A COMPARATIVE STUDY OF THE RECENT MALARIA EPIDEMICS IN JAPAN AND LOWER YANGTZE VALLEY DISTRICT

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(Received June 3, 1953)

At the end of the Second Great War a great outbreak of malaria epidemic seemed to be inevitable in Japan, because a multitude of service-men having been inflicted with malaria at the front (New Guinea, Sundaic Islands, Malaya, South and Central China) were making their way home to the four islands of Japan Proper where, together with their families who were in extreme distress on account of their defeat in the war, a potent malaria vector, *Anopheles hyrcanus var. sinensis*, was awaiting them. Nevertheless, to date, as late as seven years thereafter, no epidemic, even of the smallest scale, has been reported.

In the face of this unexpected outcome the author cannot help remembering the miserable status of endemic malaria in the Lower Yangtze Valley District. There malaria has spread all over the region for these three decades as a result of persistent war disaster and famine, in spite of apparently the same climatic, geographical and entomological conditions as exist in Japan.

Two series of malaria surveys carried out by the author, one at Wanshiching[1], a small village (population 5,000) situated 35 km south of Wuhu, Anhui Province, Central China, and another in Kurashiki[2),3)], a medium-sized town (population 50,000) in Okayama Prefecture, Japan, have happened to afford an excellent source of materials for the comparative study of malaria epidemics. The principal purpose of the present paper is to elucidate the difference in the epidemiology of malaria in the two regions, propounding some comment on the reason why a postwar malaria epidemic in Japan failed to appear.

Materials and Methods

The investigations were carried out, at wanshiching, during April 1942 to March 1943, and, in Kurashiki for the period of September 1946 to December 1947. The subjects investigated were the patients who consulted the free dispensary (Wanshiching), and the outpatients of the medical clinic of the hospital (Kurashiki).

1. Parasite detection and spleen palpation. The list of patients was renewed every month for the purpose of obviating doubled examination upon the same subjects who had already been examined in the same month. Blood specimens were taken from ear-lobes, irrespective of the kind of illness, for the thick smear films which were

stained with Giemsa's solution. When parasites were discovered under a microscope, their species were recorded. The spleens were palpated in dorsal recumbent position, and the sizes were indicated by the number of finger breadths below the costal margin.

2. Primary cases and relapsed cases. All the subjects were asked about their past illness with special reference to malaria. In persons with more than two malarial paroxysms, the later ones were regarded as relapse of the preceding attack. Subjects with both parasites and symptoms were classified as true cases. Patients without past history of malaria were grouped into primary cases, and the others into relapsed cases. Persons with parasites, yet without symptoms, were regarded as latently infected.

Results and Discussion

1. A Perspective View of Recent Epidemics (Table 1)

(1) Japan [2),3)]

Twenty per cent of the persons who returned from overseas had malarial attacks after their arrival back in Japan, and about two per cent had primary benign tertian paroxysms with prolonged incubation from the latent infection acquired overseas. Thus twenty-two per cent of the repatriated constituted an infective source of malaria (Table I). Since the repatriated numbered six millions in all, 1,270,000 persons formed the infective source. This is equal to 1.7 per cent of the total population (75 millions) who had never been abroad. Despite such a great source of infection, only 75,000 new infections occurred all over Japan. In other words, as little as 5.9 persons had new infections from an infective source which was composed of one hundred malaria patients, a considerably low rate of new infection.

Sawada (1949)[4)] on the basis of his survey throughout Japan, and independent of the present author, estimated a lower infection rate, namely 3.5 new infections per 100 infective sources. In either case it is apparent that malaria has subsided spontaneously without producing any recognizable epidemic.*

(2) Lower Yangtze Valley District (Fig. 1)[5)]

Figure 1 is the geographical schema of the comparatively recent status of endemicity. The characteristic features of the malaria in this area are: a) Malaria is more prevalent in villages and towns than in larger cities. b) Benign tertian fever is common in the ordinary year, while subtertian or, occasionally, quartan fever is predominant during epidemics. The tertian and subtertian are evenly distributed all over the district, the quartan being found in scattered distribution forming several

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* Japan was not always completely free of malaria in the days before the War. Toward the end of the last century there were 300 to 1000 malaria deaths annually, and even around the year 1937 there were 20 to 30 deaths. Subsequent to the outbreak of the Sino-Japanese hostilities (1939 and 1940) deaths rose to 200 or 300 annually. In the statistical record of the Welfare Ministry it was said that there were 20,000 malaria patients of one fever type, benign tertian malaria, all over the country in 1943, and that it was endemic in the prefectures: Shiga, Fukui, Ishikawa, Toyama, Niigata, Tochigi and Kôchi.

