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Table 1. Summary of data on sample collection and microscopy.

Demographic Profile	Stool Samples (#/%)	Prevalence (frequency/percentage)		
		Total positive samples	***Giardia***	***Cryptosporidium***
Site of collection				
Luzon**	1667 (48.2)	83 (4.98)	32 (1.92)	52 (3.12)*
Visayas**	1399 (40.5)	31 (2.22)*	23 (1.64)	9 (0.64)
Mindanao	390 (11.3)	19 (4.87)	14 (3.59)*	6 (1.54)
Overall (Philippines)	3456 (100.0)	133 (3.85)[a]	69 (2.00)	67 (1.94)
Subject classification				
Pediatric** (0-18 years old)	2160 (63.4)	104 (4.81)	43 (1.99)	63 (2.92)*
Adult** (>18 years old)	1245 (36.6)	26 (2.09)	24 (1.93)	3 (0.24)
Total	3405 (100.0)[b]	130 (3.82)[c]	67 (1.97)	66 (1.94)
Sex				
Male	1934 (56.0)	79 (4.08)	42 (2.17)	39 (2.02)
Female	1520 (44.0)	54 (3.55)	27 (1.78)	28 (1.84)
Total	3454 (100)[d]	133 (3.85)[e]	69 (2.00)	67 (1.94)

* Significantly different (site of collection; subject classification)
** Significantly different (*Giardia* vs. *Cryptosporidium*)
[a] Three (3) patients had co-infection.
[b] Fifty-one patients with unknown ages were excluded from the analysis.
[c] Three (3) patients with unknown ages were excluded from the analysis; 3 patients had co-infection.
[d] Two patients with unknown sex were excluded from the analysis.
[e] Three (3) patients had co-infection.

Table 2. Prevalence of *G. lamblia* and *Cryptosporidium* spp. among pediatric and adult patients by sex.

	Giardia lamblia		*Cryptosporidium spp.*	
Sex	Pediatric (N=2160) Freq. (%)	Adult (N=1245) Freq. (%)	Pediatric (N=2160) Freq. (%)	Adult (N=1245) Freq. (%)
Male	23 (1.06)	19 (1.53)	36 (1.67)	2 (0.16)
Female	20 (0.93)*	5 (0.40)	27 (1.25)*	1 (0.08)
Total	43 (1.99)	24 (1.93)	63 (2.92)*	3 (0.24)

* Significantly different (pedia vs. adult)

Table 3. Isolates and genotypes of *Cryptosporidium* spp. from pediatric patients in the Philippines

Isolate code	Location	Polythreonine gene		18S rRNA gene	
		RFLP	Sequencing	RFLP	Sequencing
NCR 038	Luzon		*C. parvum*		
NCR 044	Luzon	*C. hominis*	*C. hominis*		
NCR 060	Luzon		*C. hominis*		
NCR 070	Luzon	*C. hominis*	*C. hominis*		
NCR 076	Luzon		*C. hominis*		
NCR 111	Luzon	*C. hominis*	*C. hominis*		
NCR 134	Luzon	*C. hominis*	*C. hominis*		
NCR 192	Luzon	*C. hominis* & *C. parvum*	*C. hominis* & *C. parvum*		
NCR 234	Luzon	*C. hominis*	*C. hominis*	*C. hominis*	
NCR 306	Luzon			*C. parvum*	
NCR 320	Luzon			*C. parvum*	
NCR 332	Luzon			*C. parvum*	
NCR 398	Luzon	*C. parvum*			
NCR 826	Luzon			*C. hominis*	
NCR 887	Luzon			*C. hominis*	
LUZ 272	Luzon	*C. hominis*		*C. hominis*	
LUZ 419	Luzon			*C. parvum*	
VIS 046	Visayas				*C. canis*
VIS 152	Visayas			*C. hominis*	*C. canis*
VIS 682	Visayas			*C. hominis*	
MIN 016	Mindanao	*C. hominis*		*C. hominis* & *C. parvum*	*C. hominis*
MIN 176	Mindanao	*C. hominis*			

