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□ **Mini-Review** □

Unstable vivax malaria in Korea

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Abstract: Korean vivax malaria had been prevalent for longtime throughout the country with low endemicity. As a result of the Korean war (1950-1953), malaria became epidemic. In 1959-1969 when the National Malaria Eradication Service (NMES) was implemented, malaria rates declined, with low endemicity in the south-west and south plain areas and high endemic foci in north Kyongsangbuk-do (province) and north and east Kyonggi-do. NMES activities greatly contributed in accelerating the control and later eradication of malaria. The Republic of Korea (South Korea) was designated malaria free in 1979. However, malaria re-emerged in 1993 and an outbreak occurred in north Kyonggi-do and north-west Kangwon-do (in and/or near the Demilitarized Zone, DMZ), bordering North Korea. It has been postulated that most of the malaria cases resulted from bites of sporozoite-infected females of *An. sinensis* dispersed from North Korea across the DMZ. Judging from epidemiological and socio-ecological factors, vivax malaria would not be possible to be endemic in South Korea. Historical data show that vivax malaria in Korea is a typical unstable malaria. Epidemics may occur when environmental, socio-economical, and/or political factors change in favor to malaria transmission, and when such factors change to normal conditions malaria rates become low and may disappear. Passive case detection is a most feasible and recommendable control measure against the unstable vivax malaria in Korea in cost-effect point of view.

Key words: *Plasmodium vivax*, Korea, unstable malaria

INTRODUCTION

Malaria, an important communicable disease for many years in Korea, prevailed throughout the country until the 1950s. Since then, cases rapidly declined until it was declared eradicated in 1979 (WHO, 1981). Recently malaria has re-emerged in South Korea and become an important public health threat. Several review papers on malaria in Korea have been published (Paik and Tsai, 1963; Kim, 1982; Paik et al., 1988; Lee et al., 1994; Chai, 1999). Most of these review papers focussed on a specific period. Therefore, a historical review is meaningful for more comprehensive understanding of the epidemiology and potential for malaria control/eradication. In particular, the accomplishments of the National Malaria Eradication Service (NMES) activities, most of which were not officially ducumented are reported rather in detail. Only endemic *Plasmodium vivax* in Korea was dealt in this review, excluding imported cases of *P. malariae*, *P. falciparum* and other imported strains of *P. vivax*. Though there was a strong evidence that *P. malariae* was endemic in limited areas of Chungchongnam-do in 1929-1930 (Chiba and Aki, 1930; Oh, 1930), it was no longer considered as a health threat.

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MALARIA SITUATION BEFORE THE 1950S

Malaria was prevalent and a major health threat in Korea during previous centuries. The vivax malaria was first reported in 1913 by Hasegawa. He reported 1,328 cases of Korean civilians and 147 cases of Japanese soldiers at 13 locations throughout the country (Table 1). Analysis of 1,201 cases showed that (1) 74.5% was male and 25.5% female, (2) age composition was 44.9% in < 10 years, 20.9% in 11-20 years, 14.5% in 21-30 years, 8.7% in 31-40 years, 5.1% in 41-50 years, and 5.9% in > 51 years, and (3) seasonal occurrence was 1.9% in January, 2.2% in February, 2.4% in March, 5.3% in April, 7.8% in May, 21.4% in June, 15.1% in July, 16.1% in August, 14.8% in September, 9.0% in October, 2.7% in November, and 1.2% in December. Epidemiological significance was that the highest positive rate was shown in the age group under 10 years old (44.8%), and 19.7% of the total cases occurred during the period of non-transmission season (November-May), indicating that a Korean strain would be the delayed type temperate zone strain. Among the 67,531 patients who visited the Kangnung Provincial Hospital in Kangwon-do in 1917-1925, 3,083 cases (4.6%) were diagnosed as vivax malaria (Table 2). Many of the cases were reported during the non-transmission period when daily temperatures were below 15°C, suggesting the protracted incubation of vivax malaria in Korea (Himeno, 1926). Malaria parasite rates of school children in Kangwon-do were 8.1% in Korean students and 3.8% in Japanese students at Cholwon, and 16.1% in Korean students and 7.3% in Japanese students at Chunchon (Tanabe, 1927). Kodama (1928) reported that malaria was prevalent throughout Kangwon-do, particularly in counties bordering the Taibaek mountains, where rice paddies were limited. Kobayashi (1931) reported 2,322 malaria cases in 1922, 1,366 cases in 1923, 619 cases in 1924 and 635 cases in 1925 in 6 different locations (Table 3). He also mentioned that malaria cases occurred throughout the Korean peninsula with an uneven geographical distribution, and malaria was the major endemic disease in some areas, whereas very rare in many other areas, indicating focal

Table 1. Number of malaria patients treated at hospitals in 1910 (Hasegawa, 1913)

Locality	Korean civilians	Japanese soldiers
Uiju	63	—
Pyongyang	36	—
Hamhung	328	16
Onjong	—	40
Wonsan	—	31
Chunchon	294	—
Seoul	114	47
Kongju	66	—
Taejon	—	13
Chungju	93	—
Kwangju	198	—
Chinju	136	—
Total	1,328	147

Table 2. Malaria cases treated at the Kangnung (Kangwon-do) provincial hospital (Himeno, 1926)

Year	No. of patients	No. of malaria cases	%
1917	7,347	163	2.2
1918	7,871	85	1.1
1919	8,410	133	1.6
1920	9,309	362	3.9
1921	9,140	732	8.0
1922	8,590	756	8.8
1923	3,744	209	5.6
1924	6,989	335	4.8
1925	6,131	308	5.0
Total	67,531	3,083	4.6

Table 3. The malaria cases in different localities in 1922-1925 (Kobayashi, 1931)

Locality	1922	1923	1924	1925
Hoeryong	42	24	24	17
Chunchon	1,287	825	226	370
Andong	461	243	206	115
Cheju	417	187	71	26
Kumchon	63	58	56	72
Seoul	52	29	36	35
Total	2,322	1,366	619	635

Table 4. Malaria cases admitted in the Severance Hospital, Seoul, 1926-1935 (Choi, 1936)

Year	Total patients admitted	No. of malaria cases	%
1926	2,149	13	0.6
1927	2,349	7	0.3
1928	2,530	20	0.8
1929	2,641	19	0.7
1930	2,435	2	0.1
1931	2,661	2	0.1
1932	2,774	3	0.1
1933	3,140	3	0.1
1934	3,062	7	0.2
1935	3,034	8	0.3
Total	26,775	84	0.31

malaria transmissions. It is interesting to note that the highest number of malaria cases were reported in Hamhung, Hamkyongnam-do in 1910 (Hasegawa, 1913) and in 1923-1925 (Nagai, 1925). Among a total of 26,775 patients admitted to Severance Hospital, Seoul, during a 10 year period (1926-1935), 84 patients (0.3%) were diagnosed as malaria (Table 4) (Choi, 1936).

Available information reported on malaria in Korea prior to 1945 indicates that vivax malaria was endemic and prevalent throughout the Korean peninsula, demonstrating an uneven geographical distribution with a higher incidence rate in mountainous areas rather than large rice growing regions.

