

ANNUAL REPORT OF THE INSTITUTE FOR  
VIRUS RESEARCH KYOTO UNIVERSITY

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VOLUME 3

Editors :

S. AMANO  
R. KONO

N. HIGASHI  
I. WATANABE

EPIDEMIOLOGY, SEROREACTION  
AND PATHOLOGY  
IN VIRAL DISEASES

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## PREFACE TO THE THIRD VOLUME

Each volume of the Annual Report of the Institute for Virus Research Kyoto University itself was planned primarily to be a monography of specialized studies of each of the five Departments in turn. According to this rule, an opportunity to be an editor for the head of a Department comes only one time in five years. This is very inconvenient sometimes for the researchers of this developing field, because they have to wait some several years for the contribution of their precise report profitable for this publication.

On the other hand, Series A, Series B etc. on the title of each Volume arose some misunderstanding of the readers, as if each volume provided all series completely. The sign "Series" means merely that the contents of the number belong to the work of the Department of Pathology (Series A), Department of Biophysics (Series B), Department of Biochemistry (Series C), Department of Serology-Immunology (Series D) or Department of Preventive Medicine and Therapeutics (Series E), that would be published in turn.

From these two view-points we have abandoned in this volume to note the classification of Series. And accordingly, this volume contains mixed subjects from different Departments, for the time being, papers from the Departments of Serology-Immunology, Therapeutics and Pathology.

We think that this type of revolution is necessary for the existence of our Annual Report suitable for the readers and contributors. We hope that this volume would also be welcomed by the researchers of the world as before.

To the last, I should not neglect to note the effort done by Professor R. Kono, the head of the present Publication Committee of this Institute for the arrangement of this new volume.

Dec. 27, 1960

SHIGEYASU AMANO, *Director*  
*Institute for Virus Research,*  
*Kyoto University*

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# 1. Poliomyelitis in Japan

REISAKU KONO\*

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## I. INTRODUCTION

After a long lasting fight of mankind against poliomyelitis there is now definite prospects of victory on our side by the development of effective vaccine. Names like Heine, Medin, Wickman, Landsteiner, Rivers, Armstrong, Paul, Francis, Sabin, Melnick, Morgan, Howe, Bodian, Enders, and Salk, are the most memorable at the final victory. As shown in the later chapter the history of poliomyelitis is almost as old in Japan as in the Western countries. However, it had never been a big problem of public health in this country before 1938 since there was no large epidemic for a long time. And the monkey era of experimental poliomyelitis studies made its research difficult in this country, because it was hard to make available a great number of this animal in a laboratory. It is not too much to say that the United States alone was a country doing something for the studies of poliomyelitis. Consequently, Japanese polio studies were far behind the United States. The discovery of tissus culture of the poliovirus by Enders<sup>1)</sup> has made polio studies more easier than

\* Department of Serology and Immunology, Institute for Virus Research, Kyoto University (Director: Prof. R. Kono)

ever in Japan. When I was transferred to the Institute of Public Health in Tokyo in 1949, I was asked to give a lecture on poliomyelitis for the public health course. I have been engaged in a study of poliomyelitis since that time.

Until that time a few studies were done on poliomyelitis in Japan, and it was not the time when experimental studies could be began again. When I was awarded a fellowship from the Rockefeller Foundation in 1952, I had a chance to study poliomyelitis under Dr. Bodian at Johns Hopkins, Dr. Melnick at Yale and the opportunity to study tissue culture under Drs. Enders, Weller and Kibrick at Harvard. When I got back to Japan in 1953, I began to study the poliovirus using tissue culture. The Rockefeller Foundation awarded a grant in aid for this study. I shall ever be grateful for the help given by Dr. R. O. McCoy who was stationed as an adviser at the Institute for Public Health from the Rockefeller Foundation.

Poliomyelitis has been becoming an increasing menace in public health recent years. We have to do something to prevent the disease. At this moment I will review the epidemiology and virological studies of poliomyelitis in Japan by our own hand and others in this article.