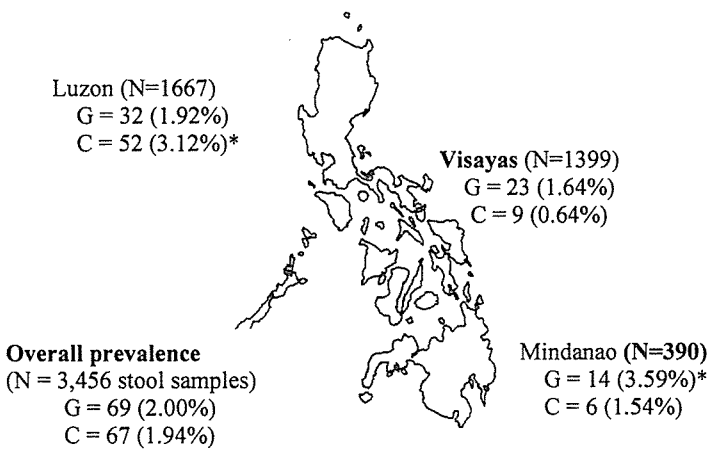

Fig. 1. Overall prevalence of *Giardia* (G) and *Cryptosporidium* (C) in the Philippines, and their distribution in the 3 major islands. (* indicates that prevalence is significantly higher.)

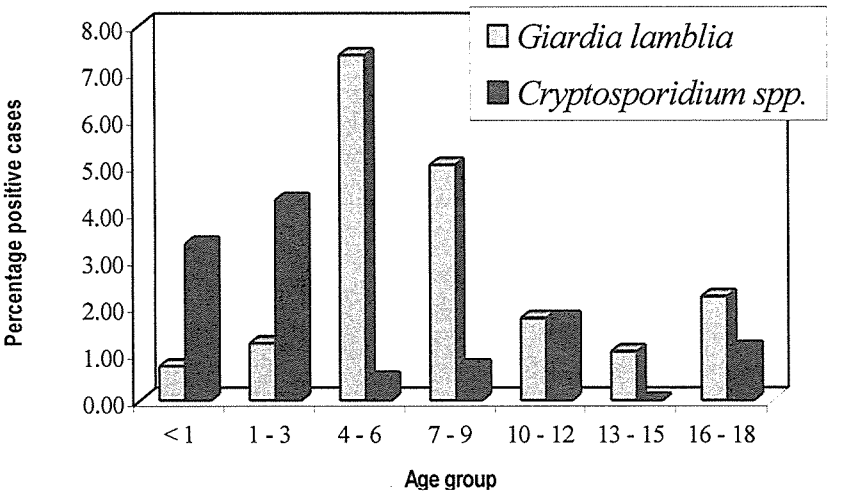

Fig. 2. Distribution of *G. lamblia* and *Cryptosporidium* spp. by different age groups of pediatric patients.

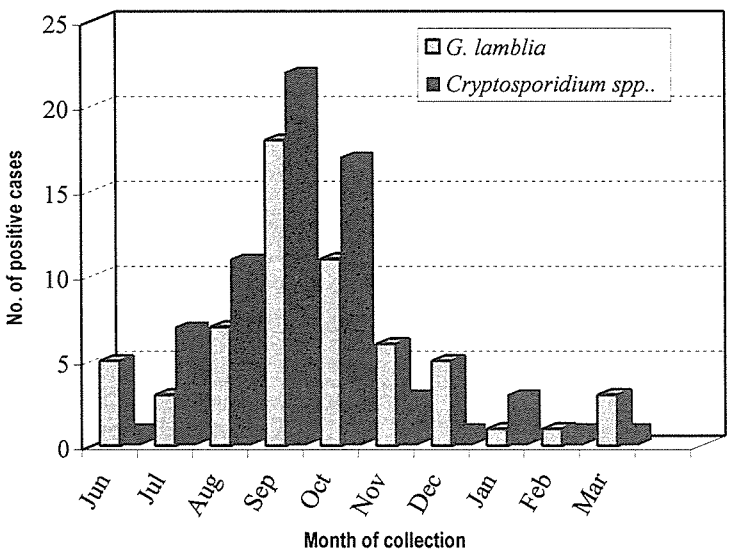

Fig. 3. Seasonal variation in frequencies of *G. lamblia* and *Cryptosporidium* spp. among diarrhea patients in the Philippines. Data shown were for stools collected from June 2004 to March 2005.

