogenic effect was determined.

## RESULTS

i *Isolation of agents* : To obtain the causative agents of the outbreak and to elucidate the interactions of agents and the syndrome induced the routine measure of the isolation from 13 fecal specimens was taken. The seven cytopathogenic agents in HeLa cultures were noticed in the first passage. By further cultivation of these agents, 4 of them were consigned to polio type I virus and the remaining three agents were excluded from the polio group. As shown in Table 1 the presence of the

Table 1. Results of Isolating the Agents from the Patients in Ehime-Syuso Area in Epidemic Time.

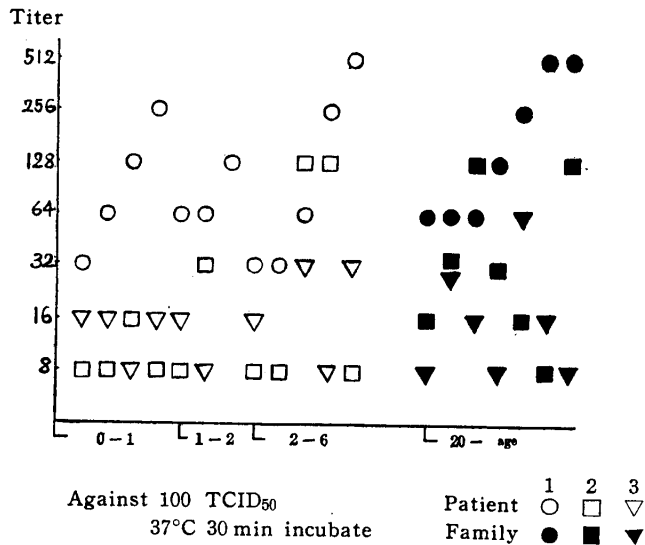
Name	Sex	Age in Yrs.	Type of Case	Source Sampling Day	Classification
E. T.	F.	2- 9/12	Spinal	Stool 9	
K. T.	F.	11/12	Spinal	Stool 10	
T. S.	M.	3- 4/12	Nonparalytic	Stool 17	Unclasif.
K. Y.	M.	4- 8/12	Nonparalytic	Stool 4	Brunhilde
T. I.	M.	6	Nonparalytic	Stool 4	Brunhilde
S. S.	M.	1-10/12	Spinal	Stool 5	
Z. M.	M.	1- 3/12	Spinal	Stool 14	Unclasif.
K. M.	F.	4/13	Nonparalytic	Stool 2	Unclasif.
Y. K.	F.	3- 3/12	Spinal	Stool 15	Brunhilde
T. Y.	M.	2	Spinal	Stool 34	Brunhilde
N. O.	M.	5- 2/12	Spinal	Stool 24	
C. Y.	F.	1	Spinal	Stool 14	
S. S.	F.	4	Spinal	Stool 14	

virus in the fecal specimens was considerably at variance in the course of illness, and the extreme case revealed an agent on the 34th day of illness.

No significant close relationship between the positive virus isolation and the appearance of paralysis was seen. Obviously the presence of no other type of polio virus was in evidence.

ii *Neutralizing antibody titer* : Twelve samples of serum from the individual patients and their visiting 7 relatives were attested for the polio antibody titer for three types in HeLa culture. The results are illustrated in Table 2. Although there is no decisive evidence without

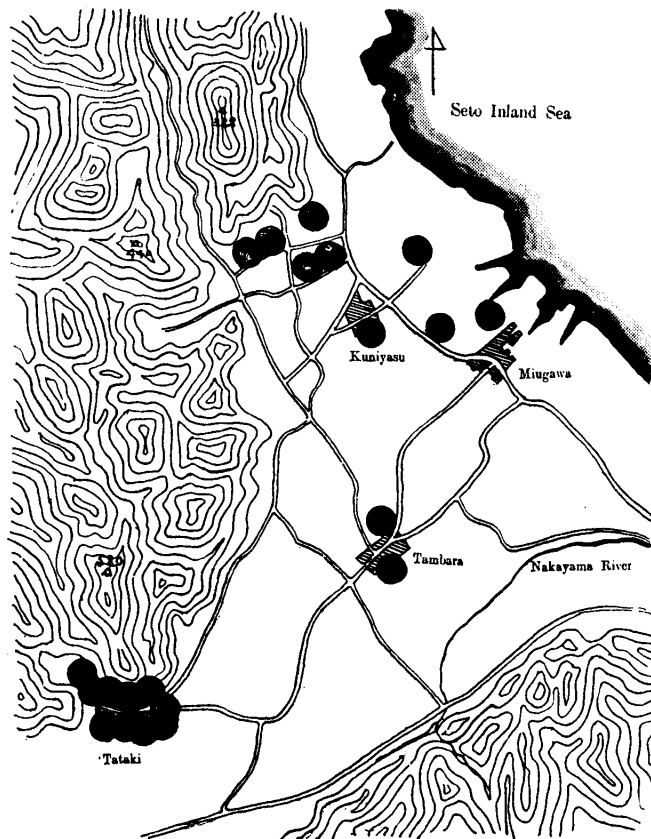
Table 2. Neutralizing Antibody Titer of Patients and their Relatives in Ehime-Syuso Area