## II. STATISTICAL ASPECTS

### A. *Historical background*

Late emeritus professor Hirai of Kyoto University read a lecture entitled "Statistical observations of Heine-Medin's disease" at the Annual General Meeting of the Japanese Pediatrics Society in 1914, which appeared in No. 175 of *Jikazasshi* (J. Pediatrics) 1914.<sup>2)</sup> Before he read the summarizing lecture he introduced the disease through an article entitled "On the Heine Medin's disease" in 1910.<sup>3)</sup> This was the year of the earliest occurrence of poliomyelitis in Japanese medical literature. Since no official statistic of poliomyelitis is available until 1947, we have to trace its prevalence on the case records from various hospitals. Kosugi<sup>4)</sup> summarized the case records at Tokyo University Hospital from 1890 to 1913 in the same journal, hence we can trace the earliest recorded case back to 1890. According to him, about several to ten cases of poliomyelitis were found every year since 1890 through 1907, and suddenly two or three times as much increase of the patients occurred around 1910. It was five years after in 1905 that outbreaks occurred in Sweden and Norway and the epidemic occurred in the same year in Minnesota, British Columbia and Alberta.<sup>5)</sup> Hirai<sup>2)</sup> also reported in his lecture that he could collect 28 cases in Kyoto, 29 cases in Osaka, 11 cases in Hiroshima, 17 cases in Okayama and 28 cases in Kumamoto, and Tomita<sup>6)</sup> reported 66 cases in Fukuoka. It would be clear from the above results that the first nation-wide prevalence of poliomyelitis would

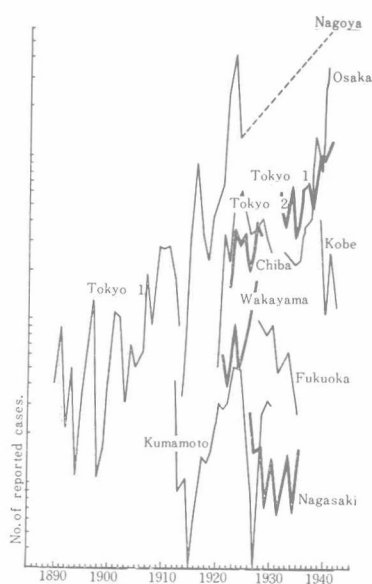


Fig. 1. The trend of the number of poliomyelitis patients collected from the case records of various hospitals from 1890 to 1943. The curves are transferred parallel to each other to avoid overlap.<sup>7)</sup>

occur around 1910. (Fig. 1)

It is clear from these descriptions that our historical background of poliomyelitis is as old as in the United States and European countries.

It is generally believed that the epidemic wave recurred in the first half of the 1920's for 69 (1922) and 133 cases (1923) were reported in Nagoya; 61 (1924) and 51 cases (1927) were recorded in Fukuoka; 48 cases (1923) in Kumamoto; 63 case (1924) in Tokyo.<sup>7)</sup>

The third flare-up was most notorious: the Kinki district which includes Osaka, Kobe, Kyoto and their vicinity, was overcome by severe outbreaks in 1938 and 1940: morbidity rates per 100,000 population were 19.7 in Kobe and 13.0 in Osaka.<sup>8)</sup> The number of poliomyelitis cases increased in the Tokyo University Hospital about the same period. Paul<sup>9)</sup> concluded in his article entitled "Poliomyelitis in Japan", that the disease was in transit-

ion from an endemic to an epidemic stage about 1940.

In conclusion, Tatumi<sup>8)</sup> cited in his review that there were three major epidemics before World War II in Japan: the first outbreak was noticed about 1910; the next epidemic appeared during several years from 1922 through 1926; the third epidemic wave recurred about 1938 and 1940. From 1923 to 1943 we were able to trace the prevalence of poliomyelitis only by the number of deaths. (Table 1)

Table 1. Number of deaths from poliomyelitis 1923-1943, in Japan.