TABLE I

Malaria among repatriated people (1946–1947, Kurashiki)

(1) Incidence of malaria patients

Areas evacuated	Number	Rate of positive malaria history (%)	Rate of relapse in Japan (%)	Rate of primary attack in Japan (%)
South Sea Area	125	74.3	49.6	1.6
Central China, South China, and Formosa	147	59.8	27.9	1.4
Korea, Manchuria, North China	370	14.6	6.2	1.9
Other Areas	3			
Total	645	36.4	19.5	1.7

(2) Fever type of malaria

Fever type	Number	Rate of relapse in Japan (%)	Rate of primary attack in Japan (%)
Benign tertian	159	49.0	6.9
Quartan	1		
Subtertian	21	61.9	
Benign tert. and Subtert.	35	68.6	
Benign tert. and Quartan	1	100.	
Obscure	18	55.5	
Total	235	53.5	4.7

(3) Enlargement of the spleen

Morbid history	Number	Number of enlarged spleens	Spleen rate (%)
Without malaria	410	17	4.1
With malaria	235	52	22.1
without relapse in Japan	98	5	5.1
with relapse in Japan	126	47	37.2
parasite carriers	22	18	81.8
Total	645	69	10.6

endemic foci. c) Malaria is common among young subjects, the poor, among soldiers and police-men, whereas it is rarely found among children, the rich and persons who make an ordinary occupations. In epidemics, however, various people are affected, irrespective of age and social class, and exceptionally high parasite rate with low spleen rate is encountered. d) The clinical manifestations are as a rule mild and death is seldom, though mortality rises to as high as six per cent in the epidemic.

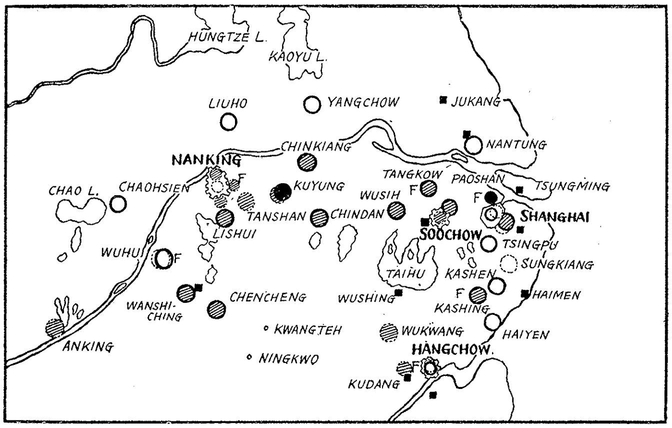

Fig. 1 Geographical schema of malaria endemicity in the Lower Yangtze Valley District.

Survey during 1930∼1934

◌ : Spleen rate <10 per cent

▒ : Spleen rate =10∼20 per cent

◉ : Spleen rate >20 per cent

Survey during 1938∼1942

○ : Spleen rate <10 per cent

◍ : Spleen rate =10∼20 per cent

● : Spleen rate >20 per cent

■ : Endemic focus of quartan malaria, F : Endemic focus of subtertian malaria.

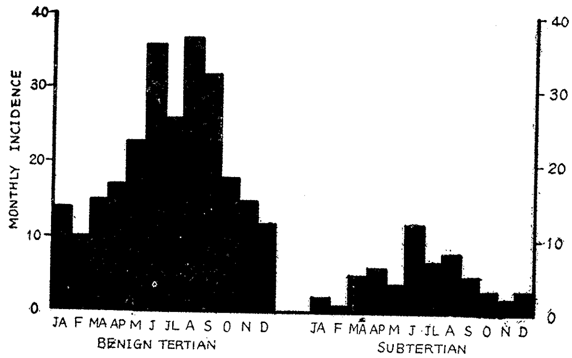

Fig. 2 Seasonal vicissitude of relapse malaria among repatriated people (Kurashiki)

2. *Seasonal Vicissitude*

(1) Japan (Fig. 2)[2),3)]

The patients and parasite carriers discovered in Kurashiki were too small in number (only 22) to discuss the seasonal vicissitude, although gametocytes were found in 70 per cent of the actually infected. Therefore, only an approximate outline of malaria relapse among the repatriated in relation to seasons is presented in Figure 2. It is apparent from the figure that relapses were frequent in the months from March to September, the period when climatic conditions are suitable for malaria propagation. So a good many cases of new infections were reasonably expected to occur in the months from June to November, and to cause, in association with relapse waves, a significant epidemic. Nevertheless, the new infections actually discovered were, as mentioned above, very few, only five per 4143, or approxmately one per 1000.

