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Epidemiological studies on subacute myelo-optico-neuropathy with abdominal symptoms (SMON) in epidemic area of Okayama Prefecture, Japan. XI. Epidemiological studies on SMON

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Abstract

Epidemiological study on the prevalence of SMON III Ibara City, Yoshii Town and Yubara Town in Okayama Prefecture was conducted and the following results were obtained. "Epidemization precession" (Die Prazession der Durchseuchung), described by Rudder which shows that ages common to this disease is shifting to younger generation as incidence rate increases, in the endemic regions was recognized in Ibara City and Yubara Town. The mode of the distribution of the interval between the primary and secondary patients in a family suggests that it corresponds to the incubation period. Distribution of the patients to the size of family is not adaptable to binomial model, but adaptable to chain binomial model, and the intra-household transmitted rate is 5 per cent, and the true intra-household transmitted rate is about two times as high as extra-household transmitted rate by the modified chain binomial model. Intra-hospital incidence among SMON patients and non-SMON patients as well as medical workers were observed at the time when the number of new patients increased in a hospital. In SMON patients, the rate of appendectomized ones was higher than that of non-SMON patients, suggesting that gastrointestinal tract has some relationship to the development of SMON disease.

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EPIDEMIOLOGICAL STUDIES ON SUBACUTE MYELO-OPTICO-NEUROPATHY WITH ABDOMINAL SYMPTOMS (SMON) IN EPIDEMIC AREA OF OKAYAMA PREFECTURE, JAPAN

(PART XI. EPIDEMIOLOGICAL STUDIES ON SMON)

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So-called subacute myelo-optico-neuropathy with abdominal symptoms (SMON) was first reported by TAKASAKI (1) in 1961 in Mie Prefecture, central part of Japan. Since then, the number of patients of SMON has been found increasing in many places throughout Japan, and the number of patients reported during 1967 to 1968 reached 4, 280 (2). As to the sex and age distribution of SMON patients, the number of female patients was predominant, the ratio being 2. 2 : 1 (3) in Okayama Prefecture, and 2. 0 : 1 in all over the country, and incidence in the sixties was highest in both male and female (2).

The clinical symptoms of SMON show signs of lateral corticospinal tracts and of posterior column disturbances (4) ensuing from abdominal symptoms, and 89.5 per cent of patients show sensory disturbance and 60.8 per cent motor disturbance and 23.5 per cent are accompanied by visual disturbances (2).

As to the causes of this disease, slow viral infection (5) mycoplasma infection and intoxication by pesticides (3, 6) and chinoform have been pointed out.

In Okayama Prefecture situated in the western part of Japan, prevalence of SMON mainly developed in two districts (3, 6—11); Ibara City -Yoshii Town and Yubara Town in 1964 to 1970 and patients amounted to 338 out of 54, 117 of inhabitants. This report describes briefly the results of our study on the epidemiological characteristics of SMON in these districts.

METHODS OF SURVEY

The clinical history of patients was examined in two hospitals, where most

of SMON in those districts were hospitalized. The patients in other hospitals were checked at Ibara City Hall and at Yubara Town Office, taking the above clinical episodes as the reference elements for diagnosis.

RESULTS

Age distribution of patients, "Epidemization precession" ("Die Präzession der Durchseuchung") (12)

Incidence of SMON patients per 100, 000 people in Ibara City was 83 in 1967, 160 in 1968, 160 in 1969, and 8 in 1970 and that in Yubara Town it was 140 in 1967, 690 in 1968, 620 in 1969, and 53 in 1970. The incidence was highest in 1968 and 1969 in Ibara City, and in 1968 in Yubara Town. The incidence of patients classified by age was highest in the range of the fifties in 1967 and was predominant in the thirties in 1968, when the incidence in all ages was found to be highest, and the incidence according to age was highest in the forties in 1969 in Ibara City. It means the distribution of common ages for this disease to be shifting to younger generations as the incidence increases and so called "Epidemization precession" being recognized in Ibara City, as shown in Fig. 1-A. In contrast, the incidence classified by age in Okayama Prefecture was highest in the sixties from 1967 to 1968 and in the fifties in 1969. A similar tendency to the one recognized in Ibara City was found at Yubara Town as shown in Fig. 1-B., and the incidence in the sixties was predominant in

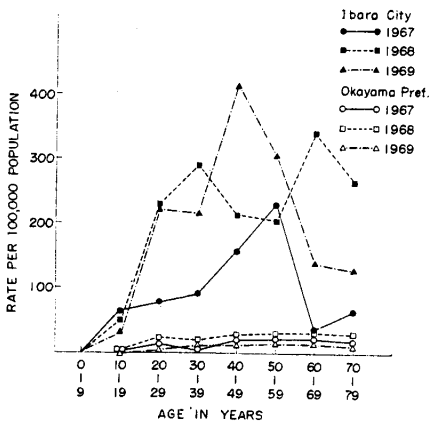

Fig. 1-A

Fig. 1 Incidence of SMON patients classified by age with lapse of year in Ibara District and Okayama Prefecture (Fig. 1-A) and Yubara Town (Fig. 1-B).