any paired sera, there would be a certain elevation of type I in contrast to other types. Non-paralytic cases revealed a tendency to show a high titer in type I. The distribution of the polio virus types in these specimens is of significance. Most of the individuals possessed all three types indicating the extent of the previous experience of the invasion of polio virus. Of course, there should be certain heterotypic reaction<sup>7,8,9,10,11</sup>. The serum was drawn from the patients chiefly on the 5—6th day of illness in the range of 3—34th day. The serially diluted sera were challenged with polio viruses of three types 100 TCID<sub>50</sub> followed by the incubation for 30 min. at 37°C. The virus-serum mixture was inoculated into tube cultures. The tubes were read on 5th day when virus control tube revealed total degeneration.

iii *Environment* : The relation of the geographical terrain and the mode of outbreak is sketched in Fig. 1. The black dots illustrate the individual patient. The village is located in the middle of the mountainside

Fig. 1. Geographical Shape and the Mode of Outbreak in Ehime-Syuso Area (1956)



and the seacoast of Setouchi and Regions is surrounded by small hills which somewhat isolate the village from the direct influence of the neighboring cities. The climate is deemed to be moderate with suitable rain-falls. The living standard in this area is thought to be Class C by Japanese standard. No credible trace of transmission of the agents could clearly be demonstrated, nor unusual seasonal changes were observed in this late spring, and on special dietary deficiencies either. No spraying of insecticides had been planned. Accepting this situation no reasonable responsible factors for this outbreak were noticeable other than the

hypothetical reasoning of the virulence of the agents and the variation of the condition of hosts.

iv *Clinical features* : The outbreak involved 78 cases in this area, of which 45 cases (57.6 percent) were paralytic and 33 cases (42.4 percent) were non-paralytic. Among these group, 28 cases were admitted to Tomita Hospital. 22 cases were paralytic, 6 cases were not. All these cases were initiated with the temperature 38°—40°C which lasted approximately 1—5 days. The majority had one fever peak while 3 cases had two fever peaks. The initial symptoms observed are shown in Table 3. The lethargic episodes were observed surprisingly in 57.1

Table 3. Onset Symptoms, Exclusive of Fever, in Order of Frequency. (28 Cases)

Symptom	Numbers	Percentage
Pain		
Headache	2	7.1
Other Localized Pain	11	39.3
Generalized Aching	1	3.6
Vomiting/Nausea/Anorexia		
Vomiting/Nausea	10	36.7
Anorexia		
Malaise	8	28.6
Stiffness of Neck or Back	11	39.3
Listlessness, Fatigue, Drowsiness	16	57.1
Localized Weakness or Paralysis	0	0
Chills	1	3.6
Fretfulness, Irritability	6	21.4
Vertigo	0	0
Cold	0	0
Diarrhea/Constipation		
Diarrhea	1	3.6
Constipation	9	32.1
Sweating	13	46.4
Eruption	1	3.6
Convulsion	2	7.2
Strabismus	1	3.6

percent and restlessness in 21 percent. The incidence of this lethargy was reported previously in the range of 5—15 percent which is considerably lower than this outbreak in question<sup>12,13</sup>. The paralysis was seen frequently after 2—4 days of illness, rarely after 6—8 days. One case revealed paralysis after 13 days in right arm, which corresponds to the reports (12, 14). As shown in Table 4. the paralytic site was frequently

Table 4. Analysis of Paralytic Site

Paralytic Site	Number	Percentage
One Leg	10	45.6
Both Legs	6	27.4
One side Leg and Arm	2	9.0
One side Leg and another side Arm	1	4.5
Face	1	4.5
Face and one Leg	1	4.5
Neck	1	4.5

seen on the one side leg and next on both side of leg, which is not in accord with the results obtained by TATSUMI'S<sup>12</sup> classification, but rather closely resembles the YAMADA'S<sup>15</sup>. Tendon-reflex of the 25 paralysed muscles was obliterated in 6, lower in 3 and normal or enhanced in 19. The reflex of non-paralytic patients revealed normal response or an increase. The recovery of the paralytic muscles was relatively rapid. Only 2 cases remained paralysed. The remainder showed the recovery of the motor system within 6—24 days.