Year	No. of deaths	Year	No. of deaths	Year	No. of deaths
1923	808	1930	438	1937	573
1924	742	1931	394	1938	715
1925	433	1932	395	1939	613
1926	346	1933	440	1940	648
1927	389	1934	499	1941	651
1928	407	1935	412	1942	708
1929	424	1936	516	1943	765

After World War II poliomyelitis had been a reportable disease in 1947 and was designated a legal communicable disease by the government in 1959. Official notification by the physician in charge is required,

but differentiation of the paralytic and non paralytic form is unnecessary for the report. Therefore, most of the statistics refer to the paralytic forms. Since the notification of poliomyelitis was more universally known among physicians after 1949, the morbidity statistics became more reliable and we would like to discuss statistical aspects of poliomyelitis in Japan mainly on the data after 1949.

As poliomyelitis has increasingly become a great problem in public health in this country, a strong antipoliomyelitis campaign has been demanded. Small scale trials of Salk's vaccine which was imported from the United States was done in 1956, and after that a considerable portion of infants were immunized by American or Canadian made vaccine. The government set up a pilot plant for the manufacturing of Salk's vaccine in the National Institute of Health last year, and its first products were proved satisfactory as an immunizing agent. The production was transferred to the private pharmaceutical companies in 1960. The children from six to eighteen months after birth will have compulsory immunization by three doses of Salk's vaccine in 1961. Live attenuated virus vaccine (Sabin type) is now about to be investigated in a small field trial.

### *B. Morbidity rate and geographical distribution*

Hachinohe was the first city attacked by the epidemic wave of poliomyelitis after the World War II in 1949<sup>10)</sup>, and it seemed to spread to the neighbouring prefectures, Hokkaido, Miyagi and other parts of Japan. The number of cases reached up to 3,127, and the attack rate was 3.8 per 100,000 persons in the whole country. In 1951, 4,233 cases were reported, attack rate 5.0. These three years from 1949 through 1951 may be regarded as epidemic years, because the annual incidence was over 3,000 cases. (Table 2) But it went into a quiescent period there-

Table 2. Number of patients and deaths from poliomyelitis, 1947-1950 in Japan.

Year	No. of cases	Morbidity*	No. of deaths	Mortality*	Fatality†
1947	275		1,009		3.7
1948	993	1.2	775	1.0	78.0
1949	3,127	3.8	1,074	1.3	34.3
1950	3,212	3.9	775	0.9	24.1
1951	4,233	5.0	570	0.7	13.5
1952	2,317	2.7	508	0.6	21.9
1953	2,286	2.6	441	0.5	19.3
1954	1,921	2.2	442	0.5	23.0
1955	1,314	1.5	314	0.4	23.9
1956	1,498	1.7	290	0.3	19.4
1957	1,718	1.9	255	0.3	14.8
1958	2,610	2.8	243	0.3	9.3
1959	2,917 $\triangle$	3.1	200 $\triangle$	0.2	6.8
1950**	5,189 (1,535)		287 (102)		

\* per 100,000 population.

† percentage.

\*\* as of 47th week.

$\triangle$  number of cases and deaths in Hokkaido.

after; the lowest incidence within these twelve years was found in 1955: the number of cases being 1,314 and the attack rate 1.5. And it turned again to an upswing after 1955, the nomination of polio as a legal communicable disease brought about an increase of the reporting in the later half of 1959 and 1960 is going to become the worst year concerning the epidemiological history of poliomyelitis in this country. The number of cases reached up to 5,189 as of the 47th week, attack rate over 5.5 and particularly Hokkaido was hit by the largest and severest polio epidemic, the number of cases were estimated 1,585 (attack rate 36.9) as of the 46th week. Its detailed stories will be presented later.