International Conference on Vivax Malaria in Asia and Pacific Area

Tuesday, January 16, 2007

0900-1700H

Time	
0900 – 0940	**Registration**
	Opening
	– Opening remarks - IPD, China CDC - Dr Tang Linhua
	– Opening remarks - NIID, Japan - Dr Tomoko Kitajima
	– Opening remarks - WPRO- Dr Kevin Palmer
	– Self introduction by participants
	– Group photograph
0940 – 1000	**Coffee/Tea Break**
1000 – 1030	**Reginal Situation** (***Moderator:*** Dr Tang Linhua , Dr Hoda Youssef Atta)
	1.Overview of vivax malaria distribution in WPRO
	– Dr Kevin Palmer
	2.Overview of vivax malaria distribution in SEARO
	– Dr Krongthong Thimasarn
1030 – 1200	**Country Presentations** (***Moderator:*** Dr Tang Linhua, Dr Kevin Palmer)
	3.Cambodia – Dr Top Sophornarant
	4.China – Dr Xia Gang
	5.DPRK – Dr Kim Yun Chol
	6.Indonesia – Dr. Bangkit Hutajulu
	7.Japan – Dr Hiroshi Ohmae
1200 – 1330	**Lunch Break**
1330 – 1500	(***Moderator:*** Dr Hiroshi Ohmae, Dr Krongthong Thimasarn)
	8.Philippines – Dr Jeniffer Luchavez
	9.ROK – Dr Dukhyoung Lee
	10.Solomons – Dr Bernard Bakotee
	11.Thailand – Dr Jeeraphat Sirichaisinthop
1500 – 1520	**Coffee/Tea Break**
1520 – 1600	**Discussion** (***Moderator:*** Dr Kevin Palmer)
1600 – 1700	Entomological factors (***Moderator:*** Dr Kevin Palmer)
	12.Overview of vector of vivax malaria in Asia and South pacific area
	– Dr Jeffrey Hii
	13. Entomological factors affecting vivax transmission in China
	– Dr Zhou Shuisen
	Discussion

Wednesday, January 17, 2007

0900-1700H

Time	
0900 –1000	**Treatment** (***Moderator:*** Dr Krongthong Thimasarn)
	14. Treatment scheme for vivax malaria in China
	– Dr Gao Qi
	15. Treatment of vivax malaria in Indonisia
	– Dr Lambok Siahaan
	16. Treatment of vivax malaria in Thailand
	– Dr Jeeraphat Sirichaisinthop
1000 – 1020	**Coffee/Tea Break**
1020 – 1200	(***Moderator:*** Dr Kevin Palmer)
	17. Antimalarial drug response of vivax malaria in ROK
	– Dr Chae Seung Lim
	18. Detection and molecular analysis of G6PD deficiency in Southeast Asia
	– Dr Fumihiko Kawamoto
	Discussion
1200 – 1330	**Lunch Break**
1330 – 1500	**Surveillance and EDS** (***Moderator:*** Dr Krongthong Thimasarn)
	19.Surveillance and early detection warning system for vivax malaria
	– Dr Tang Linhua
	20.Limitation of present surveillance system to detect vivax malaria in the Solomons - Dr Hiroshi Ohmae
	21.Overview of Vivax Malaria in EMRO
	– Dr Hoda Youssef Atta
	Discussion
1500 – 1520	**Coffee/Tea Break**
1520 – 1700	**Advances on Vivax Malaria Control and Prevention**
	(Moderator: Dr Hoda Youssef Atta)
	22.New diagnostic method using LAMP for vivax malaria
	– Dr Eun Taek Han
	23.Vaccine development – Dr Jetsumon Prachumsri
	24.Researches on vivax malaria in NIH Korea
	– Dr Tongsoo Kim
	Discussion

Thursday, January 18, 2007

0900-1700H

Time	
0900 –1000	**Working groups' discussion:**
	Group A: vivax malaria in tropical regions
	Group B: vivax malaria in temperate regions
1000 – 1020	**Coffee/Tea Break**
1020 – 1200	**Presentation of working group results in plenary session**
	(***Moderator:*** Dr Krongthong Thimasarn)
1200 – 1330	**Lunch Break**
1330 – 1730	**Sight-seeing**

Summary of the first international conference on Vivax malaria in Asia and Pacific area

Presentations and discussions on Regional Situation, 10.00-10.30 am, 16 Jan 2007 »