(2) Lower Yangtze Valley District (Fig. 3, 4 and 5)

In this area the quartan malaria[6,7] bears resemblance to the postwar malaria in Japan particularly in the excessive relapsing (Fig. 3). However the former is distinctly different from the latter in two respects: a) The great majority of relapses appear after October, namely in winter, when climatic conditions do not permit malaria transmission. b) New infections are encountered in summer and autumn, the season of transmission, though much smaller in number as compared with relapses. The morbidity curve rises in July (new infections), reaches its peak in December (relapses) and then falls sharply to zero level in an ordinary year, while in the epidemic year it exhibits a further rise in February and March.

The seasonal vicissitude of benign tertian malaria[8,10] shows a curve which has a steeper ascending limb and a gently-sloping descending limb involving three conspicuous undulations (Fig. 4). The undulations are invariably caused by the upheavals of increase in relapse. Recurrences (long-interval relapse which occurs more than six months after the former attack) increase suddenly toward the end of June and in July when new infection is about to start, and give rise to the first peak (in July), the highest throughout the year. The second (September) and the third (November) peaks are also produced chiefly by recurrence and recrudescence (short-interval relapse which appears within six months from the former attack). New infection is frequent from July to September, but it is not so potent as to modify the shape of the morbidity curve. However, in the epidemic year when new infections are numerous from July the morbidity curve rises higher and higher until it reaches its maximum peak in October, and then declines steeply, because new infections fill the valleys and are piled up on the peaks of the morbidity curve.

Subtertian malaia[7,9,10] usually makes an M-shaped vicissitude with two maximal incidences in July and October (Fig. 5), though in the epidemic year it produces a ⌉ -shaped curve with a single peak which ascends in June or July and descends abruptly after reaching the acme in November. Both relapses and new infections are simultaneously more frequent at peaks than in valleys, that is, new infection waves appear relatively independent of relapse waves, a phenomenon peculiar to subtertian malaria.

3. RELAPSE

(1) Japan (Table II, Equations I and II) [2,3,11,12]