When compared with the morbidity rates of various countries, the highest morbidity rates in Canada 60.1 (1953), the United States 36.9 (1952), Denmark 131.7 (1952), and Sweden 71.0 (1953) are far higher than ours;<sup>5)</sup> our figures resembling those of France, Italy, Spain and Portugal. Since our statistics concern paralytic forms, as previously mentioned, it is hard to compare the figures without any modification. In the severest outbreak of 1952 in Denmark 43.2 per cent of the notified cases were reported as the paralytic form; and 59.6 per cent of Swedish polio patients in 1953 were paralytic.<sup>5)</sup> Approximately about 50 per cent of the notified cases may be the paralytic form in these countries. What we have to consider next is, in my opinion, population as denominator for computation of the morbidity rate. Denmark and Hokkaido have about an equal size of population, and the two popul-

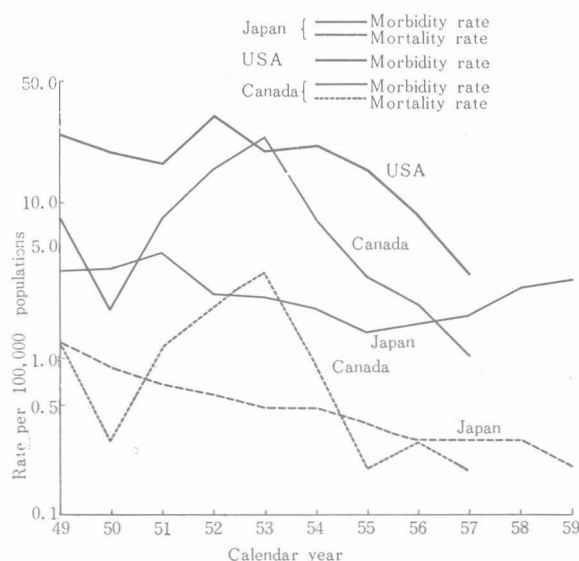
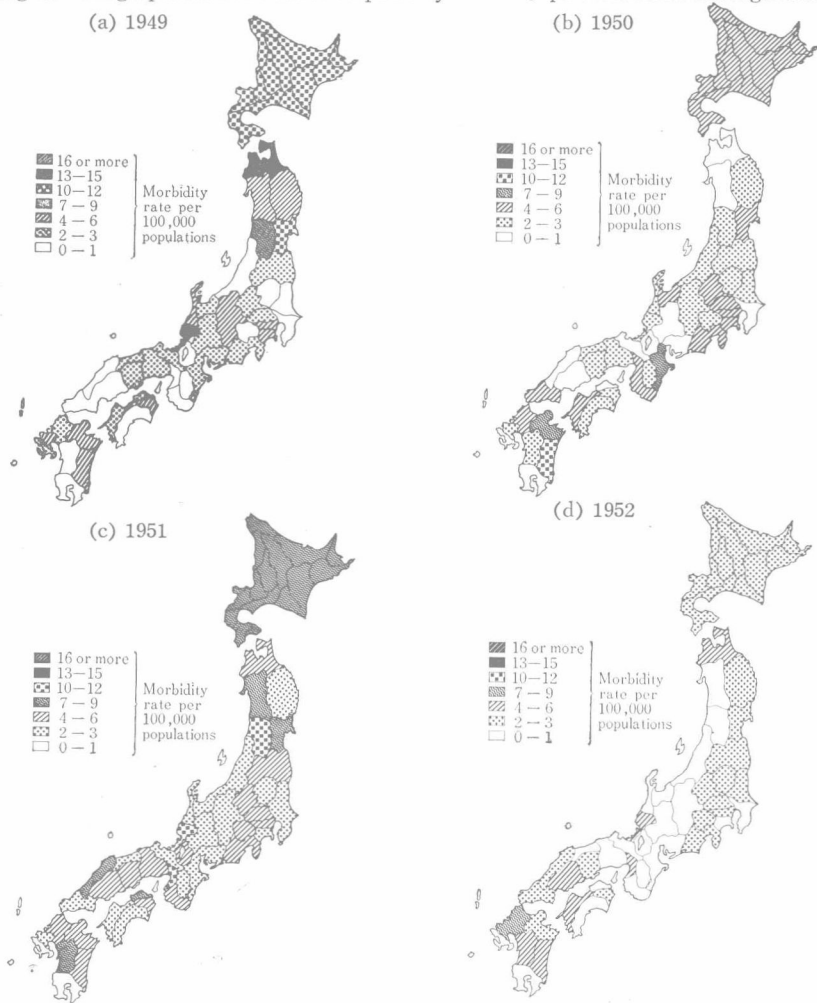


Fig. 2. Annual morbidity and mortality rate of poliomyelitis in Japan, Canada and the U.S.A.