1. Overview of vivax malaria distribution in Western Pacific Region – Vivax malaria is a major but often poorly understood public health problem in all ten malaria endemic countries of the Western Pacific Region. In 2004, the last year for which WHO has complete country malaria figures, the percentage of all confirmed malaria cases diagnosed as *P. vivax* ranged from 3% in Lao PDR to 100% of cases in the Republic of Korea. Because it rarely causes death and clinical symptoms are usually mild there has been very little emphasis placed on improving the diagnosis, treatment and prevention of vivax malaria. There is also a trend to devoting more attention to *P. falciparum* because genetic polymorphism, drug resistance variability and disease burden on human populations. There has been a dearth of information since the characterization of the Chesson strain among returning American soldiers after World War II in the Pacific. Consequently there is a need to understand the current epidemiology of the disease including the biology of the parasite and transmission dynamics, relapse rates and relapse intervals, and the impact on morbidity and mortality. There is a wide range of important research topics that urgently need to be addressed including the characterization of the parasite's biology, its interaction with various vector species, the disease it causes in humans and effective treatment measures all of which could provide the basis for better control in vivax malaria areas. Information gaps in the Pacific and East Asia are highlighted below:

Pacific	*East Asia*
1. efficacy of chloroquine and artemisinin combinations, 2. efficacy of primaquine in various regimens, identification and trials of replacements for primaquine, 3. ways to improve treatment compliance, 4. importance of G6PD and maybe new G6PD screening methods, 5. utility of rapid diagnostic tests, 6. new algorithms for improved clinical diagnosis, 7. improve treatment of severe cases, 8. dynamics of vectors, and effectiveness of ITN and LLIN.	1. Define and better understand vivax in DPRK, ROK and China. 2. Define the unique way that East Asia vivax "hibernates" resulting in extremely long incubation intervals; 3. Efficacy of chloroquine, primaquine and artemisinin to treat cases, 4. Efficacy of mass treatment with chloroquine/primaquine, 5. G6PD distribution and characterization, 6. Modification of existing interventions to address the short transmission season, 7. Utility of rapid diagnostic tests, 8. Indicators for vivax control, sampling/survey methods, 9. Identification of vectors, efficacy of ITN and LLIN, possible role of indoor residual spraying, other vector control methods

2. Southeast Asian Region – with the exception of Maldives, Although vivax malaria affects all ten malaria endemic countries of the Southeast Asian Region, this parasite has been ignored for many years. In 2004, the last year for which WHO has complete country malaria figures, the percentage of all confirmed malaria cases diagnosed as *P. vivax* ranged from 22% in Bangladesh to 100% of cases in the Democratic People Republic of Korea. India has the highest burden of vivax in SEAR and DPR Korea has a long incubation strain of vivax. Following the successful implementation of ACT in Thailand, Pf/Pv ratios have reversed progressively and high proportion of vivax was reported in multi-drug resistant falciparum areas near its eastern border. Chloroquine resistant vivax has been reported in India, Indonesia and Myanmar since 1991 but the resistance is focal except in Indonesia where chloroquine resistant vivax was reported in several islands. . There is lack of good data that reflects the true number of deaths and morbidity due to malaria. Although vivax malaria is non-fatal but the economic burden due to vivax malaria is enormous and unknown There is an urgent need for rapid diagnostic tests to detect vivax infections and to review primaquine treatment among countries in the region.

3. Discussion

4. In response to Dr Tang's question regarding WHO's plans to strengthen the control of vivax in the two regions, Dr Thimasarn explained that SEA Region revised malaria control strategy has a focus on scaling up control of vivax through supporting research in diagnosis and treatment, and establishing the Asia Vivax network. The latter was taken up seriously by WPRO who organized the first meeting of the Vivax network in January 2007. Dr Palmer reiterated the importance of Vivax network and thanked the Japanese government for supporting this meeting which is the starting point of the Asian Vivax Network.

5. Dr Xia Gang (China) pointed out the absence of WHO guidelines on malaria outbreaks and that there is no clear direction or definition of vivax epidemics. China has put in place good criteria for vivax epidemics but this varies from place to place. There is a need to attract partners' attention on this issue and point was made to advertise the Vivax Network in the second meeting in WHO HQ. However any early warning system must not excessively broaden the definition of outbreaks as this may result in over-reporting the number of outbreaks.