There were little data reported for the prevalence of malaria in Korea during the second world war (1941-1945), a period following post-indenpendence (1945-1950) and the Korean war (1950-1953). Among 3,983 students of middle schools in Seoul in 1948, 584 students (14.7%) were diagnosed as malaria (Chun, 1959). In 1952, 1,032 malaria cases were reported from April through September (peak in July) in Yangyang-gun (county), Kangwon-do, of which the highest rate was identified in children under 5 years (Kim and Han, 1953). They also conducted a mass blood survey of 208 soldiers and found 4.8% positive rate. The military medical office reported from a military population of 400,000 that there were 8,855 cases (2.2%) and 5,741 cases (1.4%) of malaria in 1953 and 1954, respectively. US troops dispatched to the Korean war were provided chloroquine chemoprophylaxis (weekly) during the transmission season. Nevertheless 1,513 soldiers were reported with vivax malaria from July 1951 through November 1952 (Hanky et al., 1953). Among 1,350 Canadian soldiers that deployed to Korea during the Korean war in 1952, 152 (11.3%) became ill with vivax malaria after returning home country (Hale and Halpenny, 1953).

Judging from such limited data, it is certain that the prevalence of malaria in Korea increased in remarkable degree as a result of the Korean war. Because of poor records and population movement, the geographical distribution is not well understood.

ACCOMPLISHMENTS OF THE NATIONAL MALARIA ERADICATION SERVICE

The National Malaria Eradication Service (NMES) was established in April 1959 as a joint project of the Republic of Korea and the UN/WHO Western Pacific Regional Office. The Service was consisted of 28 Korean members and 2-3 WHO consultants (malariologist, parasitologist and/or entomologist), assigned to parasitological laboratory, entomological and epidemiological teams. The results of NMES activities were incompletely reported in published documents (Paik and Tsai, 1963; Whang, 1962, 1963, 1964; Paik et al., 1965; Paik and van der Gugten, 1966; NMES, 1966; Hong, 1967; Chen et al., 1967; Ree and Paik 1967; Hong and Ree, 1968). The followings are the summarized results of NMES activities.

Spleen survey

One of the earliest methods used for estimating malaria endemicity in a given lo-cality is to determine the proportion of persons with a palpable enlargement of the spleen. During the period of July-October 1959, a spleen survey was conducted at 37 counties in 9 provinces. A total of 22,005 children under 15 years were examined with an average spleen rate of 1.1% (range 0.0-3.8%). The results of the spleen survey by province are shown in Table 5, and their geographical distribution by county is given in Fig. 1, which revealed that vivax

Table 5. Results of the spleen survey of children under 15 years old in July-October 1959 (NMES, 1966)

Province	No. examined	No. of enlarged spleens	Spleen rate
Kyonggi-do	4,789	86	1.8
Kangwon-do	2,919	8	0.3
Chungchongbuk-do	1,577	8	0.5
Chungchongnam-do	1,922	44	2.3
Kyongsangbuk-do	2,108	12	0.6
Kyongsangnam-do	2,435	13	0.5
Chollabuk-do	1,968	38	1.9
Chollanam-do	2,678	12	0.4
Cheju-do	1,609	28	1.7
Total	22,005	249	1.1

malaria was widely dis-tributed but hypoendemic.

Mass blood survey

A mass blood survey was carried out at 278 selected villages of 41 cities/counties in 9 provinces during 1960. A total of 18,697 children under 15 years were examined with 212 children (1.1%) positive for *P. vivax* (Table 6, Fig. 2) (NMES, 1966). The highest slide positive rate was shown in Andong-gun (11.7%), followed by Yechon-gun (10.3%), Bongwha-gun (5.4%), and Yongju-gun (2.8%), all of which are located north Kyongsangbuk-do.

Passive case detection (PCD)

PCD is not only an effective measure of malaria incidence but one of the control measures, particularly in unstable vivax malarial areas. During 1961-1962, PCD units consisted of health centers, hospital/clinic physicians, and school nurses throughout the country. The PCD network was expanded to include villages, training all village chiefs/leaders and voluntary collaborators. Efforts were emphasized especially in high endemic areas, i.e., Kyongsangbuk-do and Kangwon-do. During 1961-1965, a total of 11,259 PCD workers were trained (average 42/100,000 population; range 5-124). Of them, 3,453 workers (30.6%) participated in PCD activities, taking blood smears from all fever cases and sending the slides to NMES laboratory, as well

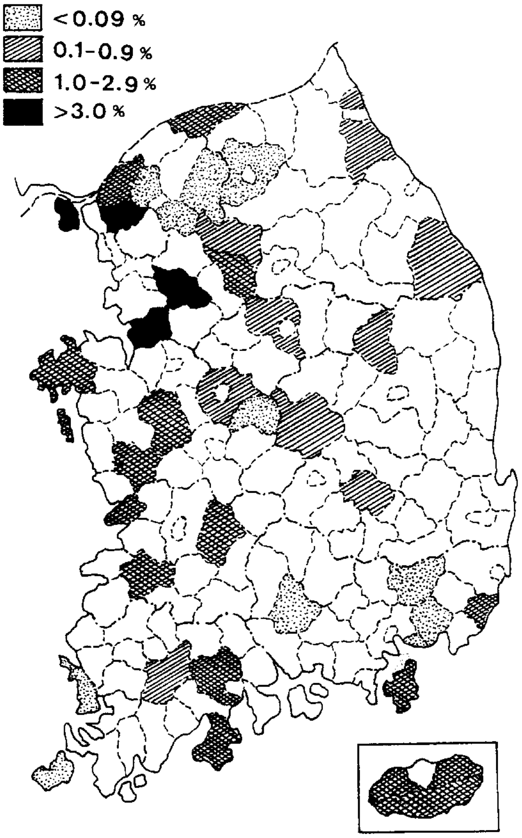

Fig. 1. Map showing the results of spleen survey for malaria endemicity in 1959 (NMES, 1966).

as the administration of chloroquine for suppressive treatment (NMES, 1966). A total 45,395 blood smears from 4,135 PCD units were examined and 13,929 cases were positive for *P. vivax*. The slide positive rate was 39.7% in 1961, 40.2% in 1962, 35.9% in 1963, 9.6% in 1964 and 22.4% in 1965, with an overall slide positive rate of 30.7% (Table 7). Geographical distribution of the malaria cases detected by PCD is given by year in Fig. 3. The fact that the malaria cases in 1964 and 1965 were significantly lower than those of the previous three years suggests that the early diagnosis and treatment may have played an important role in the decline of malaria occurrence. Monthly occurrence of the malaria cases detected by PCD is shown in Table 8. The peak of the cases was in July and August (31.0% and 30.6%, respectively).

Malaria rate per 10,000 population was

Table 6. Results of the mass blood survey in 1960 (NMES, 1996)

Province	No. of villages surveyed	Total population	No. examined	No. of *P. vivax*	%
Kyonggi-do	54 (3)*	35,101	3,631	8	0.2
Kangwon-do	22 (1)	14,880	1,532	1	0.1
Chungchongbuk-do	10 (1)	3,802	472	1	0.2
Chungchongnam-do	29 (1)	20,477	1,535	1	0.1
Kyongsangbuk-do	102 (45)	54,157	7,295	183	2.5
Kyongsangnam-do	24 (1)	14,262	1,248	8	0.5
Chollabuk-do	17 (3)	12,887	1,333	9	0.7
Chollanam-do	15 (1)	8,149	922	1	0.1
Cheju-do	4	1,059	488	0	0.0
Seoul	1	1,467	242	0	0.0
Total	278 (56)	166,241	18,697	212	1.1

*Number of positive villages.