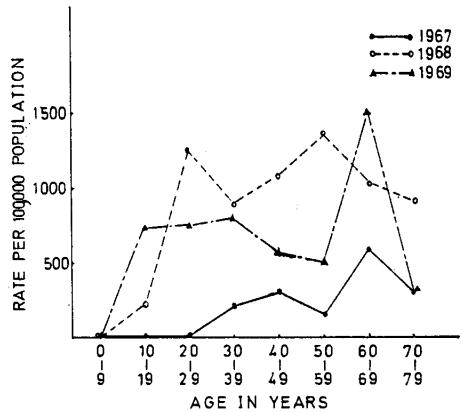

Fig. 1-B

1967 and that in the fifties and in the twenties it was predominant in 1968, and that in the sixties and in the thirties was predominant in 1969. Fatality rate of SMON in Ibara City was 15.6, 6.3, 4.8 and zero per cent in 1967, 1968, 1969 and 1970 respectively, and at Yubara Town it was 12.5, 15.0, 20.0 and zero per cent each year. Therefore, paralell relationship between fatality rate and "Epidemization precession" existed only in Yubara Town. Results of occurrence of patients in 1970 were investigated until November 1970.

It must be also noted that in Ibara City, the decrease of the fatality was followed by the gradual decline in SMON prevalence represented with incidence.

As to the age distribution of patients of intra-familial incidence, it was recognized that the secondary patients were shifting to younger ages

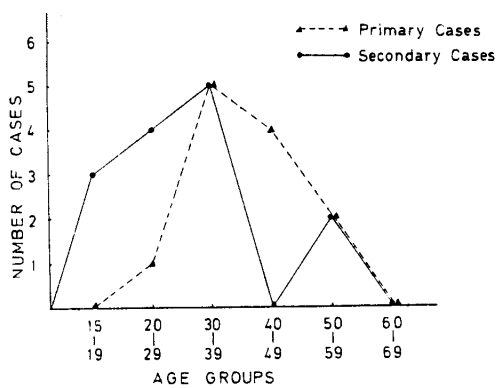

Fig. 2 Number of primary and secondary cases in intra-familial occurrence classified by age in Yubara District.

rather than the primary cases as shown in Fig. 2.

Familial aggregation

Frequency distribution of the intervals between the primary and secondary patients in one family in Ibara City, Yoshii Town and Yubara Town are shown in Fig. 3, and the two main peaks are noticed. Cases up to the second week suggest that they were transmitted at the same time as the primary cases, and the second main peak suggests that it corresponds to the incubation period.

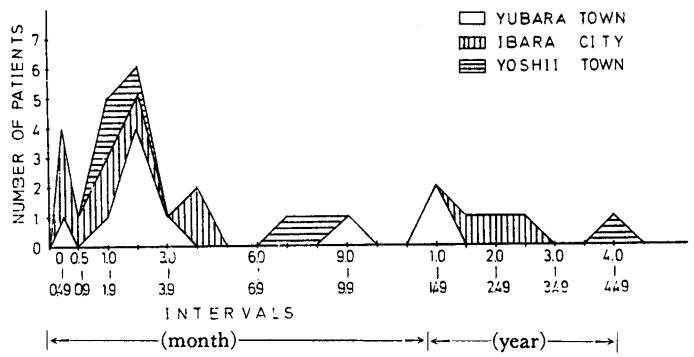

Fig. 3 Frequency distribution of interval between primary and secondary cases in intra-familial occurrence.

The secondary attack rate in the family of SMON was 2.9 per cent in Ibara City, 3.1 per cent in Yoshii Town and 7.2 per cent in Yubara Town respectively. And it was 5.80 times as high as the incidence in Ibara City, 6.74 times in Yoshii Town, and 4.80 times in Yubara Town. In Yumoto Section, the most prevalent district of Yubara Town, the secondary attack rate was 7.5 per cent and it was 2.14 times as high as incidence of Yubara Town.