6. Whilst Sub-Saharan Africa have a diversity of Plasmodium species, the situation in EMRO is different (Dr Hoda, EMRO). More than 50% of malaria infections are of P. vivax in Afghanistan and syndromic treatment is usually practiced as there is no microscopy in place. In EMR region, there is a general lack of knowledge on ACTs, the role of LLINs and G6PD countries are reluctant to comply with the 14 day primaquine treatment. Dr Hoda (EMRO) emphasized that there is an urgent need to build a Vivax Network and to increase cooperation with the inclusion of EMRO.

All country presentations on 16 January 2007

Cambodia:-

Malaria is endemic mainly in forested areas which accounts for nearly 60% of the land and 1.6 million people are at risk. . Access to remote areas is the major challenge. However Cambodia has managed to reduce the number of cases from 170,387 (1997) to 74,185 (2005) and mortality has also declined from 865 (97) to 296 (05). The percentage of *P. vivax* has increased from 20% (97) to 33% (2005). *An. dirus*, *An. minimus* and *An. sundiacus* are the major vectors. The goal of the national program is to reduce malaria related mortality by 50% and morbidity by 30% among the general population in the Kingdom of Cambodia within five years through the implementation of a comprehensive national malaria control strategy. The Strategies include increasing the level of awareness, distribution of ITN, early case detection and treatment and development of capacity at all levels. ITN distribution is based on the distance from the forest. Usage of ACT and distribution of ITN has led to the decline in cases. ACT resistance was reported in Ratnakiri but all 6 sentinel sites continue to report over 90% cure rate with ACT. The sustainability of social marketing of drugs was pointed out as a challenge in the coming years, though the program will be supported by the Global fund till 2012.

China:-

Significant decline was achieved by China from 30 million malaria cases in 1930 and in 1960-1970s there were two reported pandemics affecting 17 million and 21 million respectively. In 1990's significant progress was made in malaria control and the number of cases have declined to less than 25,000 in 2000-01. However cases have increased to 60,000 in 2006. At present 79% of cases are P.vivax and 5% is P. falciparum (17% unknown) and the period of malaria transmission is from week 28 to 48th with the peak in weak 44. A stratified random sample survey conducted by global fund round 1 project estimates the number of cases to be 15 times higher. The reason of reported cases in recent years include significant improvement in reporting system, cases caused by migration especially in Yunnan province and re-emergence of malaria in central provinces of Anhui and Henan provinces. The national program continues to faces several problems such as poor access to diagnosis and treatment, drug resistance, low coverage of vector control, weak surveillance and lack of awareness of the disease. The new national program 2006-2015 aims to reduce incidence to less than 1 per 1000 in Yunnan province, eliminate falciparum malaria in Hainan province and declare malaria elimination in other parts of the country. The strategies include greater access to diagnosis and treatment in remote areas, free distribution of LLIN, strengthening malaria surveillance and epidemic preparedness and increasing the level of awareness.

Indonesia:-

Approximately 107 million people out of 217 are at risk of malaria in 110 districts mainly in the eastern part of the country. Over 2 million cases and 700 deaths were reported due to malaria in 2005 but the estimated figure is 10 million cases and 20,000 deaths. The National Health Survey (2001) has estimated 23,483 deaths due to malaria and low

haemogloblin levels in majority of children in the age group of 1-4 years. The strategies include case detection and treatment, vector control, outbreak management, promotion and improved surveillance. Improved detection and treatment has led to the decline of cases in Java-Bali and at present the species ratio is 51:49 in favour of P.vivax. Eight districts have recorded CQ resistance in P vivax. Indonesia has over 20 malaria vectors. The over all goal of the program is to reduce mortality and morbidity by over 50% by 2010. Efforts are also underway to eliminate malaria from several islands especially in Java Bali.

Japan:-

Before World War, *Plasmodium vivax* was endemic in some of the areas of Japan(including Honshu & Hokkaido) . *P. falciparum* was endemic in Ryukyu (Okinawa) Islands. In the 1940s and 1950s, outbreaks of Falciparum malaria in Yaeyama Islands, Okinawa. After 1945, many soldiers infected with P. *falciparum* came back to Japan from Southeast Asia and Pacific area. Though there were mosquito vectors which are susceptible for *P. falciparum* in some areas of Japan, no outbreaks of malaria was recorded.