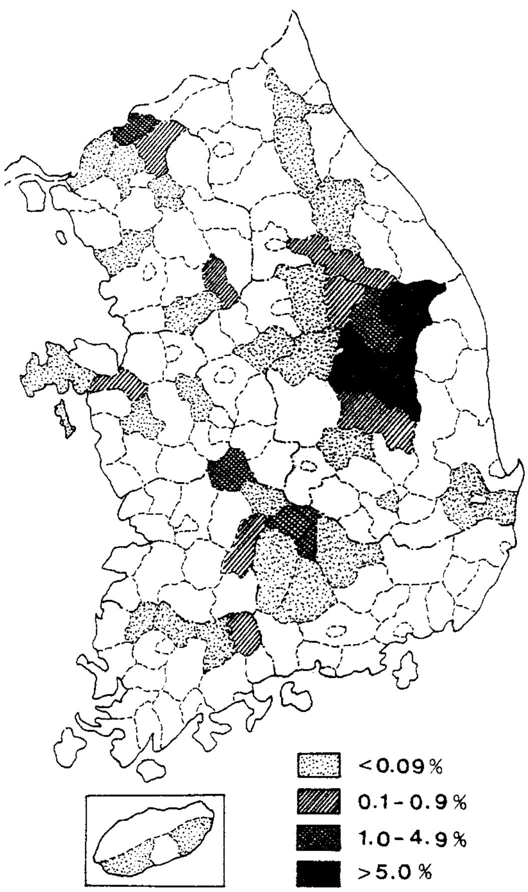

Fig. 2. Distribution of the malaria positive rate by mass blood survey in 1960 (NMES, 1966).

significantly higher in the north and north-eastern areas (13.0) than in the south and south-eastern areas (0.4) of South Korea (Table 9). Malaria endemicity was also significantly different among topographically different areas. The slide positive rate of vivax malaria by mass blood survey in 1960-1962 was significantly higher in mountainous areas (1.6%) than in hilly areas (0.7%) or flat areas (0.1%). Similarly, the number of malaria cases per 10,000 population reported by PCD during 1961 through 1965 significantly higher in mountainous areas (34.6%) than in hilly areas (10.9) or flat areas (0.5) as shown in Table 10.

During the period of 1966-1969, PCD activities were carried out in two main endemic areas (north Kyonggi-do and north Kyongsangbuk-do). Of 14,918 blood smears from fever cases, 900 (6.0%) were positive for *P. vivax*. Annual parasite incidence (API) per 1,000 population was 0.34 in 1966, 0.24 in 1967, 0.23 in 1968 and 0.13 in 1969, which indicates that malaria endemicity was significantly decreasing (Table 11). The API reported by PCD in Yongju-gun, Kyongsang-buk-do in 1968 and 1969 was 68.3 and 33.9, respectively (Table 12)(Lee et al., 1972; Kim, 1982). These API values were so unreasonably high that the source of the data would be not reliable.

Active case detection (ACD)

ACD workers periodically visited all house-

Table 7. Number of malaria cases by province and overall annual slide positive rate (SPR) as reported by the passive case detection (PCD) program in 1961-1965 (NMES, 1996)

Province	1961		1962		1963		1964		1965		Total		
	No. ex-amined	No. of positives	No. ex-amined	No. of positives	No. ex-amined	No. of positives	No. ex-amined	No. of positives	No. ex-amined	No. of positives	No. ex-amined	No. of positives	%
Seoul	67	12	211	11	162	14	286	4	366	15	1,092	56	5.1
Kyonggi-do	3,092	1,237	2,692	999	3,300	1,056	2,053	290	1,364	249	12,501	3,831	30.6
Kangwon-do	883	311	403	194	360	128	352	21	79	24	2,077	680	32.7
Chungchongbuk-do	207	43	236	43	749	193	422	39	103	35	1,717	353	20.6
Chungchongnam-do	252	14	87	15	214	58	2,284	57	102	25	2,939	169	5.8
Kyongsangbuk-do	7,918	3,503	2,453	1,240	6,239	2,524	2,028	435	1,888	820	20,526	8,522	41.5
Kyongsangnam-do	165	23	25	6	5	1	675	12	409	18	1,279	60	4.7
Chollabuk-do	174	24	249	73	64	17	1,039	24	297	15	1,823	153	8.4
Chollanam-do	247	28	100	10	54	16	11	0	808	27	1,220	81	6.6
Cheju-do	95	9	19	9	15	1	3	0	89	5	221	24	10.9
Total	13,100	5,206	6,475	2,600	11,162	4,008	8,153	882	5,505	1,233	45,395	13,929	
S.P.R.(%)		39.7		40.2		35.9		9.6		22.4		30.7	

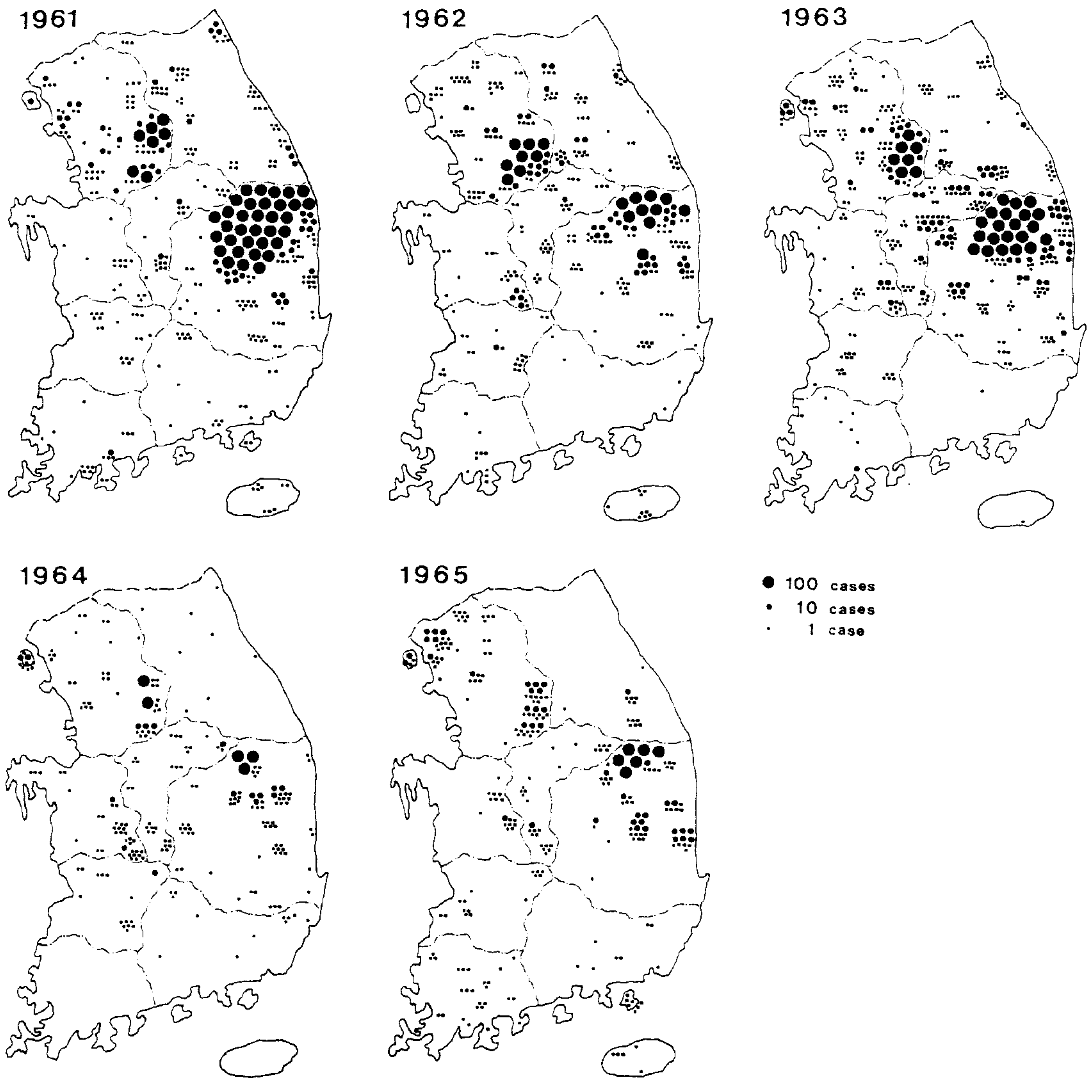

Fig. 3. Distribution of the malaria cases detected by PCD in 1961-1965 (NMES, 1966).

holds of the assigned villages to identify fever cases, take blood samples and administer antimalaria drugs (chloroquine). ACD was carried out in 3 counties of Chungchongnam-do, 5 counties of Kyongsangbuk-do and 6 counties of Kyonggi-do from 1963 through 1965 (Table 13). The results show that the highest slide positive rate was in Yongju-gun (31.9%). Malaria cases were not reported from in Yesan-gun and Asan-gun, and only one positive case from 1,036 fever cases in Tangjin-gun of Chungchongnam-do.