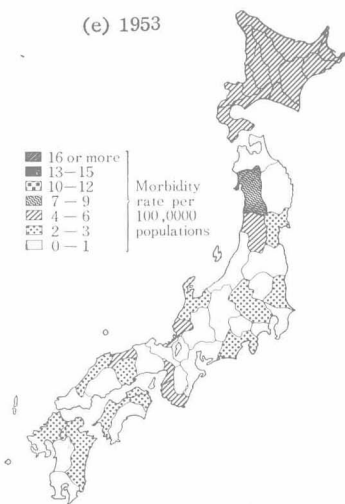
ations are considered to have been exposed to the poliovirus to almost the same extent in the 1952 and 1960 epidemics. Therefore, both the epidemics are considered reasonably comparable. The morbidity rate of Denmark in 1952 was estimated at 56.5 (paralytic form) per 100,000 and that of Hokkaido in 1960 was about 30 per 100,000. If one considers the facts that the former epidemic involved the older age groups and the later epidemic was confined to infants, the difference of the two morbidity rates is reasonable, and we shall not greatly err if we assume that the scope and severeness of the two epidemics may be the same.

As to the comparative figures of morbidity and mortality rates of the three countries, Japan, the United States and Canada, as shown in

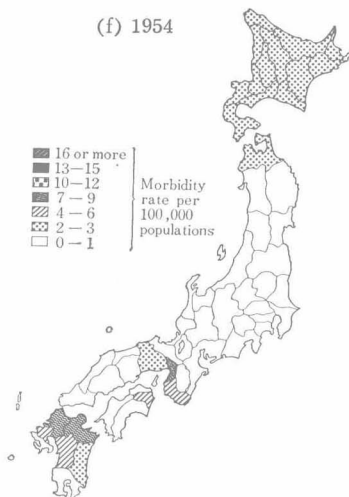
Fig. 3. Geographical distribution of poliomyelitis in Japan from 1949 through 1960