v *Findings of cerebrospinal fluid* : The figure of the pleocytosis is shown in Table 5. No difference was observable between lethargic and non-lethargic individuals. The prominent pleocytosis within the first week of illness was revealed in the group of non-paralytic individuals, which is similar to the results reported by TATSUMI<sup>13</sup>. The changes in protein and sugar contents are illustrated in the Table 4 as well. The major increase of protein was demonstrated in the second week excepting a few cases such as mentioned by TATSUMI<sup>12</sup>. The sugar contents proved to be higher in the second week in the range of normal, which corresponds to the report of FORBES<sup>16</sup>. No conclusive data were obtained in connection with the protein and sugar contents to enable to distinguish the cases of paralysis from non-paralysis on one hand and lethargic from non-lethargic on the other.



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Table 5. Transition of Cells in Spinal Fluid, Comparison of Paralytic and non-Paralytic poliomyelitis in Ehime-Syuso Area.

Name	Period	1W	2W	3W	4W	5W
Paralytic Case						
* T. S.				516		
* Y. K.			83	36		
S. S.			20			
M. H.						3
K. S.	55					
* N. O.	10	16		7		
* C. Y.	49	48		45		
* K. T.	265	13				
T. I.	143					
* T. Y.				27	13	
* T. W.	61	16		13		
* S. T.	211					
* Y. S.	20					
* Z. M.	53	18				
E. T.	31	26				
S. N.	94	11				
Y. N.	224	27		20		
Non paralytic Case						
* Y. I.	102	55				
* K. Y.	1215					
Y. K.	232					
* T. S.	372					
* M. M.	178					
K. M.	118					

\* : Patients showing the lethargic episode.

## DISCUSSION

Since the completion of the ward and laboratory works on this outbreak, two successive polio outbreaks were reported<sup>17,18</sup>. These were of similar scale and the incidence of them has been attributed to the epidemiological illustration. The form of the outbreak in Japan seems to be of explosive type in recent years. Being limited in ward works, epidemiological scope of this outbreak based on the statistical analysis will be reported elsewhere from public Health Authorities. However, the figure of the paralysis in the given population was in the ratio of 90/100,000, which far exceeds the figure obtained by TATSUMI<sup>12</sup> 10.7 in Osaka, 11.8

Table 6. Transition of Protein and Sugar in Spinal Fluid, Comparison with both Paralytic and Non-paralytic poliomyelitis in Ehime-Syuso Area.

Name	Period	1 W	2 W	3 W	4 W	5 W
Paralytic Case						
* T. S.	120		115 (46)			
* Y. K.	21		52			
S. S.			26			
M. H.						23
K. S.	29					
* N. O.	60		120	84		
* C. Y.	50		93	84 (73)		
* K. T.	31 (54)		35			
T. I.	23					
* T. Y.				68	68	
* T. W.	35 (normal Haines)		52 (97)	34		
* S. T.	30					
* Y. S.	26					
* Z. M.	33		41 (84)			
E. T.	19 (52)		21 (71)			
S. N.	32		18			
Y. N.	51		28	25		
Non-paralytic Case						
* Y. I.	31 (54)		29 (84)			
* Y. K.	33					
* T. S.	33					
* M. M.	48					
K. M.	48					

( ): Sugar content

\* : Patients showing the lethargic episode.

in Kobe/100,000 in 1938 and 1940 respectively. This figure might be compared to 52/100,000 in Köln, Germany, 1938<sup>19</sup>. The most notorious outbreak in Winston-Salem, North Carolina U. S. A. showed 55 and 62/100,000 respectively<sup>20</sup>. Usual incidence of the outbreak in large cities has been in the vicinity of 20/100,000<sup>19</sup> in U. S. A.

Concomitantly the problem of the polio type would be taken into consideration. After FORBES<sup>16</sup>, polio type II revealed 60.3 per cent of non-paralytic cases among 452 cases in 1952-53, on the contrary, polio Type I revealed merely 33.6 per cent of non-paralytic cases in 1954. This outbreak in Ehime-Syuso revealed slightly higher incidence of non-paralytic cases than the TATSUMI'S<sup>12</sup> report. The percentage of non-paralytic

of this outbreak is in between Forbes's type I and type II.