Control

PCD and ACD was carried out at 4 counties in north Kyonggi-do in 1965 in order to evaluate sensitivity and effectiveness in finding malaria cases (Table 14). Of 3,856 fever cases, 70 (1.8%) were positive by ACD while 68 (15.1%) of 451 fever cases were positive by PCD. The result indicated that case detection by PCD and ACD was not different. As ACD is much more expensive and requires much more man-power compared to those of PCD, it was concluded that PCD alone is a recommendable method for malaria control in Korea in cost-

Table 8. Monthly occurrence of the reported malaria cases by PCD in 1961-1965 (NMES, 1966)

Month	1961	1962	1963	1964	1965	Total	%
January	2	0	0	1	0	3	0.0
February	1	0	0	0	1	2	0.0
March	5	2	0	0	1	8	0.1
April	30	20	21	1	1	73	0.5
May	299	190	143	36	22	690	5.0
June	869	439	565	152	77	2,102	15.1
July	1,429	858	1,422	169	436	4,314	31.0
August	1,606	879	1,153	226	403	4,267	30.6
September	708	119	598	229	188	1,842	13.2
October	235	68	100	52	97	552	4.0
November	19	18	6	12	7	62	0.4
December	3	7	0	4	0	14	0.1
Total	5,206	2,600	4,008	882	1,233	13,929	100

Table 9. The number of malaria cases by PCD of mid and mid-eastern and south and south-western provinces of South Korea in 1961-1965 (NMES, 1966)

Province	No. examined	No. of positives	S.P.R. (%)	No. of patients per 10,000 population
North and north-eastern provinces:				
Kyonggi-do	12,501	3,831	30.6	13.5
Kangwon-do	2,077	680	32.7	4.1
Chungchongbuk-do	1,717	353	20.6	2.4
Kyongsangbuk-do	20,526	8,522	41.5	19.8
Total	36,821	13,386	36.4	13.0
South and south-western provinces:				
Chungchongnam-do	2,939	169	5.8	0.6
Kyongsangnam-do	1,279	60	4.7	0.2
Chollabuk-do	1,823	153	8.4	0.6
Chollanam-do	1,220	81	6.6	0.2
Cheju-do	221	24	10.9	0.8
Total	7,482	487	6.6	0.4

effectiveness concept.

The pilot projects to evaluate the effectiveness of indoor residual spraying for malaria control were conducted twice, first at Ponghyon-myon, Yongju-gun, Kyongsangbuk-do in 1963, and the second at Kaegun-myon, Yangpyong-gun and Taesin-myon, Yoju-gun, Kyonggi-do in 1964. All houses and animal sheds in the study areas were sprayed with DDT at a dosage of 2 g/m^2 before the beginning of the mosquito season. Both PCD and mosquito surveys were employed in both the DDT treated and the control (untreated) areas. The results of both pilot projects showed that there was no significant difference in the incidence of malaria and population density of *An. sinensis* between the DDT sprayed areas and the control areas. However, the life span of vector mosquitoes was shorter in the treated area (47.8% versus 77.8% parous rate of the treated and control area, respectively). Based on these results (ACD, PCD, and DDT residual spray), it was determined that PCD alone would effectively control unstable vivax

Table 10. Comparison of the number of malaria cases for topographical regions in 1960-1965 (NMES, 1966)

	Plain area (21)[a]			Hilly area (25)[a]			Mountainous area (20)[a]		
	No. examined	No. pos.	%	No. examined	No. pos.	%	No. examined	No. pos.	%
Mass blood survey (1960-1962)	16,047	17	0.1	19,064	133	0.7	18,042	280	1.6
PCD (1961-1965)	3,696	361	9.8 (0.5)[b]	12,098	3,716	30.7 (10.9)[b]	20,078	8,296	41.3 (34.6)[b]

[a]Number of counties investigated.
[b]Number of patients per 10,000 population.

Table 11. Number of reported malaria cases by PCD in north Kyonggi-do in 1966-1969 (Shim and Kim, 1999)

		1966		1967		1968		1969		Total			
Gun/si	Population	No. exa.	No. pos.	No. exa.	No. pos.	No. exa.	No. pos.	No. exa.	No. pos.	No. exa.	No. pos.	%	API[a]
Paju	182,804	2,452	197	2,577	168	2,061	199	3,942	119	11,032	683	6.2	0.94
Koyang	86,151	116	19	243	21	2	1	5	0	366	41	11.2	0.12
Yonchon	68,638	54	9	0	0	4	1	0	0	58	10	17.2	0.04
Pochon	134,684	335	10	137	8	165	4	10	2	647	24	3.7	0.05
Kimpo	84,928	362	42	95	8	9	4	12	1	478	55	11.5	0.16
Kanghwa	119,129	286	42	187	20	263	9	13	1	749	72	9.6	0.15
Yangju	210,470	415	6	472	4	0	0	3	0	890	10	1.1	0.01
Uijongbu	69,969	620	3	73	2	0	0	5	0	698	5	0.7	0.02
Total	956,773	4,604	328	3,784	231	2,504	218	3,990	123	14,918	900	6.0	0.24
API[a]			0.34		0.24		0.23		0.13			0.24	

[a]Annual parasite incidence per 1,000 population.

malaria in Korea.

Malaria after NMES

Subsequent to 1969 when NMES was dissolved, there were no specific activities of malaria control/eradication. Both ACD and PCD were carried out with total coverage of the population in Taesin-myon, Yoju-gun and Kaegun-myon, Yangpyong-gun, Kyonggi-do during the period of June-October 1972 to determine malaria endemicity after NMES (Table 15). The API declined to zero (2.5 in 1965) at Taesin-myon, and to 0.5 (9.1 in 1965) at Kaegun-myon (Lee et al., 1972). PCD was carried out at Isan-myon, Yongju-gun, Kyongsangbuk-do in 1976, resulting that 7 malaria cases (1.4%) out of 487 fever cases were detected showing 0.7 of API (Kim, 1982).

Among 51 malaria cases diagnosed from 29 hospitals located in Seoul in 1970-1982, 38 cases were imported from tropical countries and 13 cases were indigenous. Ten indigenous cases were found in 1970-1974, and one case each in 1976, 1978 and 1981, respectively (Ahn et al., 1982). From the chart of 26 hospitals, 27 indigenous cases were found during the period of 1970-1984, of which 2 cases were recorded in 1984 (Soh et al., 1985). It was not possible to confirm whether these two cases were precisely diagnosed by microscopic confirmation. These data indicate that the incidence of malaria had rapidly declined in 1970s. The Republic of Korea was declared malaria free by the World Health

Table 12. Number of malaria cases by PCD in Yongju-gun, Kyongsangbuk-do in 1968 and 1969 (Lee et al., 1972; Kim, 1982).