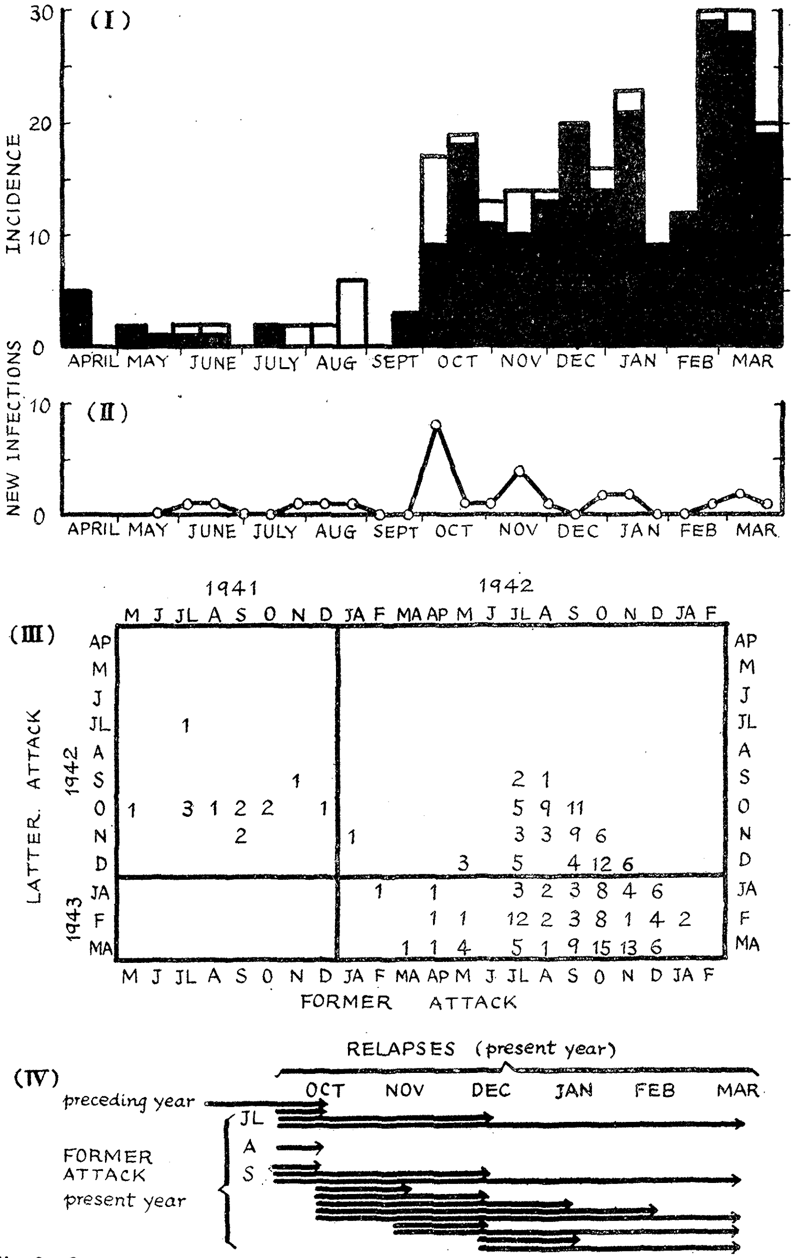

Fig. 3 Quartan malaria in the Lower Yangtze Valley District, its seasonal vicissitude,(I) new infections(II) and relapses.(III. IV)
In (I) white and black columns represent new infections and relapses respecsively.

In (IV) the notation A——→B indicates the malaria relapses in Month B from the former attack in Month A.
Only those cases whose morbid history (date of the former attack in particular) is completely clear were dealt with in (III).

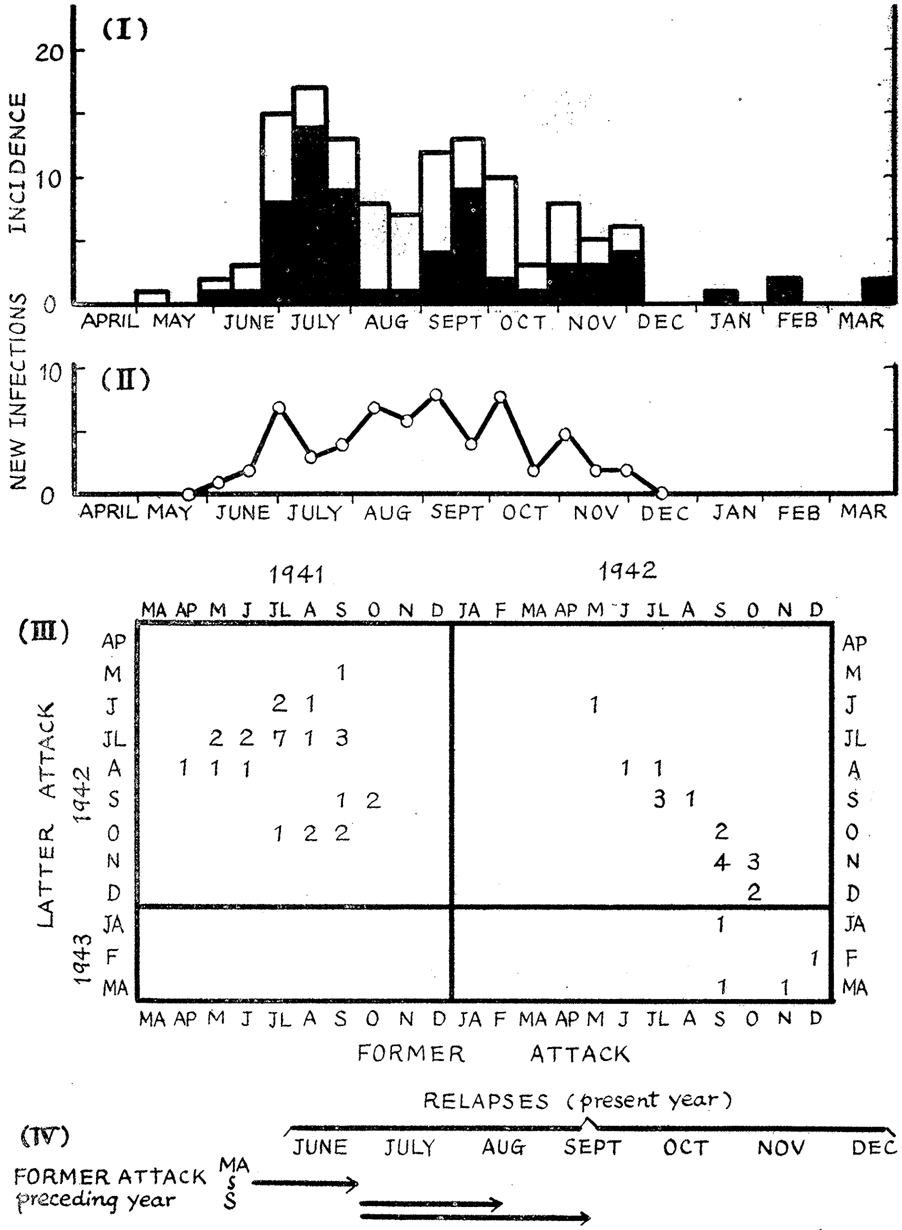

Fig. 4 Benign tertian malaria in the Lower Yangtze Valley District, its seasonal vicissitnde,(I) new infections(II) and relapses. (III. IV)
In (I) white and black columns represent new infections and relapses respecsively.
In (IV) the notation A ——B→ indicates the malaria relapses in Month B from the former attack in Month A.
Only those cases whose morbid history (date of the former attack in particular) is completely clear were dealt with in (III).