As to the clinical symptoms, the lethargy was the conspicuous character, which can be understood in this outbreak in the ratio 57.1 per cent and restlessness of 21 per cent initially, indicating the initial meningial signs. The lethargic cases in Japan so far reported by TAKAZU<sup>14</sup>, TATSUMI<sup>12</sup> proved to be 5—15 per cent restlessness to be 10 per cent. According to the literature abroad<sup>19</sup> the simple quietness and listlessness with marked drowsiness are the major symptoms in young children.

The incidence of the paralytic case followed to the curve after HAMAMOTO<sup>1</sup>, SHOJI<sup>21</sup> of the age distribution of the polio antibody titer, namely, the lowest part of age 6 months to 1 year are prone to be paralysed<sup>18,21</sup>. KONO<sup>18</sup> reported certain delay in the peak of the figure of the paralytic cases. In this outbreak the peak of the age distribution of paralytic cases was 1—2 years old children, which is in accordance with Kono's data. In the cases occurring in Winston SALEM<sup>9</sup> the peak was shown in the age 1—4.

HAMAMOTO<sup>1</sup> described the age distribution of the polio antibody titer against three types; the rise of one type at 6 M to 1 year, for two types 2—4 years and for all three types at 5—9 years. In this outbreak, subject group revealed all three types in each individual. The elevation of the antibody titer against Lansing was observed in the each age group after the polio type I epidemy by MELNICK<sup>7</sup>, who suggested the close immunological relationship between the types I and III accepting the view of TURNER<sup>10</sup> and HAMMON<sup>11</sup>. Sabin has also observed the heterotypic reaction to the latent infection in 6 cases in 1948<sup>28</sup>. It could be presumed that these factors in this epidemy would be responsible to some extent.

There are, however, a large volume of the reports about the concomitant isolation of two or three types of polio virus in one epidemy; Los Angels 2 type I and 1 type II 1947<sup>22</sup>, Boston 1 type I and 10 type III 1950<sup>23</sup>, Pittsburgh 28 type I and 9 type III<sup>24</sup>, Easton Pa., 12 type I and 1 type II and 3 type III<sup>25</sup>.

In the present outbreak due to the limited facilities, only one type could be isolated. The remaining three agents might be classified as to belong to the ECHO virus group<sup>26,27,28</sup>, or some others.

The complexity of the general picture of the epidemy of encephalomeningomyelitis would be illustrated by taking the sample of polio epidemy in the given area, to us the Setouchi area Japan. The further investigation on this problem is in progress.

SMMARY

An outbreak of encephalomyelitis in Ehime-Syuso area from April to June 1956 was clinico-virologically investigated with the materials obtained from 28 hospitalized cases and their healthy visiting relatives.

The major rise in polio type I antibody titer and the positive isolation of 4 strains of type I indicate the epidemy in this area to be the polio type I. Three undeterminable cytopathogenic agents were concomitantly obtained in the HeLa cultures. The style of this episode was duly compared with the documents already reported.

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REFERENCES

1. HAMAMOTO, E. : Studies on the polyradiculoneuritis manifested the so cold "Guilain Barré syndrom." Acta Paediatrica Japonica. 60, 661, 1956 (in Japanese)
2. TAKEMORI, N. : Personal Communication.
3. SYVERTON, J. T., SCHERER, W. F., and ELWOOD, P. M. : Studies on the propagation in vitro of poliomyelitis viruses. J. Lab. Clin. Med. 43, 286, 1954.
4. PUCK, T. T., MARCUS, P. I. and CIECIURA, S. J. : An epidemiological study of enteric virus infections. Poliomyelitis, Cocksackie, and Orphan (ECHO) viruses isolated from normal children in two socio-economic groups. J. Exper. Med. 103, 247, 1956.
5. MARCUS, P. I. CIECIURA, S. J. and PUCK, T. T. : Clonal growth in vitro of epithelial cells from normal human tissues. J. Exper. Med. 104, 615, 1956.
6. SCHERER, W. F., SYVERTON, J. T. and GEY, G. O. : Studies on the propagation in vitro of poliomyelitis viruses. IV. viral multiplication in a stable strain of human malignant epithelial cells (strain HeLa) derived from an epidermoid carcinoma of the cervix. J. Exper. Med. 97, 695, 1953.
7. MELNICK, J. L. and LEDINKO, N. : Development of neutralizing antibodies against the three types of poliomyelitis virus during an epidemic period. The ratio of inapparent infection to clinical poliomyelitis. Am. J. Hyg. 58, 207, 1953.
8. SABIN, A. B. : Transitory appearance of type II neutralizing antibody in patients infected with type 1 poliomyelitis virus. J. Exper. Med. 96, 99, 1952.
9. MELNICK, J. L. and LEDINKO, N. : Socialserology : Antibody levels in a normal young population during an epidemic of poliomyelitis. Am. J. Hyg. 54, 354, 1951.
10. TURNER, T. B., HOLLANDER, D. H., BUCKLEY, S., KOKKO, U. P., and WINSOR, C. P. : Age incidence and seasonal development of neutralizing antibodies to Lansing poliomyelitis virus. Am. J. Hyg. 52, 323, 1950.
11. HAMMON, W. McD., SATHER, G. E., and HOLLINGER, N. : Preliminary reports of epidemiological studies on poliomyelitis and streptococcal infections. Lansing neutralizing antibody and antistreptolysin "O" surveys of California ci-