Locality	Population	1968			1969		
		No. exa.	No. pos.	API[a)]	No. exa.	No. pos.	API[a)]
Yongju-ub	46,838	6,195	3,380	72.2	3,727	1,715	36.6
Isan-myon	10,467	1,897	1,143	109.2	1,126	540	51.6
Munsu-myon	8,456	1,066	690	81.6	809	372	44.0
Changsu-myon	8,368	990	639	76.4	781	371	44.3
Anjung-myon	10,960	723	387	35.3	461	185	16.9
Bonghyon-myon	8,582	636	338	39.4	226	93	10.8
Sunhung-myon	7,915	564	361	45.6	471	165	20.8
Total	101,586	12,071	6,938	68.3	7,601	3,441	33.9

[a)]Annual parasite incidence per 1,000 population.

Table 13. Number of malaria cases by ACD in 1963-1965 (NMES, 1966)

Locality	No. of fever cases	No. of positives	S.P.R. (%)
Kyonggi-do:			
Uijongbu-shi	703	1	0.1
Yangju-gun	411	1	0.2
Yoju-gun	1,831	86	4.7
Paju-gun	2,238	66	2.9
Pochon-gun	504	2	0.4
Yangpyong-gun	392	60	15.3
Chungchongnam-do:			
Yesan-gun	372	0	0
Tangjin-gun	1,036	1	0.1
Asan-gun	188	0	0
Kyongsangbuk-do:			
Uisong-gun	198	10	5.1
Yongdok-gun	288	33	11.5
Munkyong-gun	1,227	79	6.4
Yongju-gun	1,044	333	31.9
Ponghwa-gun	217	23	10.6
Total	10,649	695	6.5

Table 14. Results of ACD and PCD in selected study areas in Kyonggi-do in 1965 (NMES, 1996)

Locality	ACD		PCD	
	No. exa.	No. pos.	No. exa.	No. pos.
Uijongbu city	703	1	49	2
Yangju-gun	411	1	46	2
Pochon-gun	504	2	83	4
Paju-gun	2,238	66	273	60
Total	3,856	70	451	68
S.P.R.(%)		1.8		15.1

Organization in 1979 (WHO, 1981).

PROLONGED INCUBATION PERIOD OF KOREAN VIVAX STRAIN

A prolonged incubation period has been observed from many strains of *P. vivax*, mainly in the temperate zone, such as Dutch, Madagascar, USSR and Korea. The first observation of longterm incubation period of Korean *P. vivax* was made by Hasegawa (1913). He reported that 6 Japanese soldiers returned from Korea to Osaka, Japan in April 1910 and demonstrated the onset of malaria in June 1910. As there was no malaria in Osaka, they were suspected to be infected in Korea during the transmission season of the previous year. He also observed that out of 1,201 malaria cases 251 (20.9%) occurred from December through April during the non-transmission season. In the 1950s, several workers reported both short and long incubation periods of a Korean strain of *P. vivax* (Eddleman et al., 1951; Hall and Loomis, 1952; Brunetti, 1954; Brunetti et al., 1954; Tiburskaja et al., 1968). Brunetti et al. (1954) reported that an outbreak of vivax malaria in California, USA, resulted from veterans returning from the Korean war. Nine persons became ill after an incubation period

Table 15. Results of ACD and PCD in Taesin-myon, Yoju-gun and Kaegun-myon, Yangpyong-gun, Kyonggi-do in June-October 1972 (Lee et al., 1972)

	ACD		PCD		Total		
	No. of fever cases	No. of positives	No. fo fever cases	No. of positives	No. of fever cases	No. of positives	API[a)]
Taesin-myon	154	0	25	0	179	0	0
Kaegun-myon	139	1	118	3	257	4	0.5
Total	293	1	143	3	436	4	0.2
%	—	0.3	—	2.1	—	0.9	—

[a)]Annual parasite incidence per 1,000 population.

of 10-40 days while 26 persons became ill after an incubation period of 217-316 days. Exo-erythrocytic stages of the North Korean strain could still be found in the liver 255 days after the inoculation of sporozoites (Garhnam et al., 1975). They mentioned that the North Korean strain resembled the Dutch and St. Elizabeth strains and lied between *P. vivax vivax* and *P. vivax hibernans* because it did not always show a long incubation period. Shute et al. (1976) experimentally studied the effect of numbers of sporozoites inoculated on the length of the incubation period using the North Korean strain of *P. vivax*. All 6 subjects inoculated with 10-100 sporozoites became ill after a long incubation period (262-628 days). Among 5 persons injected with 1,000 sporozoites, 4 became ill after a long incubation (257-386 days) and one 16 days after inoculation. All 5 subjects inoculated with 100,000 sporozoites became ill after a short incubation period (13-16 days). They concluded that there are two strains (populations) of sporozoites, one governing long incubation and the other short incubation, with the strain of short incubation representing a small proportion of the whole population. Tiburskaja and Vrublevskaja (1977) experimentally infected humans with the North Korean strain of *P. vivax* through bites of the infected mosquitoes. Among 77 patients, 19 (24.7%) became ill after a short incubation period (14-22 days) and 58 (75.3%) after a long incubation period. Among 58 cases of long incubation period, 1 case (1.3%) became ill after 1 month, 11 (14.3%) after 8 months, 14 (18.2%) after 9 months, 14 (18.2%) after 10 months, 13 (16.9%) after 11 months, 3 (3.9%) after 12 months, and 2 (2.6%) after 13 months.

RE-EMERGENCE OF MALARIA SINCE 1993

One indigenous case of *P. vivax* was reported in Paju-gun, Kyonggi-do in July 1993 (Chai et al., 1994). Since then the number of cases has been rapidly increased annually, as shown in Table 16 (National Institute of Health, 1995, 1996, 1997, 1998, 2000; Lee et al., unpublished). The discharged soldiers who were infected while on army service and a paroxism was presented at home after discharge were put in the "soldier" category.

The majority of the cases were reported in military personnel, particularly at beginning of the outbreak, composed of 90% in 1994, 92.5% in 1995, 86.8% in 1996, 79.1% in 1997, 70.8% in 1998, and 57.8% in 1999. The rate of soldiers has been decreasing year after year, and the number of soldier cases decreased from 2,784 in 1998 to 2,092 in 1999. By socio-political factors, it was suggested that the rate in military personnel should have been higher than for civilians since soldiers on sentry duty were severely exposed to mosquito bites throughout the night outdoors in and/or near the DMZ where domestic animals were not available for feeding of zoophilic vector mosquitoes. After 1997, many soldiers serving in and/or near the DMZ were placed on chloroquine prophylaxis through the whole mosquito season with primaquine at end of the season (Kim et al., 1997, 1998; Lee, 1998). Chemo-prophylaxis and other measures such

Table 16. Number of vivax malaria cases in South Korea in 1993-1999[a)]

Year	Soldier cases			Civilian cases	Total	
	in service	discharged[b)]	Total		Number	Fold
1993	1	0	1	0	1	
1994	18	0	18(90)[c)]	2(10)	20	20 x
1995	88	11	99(92.5)	8(7.5)	107	5.4 x
1996	285	24	309(86.8)	47(13.2)	356	3.3 x
1997	1,156	207	1,363(79.1)	361(20.9)	1,724	4.8 x
1998	1,657	1,127	2,784(70.8)	1,148(29.2)	3,932	2.3 x
1999	1,196	896	2,092(57.8)	1,529(42.2)	3,621	0.9 x
Total	4,401	2,265	6,666(68.3)	3,095(31.7)	9,761	

[a)]US Army personnedl (107 cases) infected at/near DMZ are not included.
[b)]These soldier cases were infected while on service in and/or near the DMZ, and paroxysm was shown at home after discharge.
[c)]Numbers in parenthesis indicate percentage.

as wear of permethrin-treated uniforms resulted in continuous decrease in the number of cases in military personnel in 1999. Lee (1998) reported that chloroquine (300 mg/week) and primaquine (15 mg/day for 14 days) for chemoprophylaxis were administered to soldiers who served in high risk areas (in and/or near the DMZ). None of properly administered soldiers developed malaria, whereas 11% of inadequately administered soldiers and 89% of untreated soldiers developed malaria. The decrease in reported malaria cases in soldiers in 1999 resulted in an overall decrease to 3,621 (0.9x) from 3,932 in 1998, inspite that the malaria cases of civilians increased to 1,529 (1.3x) in 1999 from 1,148 in 1998.