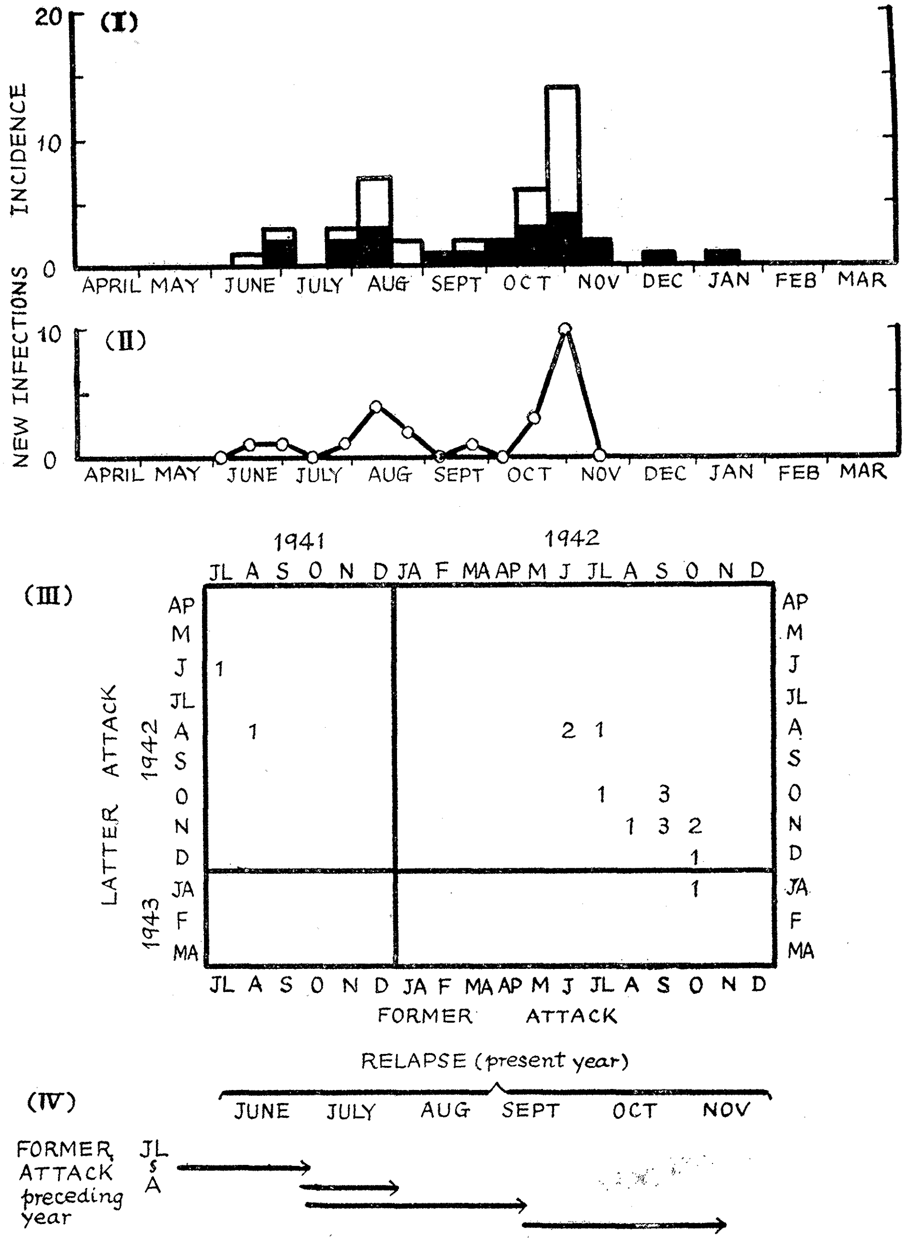

Fig. 5 Subtertian malaria in the Lower Yangtze Valley District, its seasonal vicissitude(I), new infections(II) and relapses. (III, IV)
In (I) white and black columns represent new infections and relapses respecsively.
In (IV) the notation $A \xrightarrow{B}$ indicates the malaria relapses in Month B from the former attack in Month A.
Only those cases whose morbid history (date of the former attack in particular) is completely clear were dealt with in (III).