In order to clarify the familial aggregation, we made the comparison of the intra-familial distribution of patients to the size of family, using the binomial model, chain binomial model (13) and modified chain binomial model (14). The distribution of SMON patients to the size of family cannot be adapted to binomial model, as the Chi square values (839.92) calculated by the difference between observed values and estimated ones, proves that the above difference is highly significant within 1 per cent level as shown in Table 1. And it can be adapted to GREENWOOD's model (13) as shown in Table 2, in the case of household of three, and the transmittance rate between household is about 0.05 and distribution of above rate in Ibara City and Yubara Town is shown in Fig. 4. A similar

TABLE 1. NUMBER OF HOUSEHOLD CLASSIFIED BY SIZE OF FAMILY AND BY SMON PATIENTS IN ONE HOUSEHOLD AND NUMBER OF HOUSEHOLD ESTIMATED BY BINOMIAL MODEL IN ALL DISTRICTS OF IBARA CITY, YUBARA TOWN AND YOSHII TOWN.

Patients in the household	Size of family 1	2	3	4	5	Total	Total number of patients
0	543	1209	1605	2012	1723	7092	
	(555.24)	(1217.04)	(1599.51)	(1993.58)	(1702.75)	(7091.12)	
1	17	24	35	48	51	175	175
	(4.76)	(20.87)	(41.14)	(68.53)	(72.99)	(208.29)	
2		5	1	6	1	13	26
		(0.09)	(0.35)	(0.88)	(1.24)	(2.56)	
3			0	1	2 3	(0.02)	9
			(0.00)	(0.01)	(0.01)		4
4				1	0 1		
				(0.00)	(0.00)		
Total	560	1238	1641	2068	1777		214
Total number of family size	560	2476	4923	8272	8885	25116	

$p=0.0085$ $\chi^2=839.92$

TABLE 2. AN EXAMPLE OF GREENWOOD'S MODEL OF CHAIN BINOMIAL; HOUSEHOLD OF THREE ABOVE 15 YEARS OLD IN IBARA CITY, YUBARA TOWN AND ALL DISTRICTS OF IBARA CITY, YUBARA TOWN AND YOSHII TOWN IN OKAYAMA PREFECTURE.

Type of chain	Frequency	Ibara City Observed numbers	Ibara City Expected numbers	Yubara Town Observed numbers	Yubara Town Expected numbers	All districts Observed numbers	All districts Expected numbers
1−0	q^2	40	39.38	11	11.06	57	56.5
1−1	$2pq^2$	3	4.25	1	0.88	5	5.99
1−1−1	$2p^2q$	1	0.24	0	0.04	1	0.34
1−2	p^2	0	0.13	0	0.02	0	0.18
Total	1	44	44	12	12	63	63
			$p=0.054$		$p=0.040$		$p=0.053$
		d·f=2	$\chi^2=2.19$	d·f=2	$\chi^2=0.077$	d·f=2	$\chi^2=1.63$

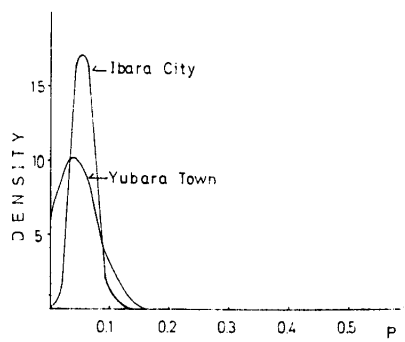

Fig. 4 Distribution of P[intra-household transmittance rate] in household of three, in Ibara City and Yubara Town.

TABLE 3. CHI SQUARE VALUES AND P VALUES CALCULATED BY GREENWOOD'S MODEL AND PE AND PI VALUES BY MODIFIED GREENWOOD'S MODEL IN IBARA CITY, YUBARA TOWN AND ALL DISTRICTS OF IBARA CITY, YOSHII TOWN AND YUBARA TOWN.