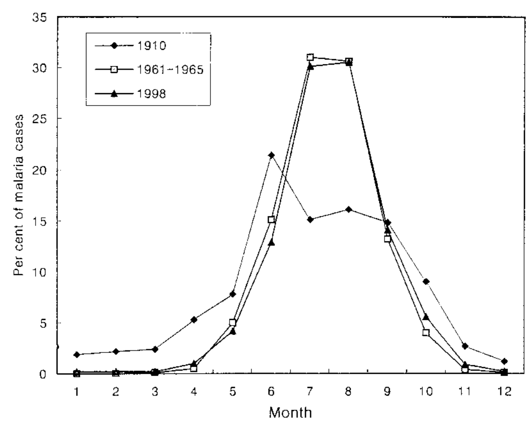

Fig. 4. Monthly occurrence of vivax malaria in 1910, 1960s and 1998 (Hasegawa, 1913; NMES, 1966; Lee et al., unpublished).

Seasonal occurrence

Total 3,932 cases in 1998 were reported throughout the year, totalling 6 cases (0.2%) in January, 8 (0.2%) in February, 9 (0.2%) in March, 40 (1.0%) in April, 164 (4.2%) in May, 509 (12.9%) in June, 1,182 (30.1%) in July, 1,199 (30.5%) in August, 553 (14.1%) in September, 219 (5.6%) in October, 34 (0.9%) in November and 9 (0.2%) in December (Lee et al., unpublished). The pattern of seasonal occurrence of the reemergence of malaria was very similar to that of 1960s (Fig. 4).

Geographical distribution

In case of soldiers, data suggest that all cases of soldiers, including discharged soldiers, were infected along the DMZ, the bordering South and North Korea (Yim et al., 1996; Kim et al., 1997; Lee, 1998). Among a total of 389 malaria cases of the soldiers in 1994-1996, 343 (88.2%) soldiers had served in DMZ and the remaining (11.8%) had served at vicinity of the DMZ (Kim et al., 1998). A total of 27 malaria cases in U.S. troops in 1993-1997 stationed along the western corridor near the DMZ (Feighner et al., 1998). Lee et al. (1998) analyzed 650 cases of civilians in 1994-1997, including ex-soldiers discharged from military service where they were potentially infected; 226 cases (34.8%) were ex-soldiers who served in/near DMZ; 317 cases (48.8%) were residents in known malarious areas of north Kyonggi-do and north-west Kangwon-do; 75 cases (11.6%) were residents outside of malaria risk area, but had a history of travel in malarious areas during transmission season; the remaining 32 cases (4.9%) were residents of non-malarial areas. Geographical distri-bution of the civilian cases from 1994 through 1997 was outlined by Kho et al. (1999) as shown in Fig. 5. Among 287 cases examined, 232 (80.8%) were located within 10 km of the southern border of DMZ and the remaining 55 (19.2%) resided between 10-20 km from the DMZ.

When the malaria cases were plotted on a map by the reported locality, they were widely distributed throughout the country including Cheju-do, as if malaria endemicity were established all over the country. In 1998 a total 3,932 cases were reported, of which 1,196 cases were soldiers serving near the DMZ, and 1,127 cases of ex-soldiers were reported in non-malarious areas (e.g., 293 in Seoul, 106 in Pusan, 96 in Kyongsangnam-do, 6 in Cheju-do, etc.), as shown in Fig. 6. However all the ex-soldiers are believed to be infected during army service in malarious areas near the DMZ. Among the 1,148 civilian cases, 809 (70.5%) patients resided in malarious areas and 339 (29.5%) resided in other areas. Among 339 patients residing in non-malarious areas, 157 responded to a questionaire that they had visited the malarious areas during the transmission season. The site of transmission of the remaining 182 civilians (4.6% of the total malaria cases) was not determined (Lee et al., unpublished).

Origin of re-emergence and possibility of endemicity

As malaria was eradicated in South Korea in 1979, it was impossible to be re-established of endemicity in 1993 and 1994. No one argues

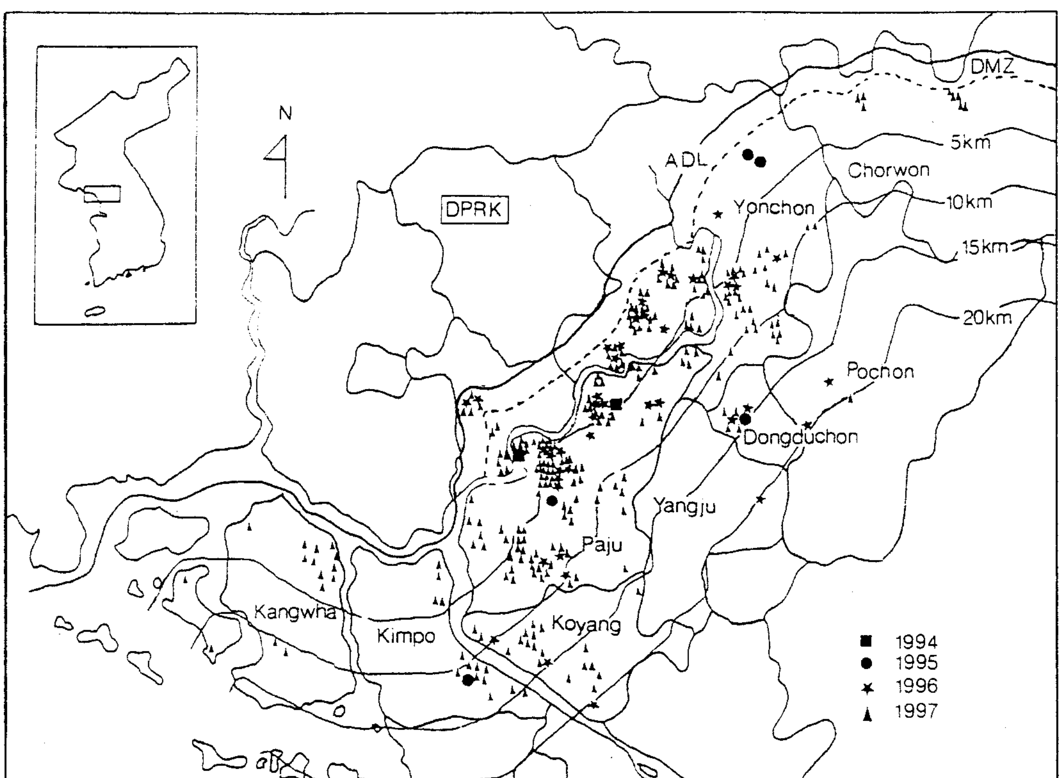

Fig. 5. Distribution of 278 civilian cases of *vivax* malaria in 1994-1997 (Kho et al., 1999).