As shown in Table II the frequency of malaria paroxysms of the repatriated people decreases with a rapid pace until the third year after their arrival back, at which time none is encountered. However, it does not necessarily substantiate the impotence of the malaria relapse. By the same token the mathematical analysis[13] of the interrelationship of relapses with reference to the interval between the former and present attacks (see Equations I and II) reveals that in postwar malaria in Japan, both the benign tertian and subtertian fevers were disposed to more frequent relapsing than were those of the Lower Yangtze Valley District, bearing close resemblance to those of equatorial or tropical regions, especially in that there is little discrimination between recrudescence and recurrence.

Equation (I)[13] .... Benign tertian malaria

$$F(m)=37.2\times\frac{e^{-0.15}\,0.15^{m-1}}{(m-1)!}+5.6\times\frac{e^{-0.15}\,0.15^{m-3}}{(m-3)!}+3.2\times\frac{e^{-0.1}\,0.1^{m-5}}{(m-5)!}+3.2\times\frac{e^{-0.1}\,0.1^{m-7}}{(m-7)!}$$

$$+2.2\times\frac{e^{-0.1}\,0.1^{m-10}}{(m-10)!}+1.1\times\frac{e^{-0.1}\,0.1^{m-13}}{(m-13)!}+1.1\times\frac{e^{-0.1}\,0.1^{m-15}}{(m-15)!}$$

Equation (II)[13] .... Subtertian malaria

$$F(m)=8.5\times\frac{e^{-0.35}\,0.35^{m-1}}{(m-1)!}+0.8\times\frac{e^{-0.35}\,0.35^{m-3}}{(m-3)!}+1.0\times\frac{e^{-0.35}\,0.35^{m-5}}{(m-5)!}$$

$$+1.0\times\frac{e^{-0.35}\,0.35^{m-9}}{(m-9)!}+1.0\times\frac{e^{-0.35}\,0.5^{m-14}}{(m-14)!}$$

TABLE II

Relapse in malaria among repatriated people

(1) Frequency of relapse occurring after arrival back in Japan

	First year			Second year		
	Cases	Paroxysms	Number of relapses per case	Cases	Paroxysms	Number of relapses per case
Benign tertian	91	225	2.4	53	30	0.57
Subtertian	15	54	3.6	10	4	0.4
Benign tertian and subtertian	20	68	3.4	12	11	0.92

(2) Time of final malaria attack

Years \ and Months after repatriation	1	2	3	4	5	6	7	8	9	10	11	12
Zero year	4	2	1	1		2	1	2	2	2	1	
One years	2			1	2			1				
Two years						1						

(3) Interval (in months) between the former and latter attacks

Fever type \ Interval (months)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Benign tertian	32	5	5	1	3		3			2			1		1	
Subtertian	6	2	1		1				1					1		

Malaria relapses discontinuously from the primary (or former) attack with a regular wavy fluctuation which is represented by a combination of Poissonian series $N \times \frac{e^{-\alpha} \quad \alpha^{m-n}}{(m-n)!}$, where the index α represents the probability of calmness of symptoms without relapsing for a month.[13] As clearly seen from the comparison of the equations (I) and (II) with those of (IV) and (V) which are concerned with the relapses in the Lower Yangtze Valley Districts, this index α is distinctly smaller (more inclined to relapsing) and more uniform (recrudescence is hardly discriminated from recurrence because of the almost equal probability of calmness in any individual relapse waves) in the postwar malaria in Japan than in the endemic malaria of the Lower Yangtze Valley District.

Gametocytes were demonstrated in 15 cases out of 22 relapsed cases (including parasite carriers without symptoms) in Kurashiki. Accordingly the gametocyte carriers are estimated to be approximately 70 per cent of the relapsed cases.

(2) Lower Yangtze Valler District (Figs. 3, 4 and 5; Equations III, IV and V)

The analysis of quartan relapse[6),13)] by means of the tabular diagram of Figure 3 discloses that the unevenness of the morbidity histogram is caused by the summation of complicated relapses, as schematized at the bottom of the same figure, although mathematically it assumes a far simpler expression as equation (III).

Similar analyses with respect to benign tertian[8),13)] and subtertian[9),13)] malaria give the schemas presented in Figures 4 and 5 as well as the equations (IV) and (V). In (IV) the relapse waves whose Poissonian index α is 0.4 indicate recrudescence, and those of $\alpha = 0.6$ indicate recurrence. Lower α value for recrudescence than for recurrence shows that the former is more disposed to relapsing than the latter.