Because of progress of malaria control programme, the number of Vivax malaria had decreased. Except for imported cases and some suspected cases of airport malaria, no cases of Vivax malaria have been reported since 1961 in Japan. But there are many habitats of mosquito vectors of malaria parasite in Japan. The presentation clearly highlighted the need to improve detection of vivax malaria at airports and quarantine areas.

DPRK:-

Malaria was eradicated for 30 years but P.vivax malaria reappeared in 1998 and it 2001 over 300,000 cases was reported. Since 2002 malaria has declined in DPRK and further 18.7% decline was reported last year. The annual incidence rate in 2006 was 0.4 per 1000. An.sinensis, An. lesteria and An. Yatsushiroensis are the major vectors and the disease peaks in the month of August soon after rains. The goal of the national program is to substantially eradicate the constant threatening sources of potential malaria pandemic in the country, by sustaining the already-achieved successes in all the malaria-affected areas and focusing the control program around the borderline areas. The current strategies include diagnosis and treatment and chemophylaxis with Primaquine and development of human resources.

ROK:-

Malaria was eradicated from 1978 to 1992, but one case was recorded in 1993 from the DMZ. Cases of vivax malaria was recorded ever since with the peak in 2000 of 4142 cases and 1962 cases were recorded in 2006. 21 cities and counties are at risk of malaria and they are stratified as high risk, risk and potential risk areas. Malaria incidence is high in western areas and low in eastern areas. Seoul Metropolitan area seems to function as a defensive shield against malaria, preventing its spread to areas south of the

metropolitan area Joint activities involving both ROK and DPRK are going on with a significant success.

Philippines:-

57 of the 79 provinces are endemic for malaria and 46,342 cases were recorded in 2005. 73% of these cases are falciparum and 23% are vivax malaria. There are five major vectors and the country is categorized into provinces with over 1000 cases, 100 to 999 cases and less than 100 cases respectively. Computation of past five years of data shows the northern Luzon group of islands accounts for 60% of the cases and 39% are recorded in the southern Mindanao group. There are four sentinel sites for drug resistance studies and studies on CQ resistance in P.vivax is currently in progress and so far all cases (n=27) are still sensitive. Philippines have currently three on going global funds projects and support from AusAID -WHO RBM project. The national goal is to eliminate malaria by 2020.

Solomon Islands:-

Solomon Islands have the highest incidence of malaria outside of African continent. The country was badly affected by ethnic crisis from 1999 to 2003 and the annual incidence rate in 2006 was 150/1000 cases. P. vivax ratio ranged from 48% (1996) to 29.3% (2005). The presentation hypothesized the greater the reduction of malaria the more chances of P. vivax predominance. Primaquine treatment for 14 days was found to be very effective.

Thailand:-

Thailand has a total population of 65 million and malaria mortality has declined 120/100,000 from 1955 to only 161 deaths in 2005. The ratio of P. vivax has increased from 31% (1981) to 50% in 2005. The percentages of imported cases (from foreigners) have increased from 24% to 54% in 2006. 97% of imported cases are from Thailand – Myanmar border. Artesunate resistance was also reported recently.

Entomological factors on P. vivax transmission

- Through the presentation and discussion on the overview of vectors of vivax malaria in Asia and South Pacific area, and in China respectively by Dr. Jeffrey Hii and Dr. Zhou Shuisen, main points could be summarized as follow:
- The distribution of primary or secondary vectors responsible for malaria transmission varies and depends on many factors including ecotypes, geographies, social developments, and disease interventions. Under such conditions, the transmission role of a main vector could be switched to other potential discriminated vector(s).
- The biology and behavior of the main vectors, particularly on the transmission characteristics associated with certain factors such as disease interventions and environmental modification either under natural or men-made conditions.