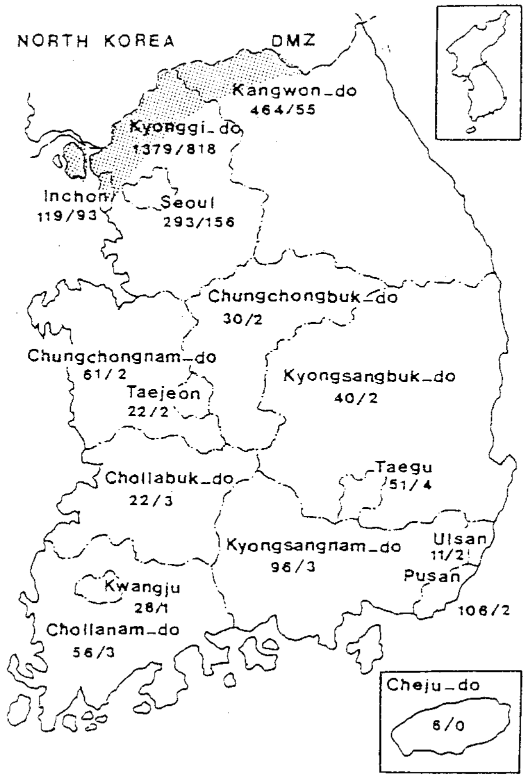

Fig. 6. Map showing the number of malaria cases in 1998 by province/special city. No. of sodier cases/No. of civilian cases(Lee et al., unpublished).

the fact that re-emergence of *P. vivax* originated from North Korea. As people could not transfer from North to south Korea, the only possible source of infection would be the sporozoite-infected mosquitoes dispersed from North Korea to South across DMZ (Chai, 1997, 1999; Ree, 1998; Kho et al., 1999). This plausible speculation is based on the other postulation that malaria had persisted with low endemicity in North Korea until 1993 and a big epidemic occurred when epidemiological and/or environmental factors changed in favorate of the vector mosquitoes and the parasite (Ree, 1998).

We have a typical unstable malaria in Korea. Some characteristics of the unstable malaria are well summarized by Macdonald (1957) and Gilles and Warrell (1993) (Table 17). The vector species, *Anopheles sinensis*, is highly zoophilic (Ree et al., 1967), moderate longevity (Hong, 1977) and high population density. Transmission season is short (June-September). Table 18 summarized the differences of entomological, socio-ecological and medical factors between South and North Korea influencing malaria endemicity/ epidemicity, which helps to understand malaria epidemiology of South and North Korea. Some recent meteorological data that would cause an epidemic in north Kyonggi-do, Korea were given by Ree (1998).

Our primary concern is that malaria is now endemic in South Korea, particularly in north Kyonggi-do and north-west Kangwon-do (within 20 km from DMZ), and what are the main source of infection of most malaria cases. Malaria outbreak would be resulted from either way, one by direct bites of sporozoite-infected mosquitoes dispersed from North Korea across the DMZ through the entire transmission season (Ree, 1998; Kho et al., 1999), the other by endemicity maintained by local mosquitoes producing secondary, tertiary, and further successive cases (Chai, 1999). For producing a secondary case, the same mosquito should bite humans twice with a 12 day interval. As human blood index of *An. sinensis* was 0.007 in 1999 (Ree et al., unpublished), proportion of two human bites by the same mosquito would be 0.000049. As proportion of daily survival was 0.871 in 1999 (Ree et al., unpublished), proportion of survival for 12 days of the sporogonic period would be 0.191. Therefore, proportion of two human bites with a 12 day interval would be 0.000009. On the other hand, when we speculate that malaria transmission is resulted from bites of sporozoite-infected mosquitoes dispersed from North Korea, just one bite by chance produces a new case. The proportion of this chance would be 0.007. Although the flight range of mosquitoes differs by species and by environmental factors, it is well known that *Anopheles* mosquitoes fly quite far distances (20-30 km is not uncommon) (Swellengrebel et al., 1938; Simmons et al., 1939; Hocking, 1953). A dispersal range of mosquitoes is decided either by a single flight by wind, or by many times of flight activities. It requires at least 12 times of flights during 12 days of sporogonic period (4 gonotrophic

Table 17. Some characteristics of unstable and stable malaria (Macdonald, 1957)

Characteristics	Unstable	Stable
Type of vector	Vector with infrequent human biting habit and/or low daily survival rate	Vector with frequent human biting habit and high daily survival rate
Environmental conditions	Not favourable for a rapid sporogonic cycle	Favourable for a rapid sporogonic cycle
Endemicity	Usually low to moderate; high endemicity may occur	Very high endemicity common; low to moderate may occur
Determining causes	Vector of low anthropophily and low to moderate longevity. Climatic conditions favourable for short periods of transmission	Vector of high anthropophily and moderate to high longevity. Climatic conditions favourable for long periods of transmission
Anopheline density (needed to maintain transmission)	High (1-10 or more bites/person/night)	Low (as low as 0.025 bites/person/night)
Seasonal changes of incidence	Pronounced	Not very pronounced, except for short dry season
Fluctuations in incidence and predominant parasite	Very marked and uneven. Most often *P. vivax* as main parasite	Not marked and related to seasons. *P. falciparum* prevalent parasite
Immunity of the population	Variable with some groups of low immunity	High, though varying in degree in different age groups
Epidemic outbreaks	Likely when climatic or other conditions suitable	Unlikely to occur in the indigenous population
Amenability to control or eradication	Not unduly difficult by imagocides and larvicides combined with chemotherapy. Daily anopheline mortailty of 20-25% may be adequate for control of transmission	Very difficult to control, especially in rural areas. Eradication unlikely unless socio-economic conditions favourable. Daily anopheline mortailty of at least 50% needed for a degree of control

cycles) for seeking hosts, resting places, and breeding places. In 1998, a flight range of *An. sinensis* was studied in Korea using a mark-release-recapture method, and 20 km of a flight range was observed (unpublished).

A plausible speculation is that many (not all) cases near the DMZ of South Korea may be due to the dispersal of sporozoite-infected mosquitoes from North Korea. If this speculation is true, number of malaria cases in South Korea relies on the degree of epidemicity (infection rate of *An. sinensis*) in North Korea. The more malaria cases in North, the more in South in a certain degree, because north Kyonggi-do is located at a peripheral edge of North Korea.

SYMPTOMS, TREATMENT AND RELAPSE

Predromal symptoms of 87 patients of vivax malaria was observed (Lim et al., 1996). Thrombocytopenia appeared in 72.4% of the patients with 124,000±71,000/μl, anemia in 92% with 12.4±2.2 g/dl of hemoglobins, and splenomegaly in 72%. High fever ($\geq$ 40°C) was shown in most of the patients, with 48 h periodicity in 72.4%, 24 h periodicity in 10% and no periodicity in 17.6%. Kim and Lim (1997) studied symptoms of 26 patients of ROK Army and observed myalgia (88.5%), vomiting (34.6%), diarrhea (3.8%), and oral herpes simplex (3.8%), besides typical malaria symptoms such as fever, chills, headache, etc. Hematologic findings were anemia (92.3%), thrombocytopenia (61.5%), leukopenia (50%), and leukocytosis (19.2%). Song (1965) reported that parasite density in blood of 171 patients in Korea was 3,853/mm^3, of which number of gametocytes were 135/mm^3 (3.5% of the total). On the other side, Lim et al.