Equation (III)[13)] $\cdots\cdots$ Quartan malaria

$$F(m) = 117 \times \frac{e^{-1.3} \; 1.3^{m-1}}{(m-1)!} + 55 \times \frac{e^{-1.3} \; 1.3^{m-4}}{(m-4)!} + 13.5 \times \frac{e^{-0.3} \; 0.3^{m-7}}{(m-7)!} + 22 \times \frac{e^{-1.3} \; 1.3^{m-9}}{(m-9)!}$$

$$+ 7.4 \times \frac{e^{-1.3} \; 1.3^{m-12}}{(m-12)!}$$

Equation (IV)[13)] $\cdots\cdots$ Benign tertian malaria

$$F(m)=10.4\times\frac{e^{-0.4}\,0.4^{m-1}}{(m-1)!}+9.4\times\frac{e^{-0.4}\,0.4^{m-2}}{(m-2)!}+3.0\times\frac{e^{-0.4}\,0.4^{m-4}}{(m-4)!}+5.5\times\frac{e^{-0.6}\,0.6^{m-8}}{(m-8)!}$$

$$+14.5\times\frac{e^{-0.6}\,0.6^{m-10}}{(m-10)}+5.5\times\frac{e^{-0.6}\,0.6^{m-12}}{(m-12)!}$$

Equation (V)[13] .... Subtertian malaria

$$F(m)=9.2\times\frac{e^{-0.5}\,0.5^{m-1}}{(m-1)!}+5.7\times\frac{e^{-0.5}\,0.5^{m-2}}{(m-2)!}+2.0\times\frac{e^{-0.5}\,0.5^{m-11}}{(m-11)!}$$

4. *New Infection*

Inasmuch as there were few new infections of malaria in postwar Japan, only those of the Lower Yangtze Valley District will be dealt with in detail, with special reference to benign tertian and subtertian malaria.

(1) Japan (Table III)[2),3)]

New infections in Kurashiki are summarized in Table III together with the primary attacks with prolonged incubation period; however, the latter do not belong to the strictly new infections in Japan, for they are caused by the latent infection acquired overseas.

Table III

New infections in Kurashiki

(1) Real new infection

Case	Primary attack	Relapse	Splenomegaly	Fever type
1	Early in Sept. 1946	Late in July 1947	−	Benign tertian
2	Early in April 1947		+	Benign tertian with prol. incub.
3	Early in August 1947	Early in Oct. 1947	+	Benign tertian
4	Late in August 1947	Late in Oct. 1947	+	Benign tertian
5	Middle of Sept. 1947		+	Benign tertian

(2) Primary attack caused by the latent infection acquired overseas

Areas evacuated	Interval between repatriation and attack, in months										
	1	2	3	4	5	6	7	8	9	10	11
Korea, Manchuria, and North China	1				1	1	1	1	1	1	
Central China, South China, and Formosa	1	1									
South sea islands	1	1									

(2) Lower Yangtze Valley District (Table IV)[1)]

Since atmospheric temperature required for the sexual cycle (in the anopheline body) of *Plasmodium vivax* and *Plasmodium falciparum* is over 16°C and 18°C respectively (Gill 1938),[14] it is readily presumed from Table IV that the season of transmission falls between May and October, both for benign tertian and subtertian malaria when the malaria transmitter is found in a sufficent number. The validity of this presumption is corroborated by the Figures 4 and 5.*

Primary attack is not necessarily related to the appearance of relapse waves in malaria in the Lower Yangtze Valley District, especially in subtertian malaria, in which both appear almost independently (compare the morbidity curve with the curve of primary attack in Figs. 4 and 5), and new infection is, rather, more dependent on the fluctuation of the subtertian gametocyte rate (Table IV)**.

Summary and Conclusion

With contemplation of the factors governing the incidence of malaria (excluding those concerning anopheline, climatic, geographical and economic conditions) the following summary is derived from what has been stated in the preceding sectons.

(1) Endemicity. After the ending of the Second Great War malaria has failed to establish its endemic on Japanese soil and has not produced even the smallest epidemic. On the contrary, in Lower Yangtze Valley District malaria has become solidly endemic for these three decades, particulary in the rural and suburban districts where a spleen rate of 10 to 20 per cent is commonly demonstrated. Although benign tertian malaria is prevalent, subtertian malaria is almost equally common.