- ties, Texas, North Carolina, Mexico, Pacific Island and Japan. *Am. J. Pub. Health.* 40, 293, 1950.
12. TATSUMI, M. : Studies on the Heine-Medin disease. *Acta Paediatrica Japonica.* 51, 22, 1947 (in Japanese).
  13. TATSUMI, M. : Studies on the Heine-Medin disease about the patients admitted in the pediatric department of Osaka University in 1940. *Acta Paediatrica Japonica.* 47, 117, 1941 (In Japanese).
  14. TAKAZU, T. : Polio, Nagai Company. 1956 (in Japanese).
  15. YAMADA, S. : Clinical observation of Heine-Medin disease. II. *Acta Paediatrica Japonica,* 52, 146, 1948. (in Japanese)
  16. FORBES, J.A. : Clinical aspects of non-paralytic poliomyelitis and a clinical comparison of poliomyelitis epidemics due to type I and type II virus. *Med. J. of Australia.* 42, 719, 1955.
  17. TAKAZU, T. et al. : Symposium. *Nippon Rinsyo.* 15, 198, 1957 (In Japanese)
  18. KONO, R. et al. : Serological studies on poliomyelitis. (1) Isolations and typing of the current stains of poliovirus and age distribution pattern of neutralizing antibodies against three types of poliovirus in Japan. *Virus.* 7, 223, 1957. (in Japanese)
  19. STOKES, JR., Pathogenesis and onest symptoms of poliomyelitis. *Pediatrics.* 6, 488, 1950.
  20. MELNICK, J.L. and LEDINKO, L. : Social serology : Antibody levels in a normal young population during an epidemic of poliomyelitis. *Am. J. Hyg.* 54, 354, 1951.
  21. SYOZI, Z. : Studies on age distribution of neutralizing antibodies against three types of poliomyelitis virus in Tokyo, Japan. *Acta Paediatrica Japonica.* 60, 864, 1956 (in Japanese).
  22. The committee on Typing National Foundation for infantile Paralysis, *Am. J. Hyg.* 54, 191, 1951.
  23. RROBBINS, F.C., ENDERS, J.F., WEIHER, T.H. and FLORENTINO, G.L. : Studies on the cultivation of poliomyelitis viruses in tissue cultures. *Am. J. Hyg.* 54, 286, 1951.
  24. YOUNGNER, J.S, WARD, E.N. and SALK. J.F. : Studies on poliomyelitis viruses in cultures of monkey testicular tissue. II. Differences among strains in tissue culture infectivity with preliminary data on the quantitative estimation of virus and antibody. *Am. J. Hyg.* 55, 301, 1952.
  25. RIORDON, J.T., LEDINKO, N., and MELNICK, J.L. : Multiplication of poliomyelitis viruses in tissue cultures of monkey testis. II. Direct isolation and typing of strains from human stools and spinal cords in roller tubes. *An. J. Hyg.* 55, 339, 1952.
  26. MELNICK, J.L. et al. : Application of tissue culture methods to epidemiological studies of poliomyelitis. *Am. J. Publ. Health.* 44, 571, 1954.
  27. RAMOS, ALVAREZ, et al. : Characteristics of poliomyelitis and other enteric viruses recovered in tissue culture from healthy American children. *Proc. Soc. Exp. Biol. & Med.* 87, 655, 1954.
  28. HONIG, E.I.H, et al. : An endemiological study of enteric virus infections. Poliomyelitis, Coxsackie, and Orphan (ECHO) viruses isolated from normal children in two socio-economic group. *J. Exper. Med.* 103, 247, 1956.