Table 18. Comparison of factors governing malaria endemicity/epidemicity between North and South Korea

Factor	North Korea	South Korea
I. Vector:		
Population density	High	High
Daily survival	moderate (?)	moderate to low
Human blood index	unknown[a)]	extremely low
II. Socio-economic and medical factors:		
Anti-malaria drugs	scarcity[b)]	surplus
Medical care	poor	good
PCD network	unknown	well established
Nutrition	mal-nutrition	good-nutrition
Housing (mosquito-proof)	poor	moderate to good
Personal protection	unknown	good
Animal industry (cow, pig, etc.)	few, sporadic	large, focal distribution
Insecticide application for agriculture/sanitation	none	heavy

[a)]As there are few heads of cows and pigs in North Korea, human blood index of *An. sinensis* females might be high.
[b)]Recently WHO provided chloroquine.

(1996) reported that gametocytes were most frequently found (95.7%), and the next was ring form trophozoites. Kim and Lim (1997) also observed that the majority of parasite stage was gametocytes (92.3%) in their blood smears and the next young trophozoites (26.4%). As these gametocyte rates were unusually high, re-observation of the slides for confirmation is required.

Hankey et al. (1953) reported that 355 veterans infected with *P. vivax* were treated with 1,500 mg of chloroquine (base) in 3 days (3 doses of 300 mg during the first 24 h, a single dose of 300 mg daily for 2 days), and 137 (38.6%) relapsed at least once. The mean duration from the first attack to the second was 68.6 days in average (range 39-247 days). Tiburskaja and Vrublevskaja (1977) observed that out of 74 patients treated with chloroquine after the first attack, 23 (31.1%) relapsed, of which 11 cases relapsed once, 11 cases twice and 1 case 3 times.

Among 272 patients treated with chloroquine 1,500 mg in 3 days plus primaquine 27 mg/day for 14 days, 2 cases relapsed, whereas no one relapsed among 348 patients treated with chloroquine 1,500 mg in 3 days plus primaquine 15 mg/day for 14 days (Alving et al,. 1953). In the course of these studies, only minimal evidence of drug toxicity was observed. One patient treated with chloroquine alone developed mild generalized pruritus which subsided 4 days after the drug was stopped. A similar mild pruritus developed in a patient treated with chloroquine and primaquine. It disappeared after chloroquine was stopped and before the administration of primaquine was completed. There was no evidence of hemolytic anemia in any patient. Approximately 15% of the patients had a mild to moderately severe anemia (hemoglobin concentration of 6.4-12 gm/100 cc) at the time treatment was instituted.

The patients of veterans with vivax malaria acquired in Korea were treated at the time of a late acute attack and followed for more than 4 months thereafter. The effect of a daily dose of 10-30 mg of primaquine for 14 consecutive days on the relapse rate is shown in Table 19. Among a total of 334 patients treated with chloroquine alone, 146 (43.8%) relapsed at least once after treatment. None of the patients treated with 20 or 30 mg of primaquine daily for 14 days relapsed (Jones et al., 1953). A regimen of 20 mg of primaquine daily for 7 days was studied in order to determine whether a shorter period of treatment was equally effective. Thirty-six patients (51.4%)

Table 19. Fourteen days treatment of Korean vivax malaria with primaquine in 1951-1952 (Jones et al., 1953)

	Chloroquine 1500 mg (base)/3d	Daily dose (mg base) of primaquine[a)]			
		10	15	20	30
No. treated[b)]	334	157	182	131	41
No. relapsed	146	4	2	0	0
%	43.7	2.5	1.1	0	0

[a)]Plus chloroquine 1500 mg (base) in 3 days.
[b)]Only patients who were followed more than 4 months after treatment are included.

treated with chloroquine alone relapsed, and 2 (2.9%) of 68 patients treated with 20 mg of primaquine daily plus chloroquine 1,500 mg in 3 days relapsed 51 and 68 days after treatment, respectively. A regimen of 15 mg of primaquine daily for 7 days resulted in 1 relapse (3.2%) out of 31 patients 49 days after treatment (Lorenzo et al., 1953). Curative effect of primaquine 15 mg daily for 14 days was tested with 625 veterans of long-term latency, who had been exposed to malaria in Korea in the summer of 1951 and returned to USA before January 1952. None of the 294 men treated with primaqine developed malaria during the 6 months' period following treatment, whereas 58 (17.5%) of 331 men treated with a placebo gave a history of malaria (Coatney et al., 1953).

VECTOR MOSQUITOES

Anopheles sinensis had been suspected as the vector species of malaria for many years in Korea (Hasegawa, 1913; Kobayashi, 1932; Yokoo, 1944). In 1962, *An. sinensis* was confirmed for the first time as a malaria vector species; total 5,086 females collected at Kaegun-myon, Yangpyong-gun, Kyonggi-do during the period of 1960-1962 were dissected for salivary gland, and sporozoites were observed from one female, showing a 0.02% sporozoite rate (Ree et al., 1967). In 1967, 4,018 females of *An. sinensis* were dissected in Chongsong-gun, Kyongsangbuk-do and sporozoites were found in 2 females, showing a 0.05% infection rate (Hong, 1977). He also dissected 89 *An. yatsushiroensis* and found one positive for oocysts (not sporozoites). In an experimental infection study, sporozoites developed in 2 females out of 9 *An. yatsushiroensis* (Hong, 1977). These two study results strongly suggest that *An. yatsushiroensis* is also a vector species of malaria in Korea.

Study results on bionomics and/or behaviour of *An. sinensis* are available in many references (Yokoo, 1944; Whang, 1962, 1964; Paik et al., 1965; NMES, 1966; Chen et al., 1967; Ree and Paik, 1967; Hong, 1967, 1977; Ree et al., 1981; Lee and Ree, 1991; Ree and Lee, 1993; Shim et al., 1997), summary of which are as follows: (1) broad range of breeding places such as rice paddy, marsh, stream, reservoir, pond, water pool with vegetation, temporary rain pool, etc., (2) highly zoophilic with particular preferences of cows and pigs, (3) feeding activity throughout night with a peak during 1100-0300 hours, (4) rather strong phototaxis, (5) moderate to low daily survival, (6) 2.5-3 days of gonotrophic cycle, (7) mainly outdoor resting habit, (8) seasonal prevalence of May-October, with a large peak in late June-early July and a small peak in late August-early September, (9) population density extremely high, and (10) hibernating mainly outdoors, such as grasses, bushes, dike and others.

CONCLUSION

Korean vivax malaria had been endemic for longtime with low incidence and prevailed throughout the country including Cheju-do and became epidemic during the Korean war (1950-1953). In 1959-1969, when NMES activities was implemented, malaria endemicity was declining, with very low endemicity in south-west and south, plain areas and high endemic foci in north Kyongsangbuk-do and north and east of Kyonggi-do. NMES activities greatly contributed to accelerating disapperance of malaria endemicity particularly in the focal areas, and resulting in the malaria eradication from the Republic of Korea (South Korea) in 1979.

Since 1993, malaria has re-emerged mainly in north Kyonggi-do and north-west Kangwon-do, located bordering the DMZ. It is postulated that malaria in North Korea had persisted with low endemicity until an epidemic started in 1994, as meteorological and socio-economical factors changed in favor of vectors and parasites, resulting in an outbreak in north Kyonggi-do. This outbreak may have resulted from sporozoite-infected mosquitoes dispersing from North Korea across the DMZ to South Korea.

All historic records tell that vivax malaria in Korea results in unstable malaria, with epidemics occurring when environmental factors such as climatic, socio-ecological, political (wars), entomological and parasitological factors change in favor of vectors and/or parasites. PCD is a feasible and recommendable control measure in cost-effect point of view against the unstable vivax malaria in Korea.

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