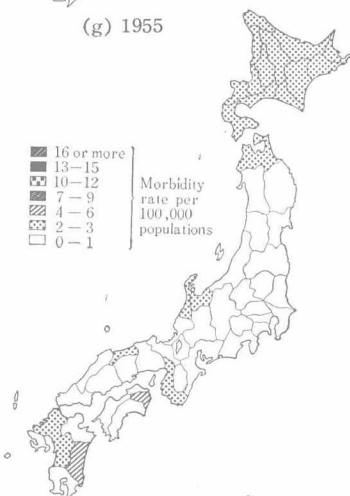
(e) 1953



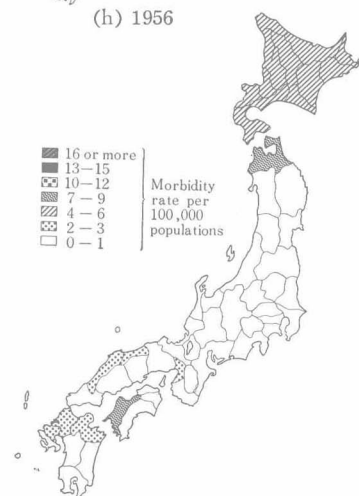
(f) 1954



(g) 1955



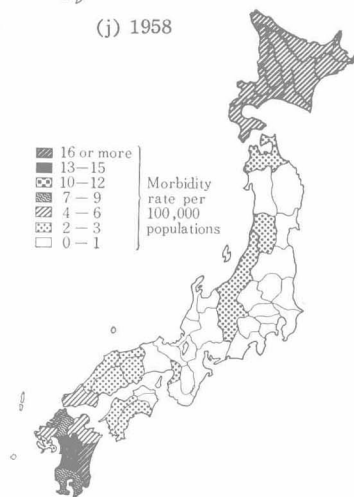
(h) 1956



(i) 1957



(j) 1958



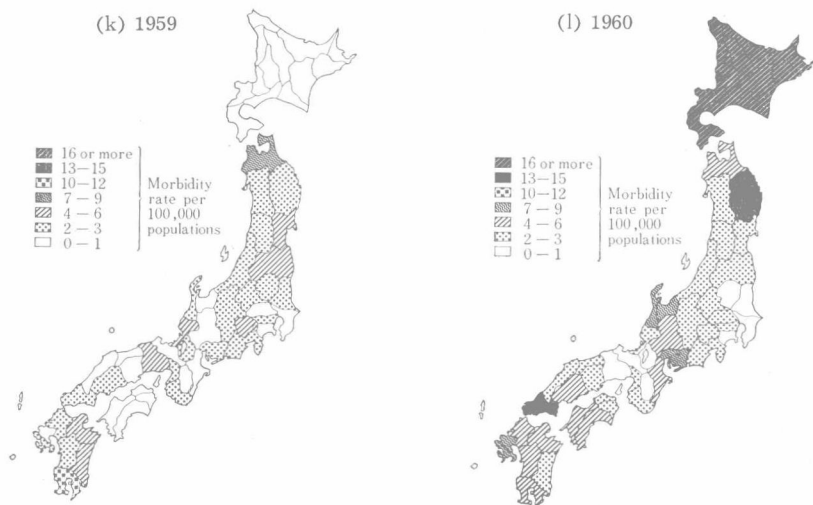


Fig. 2, the morbidity and mortality rates in the United States and Canada are going down strikingly rapid in recent years, due probably to a great extent to the extension of vaccination. It is quite important for us that the Japanese figures do not show any decrease but a small increase.

The geographical distribution of polio incidence during the twelve years since 1949 was investigated. As shown in Fig. 3 and Table 3 the incidence was higher in the northern part, the Hokkaido and Tohoku district, and in the southern part of Japan, namely, Kyushu Island and the western part of the Chugoku and Shikoku districts. That is to say, that two endemic foci of poliomyelitis seem to exist in the both ends of the Japanese Islands, and one may be able to add the Hokuriku district which locates at the middle-north of Honshu to the above as another prevalent area.

The prefectures which showed higher attack rate than the national average of 2.8 per 100,000, during the 11 years from 1949 to 1959, were Hokkaido (4.8), Aomori (5.1), Miyagi (3.5), Fukui (3.7), Osaka (5.2), Yamaguchi (5.0), Ehime (4.4), Fukuoka (5.0), Kumamoto (4.6), Oita (4.7) and Miyazaki (6.4). Prefectures with twice or more than the annual attack rates of the whole country were as follows: Osaka and Aomori five times, Fukuoka four times, Hokkaido, Saga, Oita and Miyazaki three times, Wakayama, Fukui, Yamaguchi, Tokushima, Ehime, Kagoshima and Kumamoto two times, Miyagi, Akita, Yamagata and Tottori, once. On the contrary, the prefectures having lower attack rates were Chiba, Kochi, Kagawa, Shiga, Nagasaki, Ibaragi, Nara and Kyoto. (Table 3, Fig. 3)

As far as five large cities were concerned, Osaka usually was superior in attack rate, Kobe also revealed a higher attack rate than that

Table 3. Annual morbidity rates of poliomyelitis in prevalent prefectures of Japan from 1949 through 1950.