Districts	Size of family	Greenwood chain binomial		Modified chain binomial		
		p	χ^2	pE	pI	χ^2
Ibara city (over 15 years old)	3	0.054	2.19 (d·f=2)	0.019	0.034	0.046 (d·f=1)
	4	0.017	0.11 (d·f=1)			
	5	0.057	1.51 (d·f=2)			
Yubara town (over 15 years old)	3	0.04	0.077 (d·f=2)	0.036	0.065	5.08 (d·f=2)
	4	0.109	3.88 (d·f=3)			
	5	0.062	0.61 (d·f=1)			
All districts (over 15 years old)	3	0.053	1.63 (d·f=2)	0.016	0.031	0.99 (d·f=1)
	4	0.045	12·05 (d·f=3)			
	5	0.052	2.65 (d·f=1)			
All districts (all ages)	3	0.014	0.02 (d·f=2)	0.012	0.043	7.38 (d·f=2)
	4	0.059	6.79 (d·f=3)			
	5	0.022	7.98 (d·f=1)			

TABLE 4. AN EXAMPLE OF THE MODEL OF MODIFIED GREENWOOD TYPE OF CHAIN BINOMIAL, HOUSEHOLD OF THREE ABOVE 51 YEARS OLD IN ALL DISTRICTS OF IBARA CITY, YUBARA TOWN AND YOSHII TOWN IN OKAYAMA PREFECTURE.

Type of chain	Frequency	All districts	
		Observed numbers	Expected numbers
0	qE^3		1277.11
1−0	$3pEqE^2(qEqI)^2$	57	56.64
1−1−0	$6pEqE^2(1-qEqI)(qEqI)^2$	4	5.32
2−0	$3pE^2qE(qEqI)$	1	0.96
1−1−1	$6pEqE^2(1-qEqI)^2(qEqI)$	1	0.26
1−2	$3pEqE^2(1-qEqI)^2$	0	0.14
2−1	$3pE^2qE(1-qEqI)$	0	0.05
3−0	pE^3	0	0.01
Total	1		1340.49

pE=0.016
pI=0.031
χ^2=0.99

tendency was observed in all the districts and in all the cases shown in Table 3. And we investigated the intra-household transmittanced rate and extra-household transmitted rate by modified GREENWOOD model (14) and found that the former is about two times as high as the latter in all families as shown in Table 4.

Intra-hospital occurrence :

Outbreaks of SMON were recognized from two hospitalized patients of non-SMON diseases, one hypertension and one angina pectoris, and the wife in attendance on her invalid husband (apoplexia) and also five medical workers in one hospital in Okayama Prefecture when the number of newly hospitalized patients increased in this hospital as shown in Fig. 5.

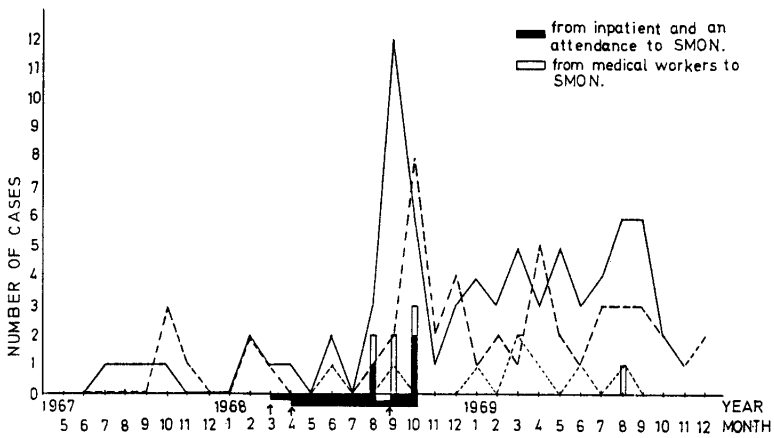

Fig. 5 Number of patients entering hospital (solid line), those of leaving hospital (dotted line), those in hospital (chain line), intra-hospital occurrence of non-SMON patients (solid column) and medical workers (open column) and arrow shows the date entering hospital of non-SMON patients.

Episodes of SMON patients

Episodes of SMON patients were investigated in a hospital located in Yubara Town and it was found that episodes of appendectomy in SMON patients are more frequent than those of non-SMON patients, and the frequency in the former group was 50 per cent (23/46) and that in the latter was 12 per cent (5/43), and the difference between the two was significant within 1 per cent level, when comparable sex and age as non-SMON control group were checked. Interval between onset of disease and appendectomy is 9.1 ± 6.6 $(m+\sigma)$ years on average in all SMON patients, 7.9 ± 4.1 years in patients below age 30 and 9.8 ± 7.5 years in patients above age 30 respectively.

DISCUSSION

Age distribution

"Die Präzession der Durchseuchung" (Epidemization precession) reported by RUDDER (12) was recognized in patients of diphtheria, scarlet fever and measles. One of the causes of "Die Präzession der Durchseuchung", lies in the fact that the primary patients are rather old, and consequently the secondary patients are rather younger members in one household, and a similar tendency was observed in the familial cases of Yubara Town. Relationship between development of immunity in inhabitants and this tendency is yet to be investigated.