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* Though a small number of primary benign tertian attacks are encoutered after October, they are the clinical manifestations of the infections acquired in October. Primary quartan attacks which occur after October are interpreted as being due to the noxious anopheline bites in September and October with more than four weeks of incubation period. This will be discussed in another paper.

** Frequent primary attacks will be expected in autumn, for the subtertian gametocyte rate is the highest from August to October, while the anopheline population is fairly abundant throughout the transmission season. The fact that there were few primary attacks in September, in the midst of the high gametocyte rate, will be accounted for as folows:

The primary subtertian patient in September is expected to have had a noxious anopheline bite in August, since at least two weeks are requisite for the incubation period. However, the climatic condition is so hot (28.5 C) and dry (below 70 per cent of relative humidity) in this month that the parasite may undergo degeneration, thus resulting in the interruption of transmission and lack of primary subtertian cases in September. The death of anophelines in the course of the parasite's sexual reproduction is excluded, because transmission of benign tertian malaria is definitely demonstrated in August (Fig. 4).

On the contrary, when it is cool and humid in summer, particularly in August, transmission is not discontinued, because parasites maintain their infectivity by virtue of optimum temperature and humidity. Thus the incidence of numerous new infectious will change the morbidity curve into a ∧-shape, filling up the valley of an ordinary M-shaped curve. This is usually the case in an epidemic.

TABLE IV

The gametocyte rate, the number of anophelines (female A. hyrcanus var. sinensis) and the climatic condition at Wanshiching

	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.
Average atmospheric temperature (°C)	14.5	19.5	23.5	29.0	28.5	23.5	18.5	12.0	4.5
Average atmospheric humidity (%)	85	71	87	76	67	78	72	72	73
Gametocyte rate (%) *Plasmodium falciparum*	3.2	1.8	1.6	1.1	2.3	3.3	2.9	5.9	1.7
Plasmodium vivax	1.0	0.6	4.7	4.8	4.5	7.0	2.0	1.7	0.8
*Days necessary for complete sexual cycle of *Plasmodium falciparum*		35	18	15	13	18	48		
of *Plasmodium vivax*		20	12	10	10	12	26		
Female anophelines caught in dwelling houses	97	340	292	639	726	755	314	9	12

*After Stratman-Thomas: Amer. J. Trop. Med. 20: 703–715, 1940

Quartan malaria is found in scattered distribution, forming several endemic foci in certain villages and towns.

(2) Seasonal variation. Inasmuch as eventually quite few new infections (only 5.9 per 100 infective sources) had appeared in Japan despite the presence of a firmly established infective source (1.7 relapsed persons who returned from overseas against 100 subjects who had never been exposed to malaria), the data available for the analysis of seasonal variation was restricted to those of relapsed malaria. The malaria relapses among the repatriated people were frequent from May to October, the season when the climatic condition is specially suitable for the transmission of both benign tertian and subtertian malaria, and assumed nearly the same features of seasonal variation as in the Lower Yangtze Valley District.

(3) Relapse. In the Lower Yangtze Valley District malaria relapses vigorously from late in June through November, although the acme is found in early summer for benign tertian and in autumn for subtertian. The mathematical analysis of the attitude of relapsing (in the Poissonian series) has revealed that the relapsed malaria among the repatriated people was closely related to the malaria of the equatorial zone rather than to that of the Lower Yangtze Valley. In other words, it was disposed to less calmness (or subsidence) of paroxysms than was the Lower Yangtze Valley malaria, and the discrimination of recrudescence from recurrence in benign tertian malaria was hardly noticed, whereas it is very distinct in the Lower Yangtze Valley. A high gametocyte rate (70 per cent) was demonstrated in the relapsed persons.

(4) New infection. That few new infections were found in Japanese postwar malaria is an evidence for the lack of malaria transmission in Japan. In the Lower Yangtze Valley District, however, the active transmission in summer and autumn

(from June to October) produces the primary cases which occur in the period between the latter part of June and December. But primary quartan cases are extremely rare as compared with the abundant relapses, and primary subtertian cases temporarily disappear in September on account of the unfavorable climatic condition for the parasites' sexual reproduction in August.

(5) The reason for the lack of a postwar malaria epidemic in Japan. Since it is apparent from (2), (3) and (4) that there was an infective source which was potent in quantity as well as in quality at least for a few years after the ending of the Second Great War, the lack of a postwar malaria epidemic in Japan seems rather strange. However, from what has been stated there is no room for doubt about the fact that its cause resides outside the "special feature of malaria in the repatriated people". Therefore it must be sought in either of the following factors: the habit of anophelines, geographical features, climatic conditions or the economic state of inhabitants, which may contribute to the interruption of malaria transmission.

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