Year	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959	Ave- rage	Frequency showing 2 fold or more than the average
Whole country	3.8	3.9	5.0	2.7	2.6	2.2	1.5	1.7	1.9	2.8	3.1	2.8	
Hokkaido	12.0	4.4	8.7		5.7	2.4	2.3	4.1	2.5	4.1		4.8	7
Aomori	14.9		5.3	4.7		2.9	3.2	8.9	5.2	2.9	9.8	5.1	9
Iwate	5.4										3.8		2
Miyagi	10.0	6.6	8.3		3.7						5.4	3.5	5
Akita	5.8		8.1		7.8								3
Yamagata	7.5		11.0		4.1				2.1		3.2		4
Fukushima		3.4	4.2								4.1		3
Ibaragi		3.5											1
Tochigi		2.8		2.8							3.8		1
Gunma	3.1	6.6	5.0	3.5			1.5				3.2		5
Saitama	2.8	5.5	4.0	3.1									3
Chiba													0
Tokyo	4.9	6.0	4.6	2.7	2.9						3.6		5
Kanagawa	4.2	4.4	3.1										3
Niigata			3.5				1.8				3.9		2
Toyama	3.7	4.5	3.7		2.7		3.2						4
Ishikawa	6.9		3.4		3.2		2.1				3.6		4
Fukui	7.4	3.5	10.9	4.1	4.4		1.7		2.1		6.9	3.7	6
Yamanashi		3.9	4.3	3.8							6.9		4
Nagano	4.7		3.4										2
Gifu			3.5				1.5						1
Shizuoka	3.3	4.5	4.1		2.6								3
Aichi	3.5		2.9										2
Mie	3.0	7.4											2
Shiga			4.2								2.8		1
Kyoto			3.7										1
Osaka		4.5	12.6	5.7	6.1	8.1	3.9	3.2	3.1	3.1	3.0	5.2	10
Hyogo	3.1		5.9			2.4			3.1		4.4		4
Nara			3.7										1
Wakayama		4.1	5.5		6.1	4.4	2.1						4
Tottori			3.3		5.3		2.3	2.7		3.4			3
Shimane			7.9		2.8			2.7					1
Okayama	3.7	3.7	6.8	2.7	3.5					2.8			4
Hiroshima			4.9	4.5					2.4	3.3	2.8		3
Yamaguchi		6.6	2.9	2.8				1.9	15.3	10.8	3.1	5.0	5
Tokushima	4.0	3.9	4.2		3.0	5.1	4.1	1.7					6
Kagawa			2.9										1
Ehime	3.9	6.6	8.2	4.0	3.1			8.8	4.5			4.4	7
Kochi													0
Fukuoka	3.3	6.4	4.1	7.6		7.6	2.9	3.7	3.3	8.3	3.6	5.0	10
Saga	4.4	3.3	3.9	7.4	3.9	5.8	2.6	3.4	3.7				8
Nagasaki							1.5						0
Kumamoto		3.3	7.3	5.2		4.0	2.2	1.7	3.8	14.5	3.9	4.6	7
Oita	6.3	9.2	5.0	3.1	3.2	7.0		2.9	3.8	5.1	5.5	4.7	10
Miyazaki	6.6	11.4	4.7	5.6	3.3	3.6	4.8	1.9	3.6	21.5	4.3	6.4	10
Kagoshima										7.8	11.3		2
Number of pre- fectures showing 2 fold or more attack rate than the national average	3	2	3	4	5	6	4	5	5	5	4		

of the whole country, but Tokyo, Yokohama, Nagoya, and Kyoto suffered less than the above cities, particularly Yokohama, Nagoya and Kyoto have never shown higher attack rates. It is worthy of note that a higher attack rate in Osaka does not necessarily mean an epidemic occurrence of polio there. Very many cases were reported from the Pediatrics Clinic of Osaka University where polio patients were sent from outside of Osaka. Only 197 of the 387 reported cases (48 per cent) from 1957 to 1959 were those who were living in Osaka.<sup>11)</sup> Therefore, it is dangerous to conclude that there is an unusual excess in the morbidity in Osaka comparing with other places in this country, and its epidemiologic pattern of poliomyelitis has never been different from other cities. However, Kobe is rather exceptional, because there were three outbreaks in which the attack rates exceeded twice as much that of the whole country. Virulent poliovirus may be endemic in this port town. (Table 4)

Table 4. Number of polio patients in the five large cities.