Familial aggregation

The survey of the distribution of SMON patients according to the family size in Ibara City and Yubara Town indicates that it is not adaptable to binomial model and is adapted to chain binomial model. This means that the intra-familial occurence may be chain transmission. The rate of intra-household transmission of GREENWOOD's model (13) was about 5 per cent, and compared with the above rate with that of measles (80 per cent) (15) and that of influenza (10 per cent) (16), the rate of the SMON is lower than that of measles and influenza. When the rate of intra-household transmission rate by GREENWOOD's model is divided into true intra-household transmittance rate and extra-household transmitted rate by modified GREENWOOD's model and calculated, it can be seen that the former is 2 times as high as the latter. Therefore, familial aggregation is also verified by this model.

Past history

The influence of appendectomy on the development of SMON is obscure. With the evidence that SMON patients had the past history of gastrointestinal disturbances followed by this disease which ensued from abdominal symptoms (diarrhea and abdominal pain), it is suggested that the primary locus of this disease is intimately related to gastrointestinal tracts.

Comparison of outbreak of patients among poisoning and chronic infectious diseases

We compared the onset mode of this disease with that of Minamata disease (17) which is due to intoxication by methyl mercuric chloride and with that of infectious hepatitis (18). As shown in Table 5, it is observed that the outbreak of patients in hospital is found in the case of infectious hepatitis and SMON. Familial aggregation is recognized in all diseases

TABLE 5. COMPARISON OF MODES OF EPIDEMIC, MINAMATA DISEASE, SMON AND INFECTIOUS HEPATITIS

	Minamata disease	SMON	Infectious hepatitis
Yearly incidence		Peak after few years	Peak in about a year
Monthly incidence	Commonly found in summer	Commonly found in Feb., May, Sept.	Commonly found in July, Aug.
Incidence in various areas	On seashore	Epidemic and sporadic	Epidemic and sporadic
Occupational incidence	65 % in fishery	Farmer, medical and office worker	Not specific
Incidence in ages	All ages (especially in below 10 years)	Above 15 ages	All ages
Incidence in sex	♂ ; ♀ = 1 : 1	♂ : ♀ = 1 : 2(common in appendectomy cases)	♂ : ♀ = 1 : 1
Die Präzession der Durchseuchung	Unknown	Appearent	Appearent
Family aggregation	About 40 %	About 20 % (chain binomial)	About 30—60 %
Interval between primary and secondary patients in family	Not specific	About 2½ months	about 2 months
Hospital infection	Unknown	Positive	Positive

Minamata disease (Kitamura (17))
Infectious hepatitis (Kosaka (18))
SMON (Epidemic area in Okayama Prefecture (3, 6—11))

but in the intervals between the primary and the secondary patients, two peaks; of which the first peak depicts the outbreak at the same time and the second peak suggests an incubation period, as recognized in both infectious hepatitis and SMON, and only the first peak is found clearly in Minamata Disease. "Die Präzession der Durchseuchung" was found in both SMON and infectious hepatitis. All these epidemiological evidences suggest the infectious nature of SMON. In additoin to this, inhabitants in Minamata endemic area of Kumamoto Prefecture consume fish and shells containing mercuric chloride at their meals so that they suffer from Minamata disease and most noteworthy is the fact that 65 per cent of Minamata disease patients are fishermen. However, patients of SMON and infectious hepatitis have no specific association with occupation, except that comparatively many medical and official workers are found in the patients of SMON. This also suggests that the trigger of SMON is rather close to the infectious one. Further survey about this problem will be investigated.

CONCLUSION

Epidemiological study on the prevalence of SMON in Ibara City,

Yoshii Town and Yubara Town in Okayama Prefecture was conducted and the following results were obtained.

"Epidemization precession" (Die Präzession der Durchseuchung), described by Rudder which shows that ages common to this disease is shifting to younger generation as incidence rate increases, in the endemic regions was recognized in Ibara City and Yubara Town.

The mode of the distribution of the interval between the primary and secondary patients in a family suggests that it corresponds to the incubation period. Distribution of the patients to the size of family is not adaptable to binomial model, but adaptable to chain binomial model, and the intra-household transmitted rate is 5 per cent, and the true intra-household transmitted rate is about two times as high as extra-household transmitted rate by the modified chain binomial model.

Intra-hospital incidence among SMON patients and non-SMON patients as well as medical workers were observed at the time when the number of new patients increased in a hospital.

In SMON patients, the rate of appendectomized ones was higher than that of non-SMON patients, suggesting that gastrointestinal tract has some relationship to the development of SMON disease.

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