Year	1949	1950	1951	1952	1953	1954	1955	1956	1957	1958	1959
Whole country	3,127 3.8	3,212 3.9	4,233 5.0	2,317 2.7	2,286 2.6	1,921 2.2	1,314 1.5	1,497 1.7	1,718 1.9	2,610 2.8	2,911 2.6
Tokyo	285 5.1	377 6.0	311 5.0	182 2.7	205 2.9	83 1.1	108 1.3	71 0.9	75 0.9	92 1.0	338 3.7
Yokohama		12	20	20	13	7	6	4	3 0.2	9 0.7	19 1.5
Nagoya		5	25	4	14	4	3	5	8 0.6	10 0.7	24 1.7
Kyoto		11	44	15	22	26	11	6	15 1.2	18 1.4	22 1.7
Osaka	32 1.7	151 7.7	472 22.6	218 9.9	243 10.5	343 14.2	135 5.3	127 4.9	391 15.2	127 4.5	121 4.0
Kobe	40 6.0	28 3.5	86 10.0	27 3.0	23 2.5	41 4.2	6 0.6	8 0.8	76 7.6	19 1.8	108 9.8

Since the poliomyelitis epidemic was recorded in Hachinohe, (Aomori Prefecture) and Miyazaki (Miyazaki Prefecture) around 1949 and 1950, the virulent poliovirus seems to have settled there endemically, and small outbreaks have been noticed almost every other year from one place to the others in the both of the prefectures and their neighborhood. It is highly probable that the virulent virus would circulate in these regions. Poliomyelitis had never been known epidemically in these two districts, although sporadic cases were seen.

Fig. 4 illustrates the time sequential pattern of poliomyelitis in several prefectures which represent different epidemiological states. Chiba and Kochi had never shown epidemic prevalence up to now, so that the curves show little up and down variation. The prefectures like Kagoshima and Yamaguchi indicate transitional change to an epidemic

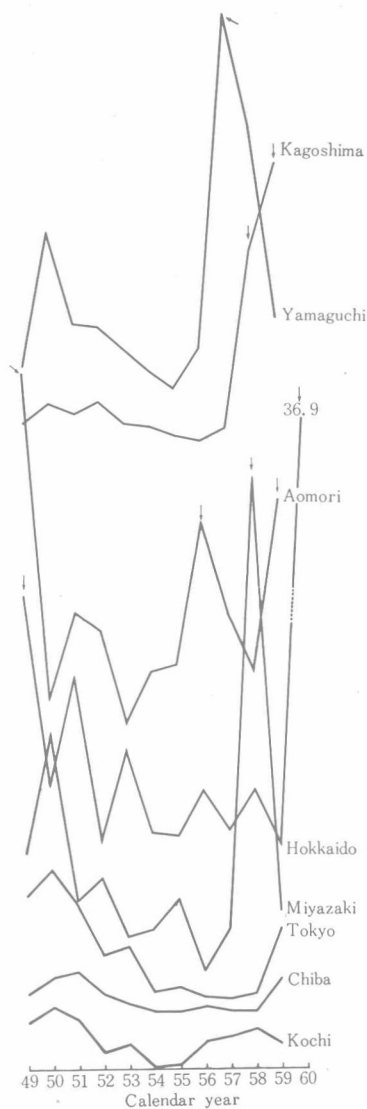


Fig. 4. The trend of annual incidence rate (per 100,000) of various prefectures which represent different epidemiological state. (The curves are transferred each other in order to avoid overlap).

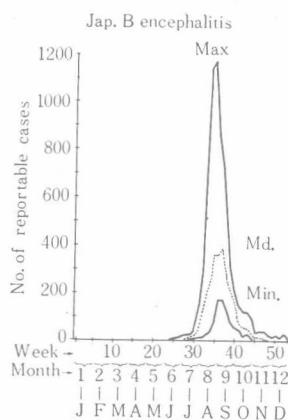
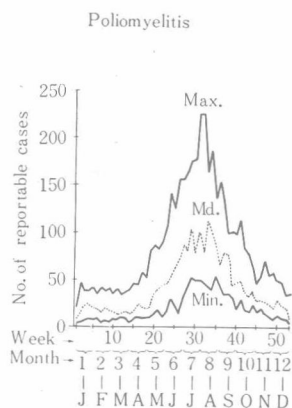


Fig. 5. Variation chart of poliomyelitis and Japanese B encephalitis in Japan.

increase of patients from the low endemic level. On the other hand, in the epidemic areas like Miyazaki, Aomori and Hokkaido, the curves