- The identification and classification of the vectors is more reliable if PCR-RFLP method is used rather than that of morphological method.
- Main vectors responsible for P. vivax transmission and its distribution are also varied. The studies in PNG convinced that in coastal ecotype, An. farauti sub-complex species are the main responsible and other two vectors, An. punctulatus and koliensis are the discriminated vectors both in coastal and inland ecotypes.
- The other entomological study in PNG found that the characteristics of the main vector, An. punctulatus, infected with P. vivax are younger parous and earlier biting if compared to the An. punctulatus infected with P. falciparum.
- Evidence from laboratory-based study on susceptible infected to plasmodium parasites in Thailand indicated that two main groups, An. barbirostis and campestris, which are highly fecundity, indoor biting, and anthropophily, are susceptible only to P. vivax. From such study design, the identification of other responsible vectors is potentially explored to understand more on the other vectors, currently known as primary or secondary responsibility on malaria transmission, to be specific on the susceptibility of P. vivax transmission. However, laboratory-based study is complicated and challenging in implementation.
- Field studies indicated that other main vectors in the regions such as An. dirus, An. leucosphyrus, An. minimus, An. kochi, An. annularis, An. sawadwongporni, An. vagus, An. Willmori, An. barbirostris, and An. campestris, are also associated with P. vivax transmission.
- In China, four main vectors associated with P. vivax transmission are An. sinensis, anthropophagus, minimus and dirus. An. sinensis extensively distributes in the country while An. dirus are geographically confines to hilly and forested areas and An. minimus mainly distributes in Southern part of 33^{O}C and Northern part of 25^{O}C, predominant in the Southern provinces. The distribution of An. anthropophagus extends northward from South 33^{O}C to 42^{O}C and it may be correlated with the global warming.
- Feeding and resting behaviors of these vectors are varied. An. sinensis can rest in both animal sheds and human house; and it is neither typical exophagic and exophilic nor typical endophagic and endophilic malaria vector. However, An. anthropophagus feeding and resting behaviors, which is very typical endophilic and anthropophilic habits in the past, actually are endophilic in the Southern and Central parts and exophilic in the Western and Northern parts. An. minimus and An. dirus are considered to be as highly anthropophilic and typically exophilic for An. dirus.
- Other factors, such as genetic variation, ecological change, and global warming, have been considered as potential associated P. vivax transmission. Change in feeding and resting behaviors and insecticide resistance indicate the implication of the strategic intervention.

Treatment, sensitivity of *P. vivax* to chloroquine and primaquine and prophylaxis

1. China:

The treatment of vivax malaria is a topic that looks like simple but actually complex. The drugs applied in the region are chloroquine for the clearance of clinical manifestation and asexual malaria parasites and primaquine for cure of liver stage of the parasites (dormant). It is complicated with the variation in strains with different incubation time and with the various patterns of relapse.

Clearance of clinical manifestation asexual malaria parasites: Chloroquine has been the first-line therapy for vivax malaria since 1946. It is given to patients with a total dosage of 1.2 g in China and 1.5 mg recommended by WHO.

Anti-relapse treatment: in 1970s to 80s, Scientists in China studied treatment of vivax malaria with different dosage of primaquine ranging from 75 mg/day to 210 mg/day (WHO recommended), different treatment course ranging from 3 days to 14 days, and different subjects recruited into tests ranging from 8 to 210. The relapse rates varied from 0 to 27%. The WHO recommended dosage (210 mg/14days) showed different outcome of relapse in areas with different endemicity. Two administrations of primaquine (22.5 – 30 mg/day) treatment courses (4, 7, 8days) to patients with an interval (1-4 months) in between showed better results than one administration. The 180 mg/8 days and 120 mg/4 days 2 times administration were better than others. No difference in relapse rates observed between 8-day consecutive administration of primaquine (22.5 mg/day) and double 4-day administrations of the drug (22.5 mg/day) with a one-month interval between the two administrations.

China is now apply a treatment course of chloroquine 1.2 g (with 0.6g on day 1 and 0.3 g on day 2 and 3 and primaquine 180 mg/8 days (22.5 mg/day). All patients are given a course of primaquine (22.5 mg/day for 8 days) for radical cure. Piperaquine (4 tablets/month) has been used for chemoprophylaxis in target group or target areas in transmission season.

Resistance to chloroquine by *P. vivax* was first confirmed among Australians repatriated from Papua New Guinea and followed by several countries including Indonesia. Preliminary study in 2005 and 2006 in China showed resistance of *P. vivax* to chloroquine.

2. Indonesia

From 1997 to 2001, 8 districts reported resistance of *P. vivax* to chloroquine. For treatment of uncomplicated vivax malaria, both chloroquine3 days and primaquine 14 days, and quinine 7 days and primaquine 14 days are recommended for adults and children. For pregnant women infected with vivax malaria, chloroquine of 3 days and quinine of 7 days without primaquine are recommended. For children, primaquine is not recommended for those of <1 year of age.

The studies conducted from 2002 to 2003 in Bangka showed ACPR of 81% of chloroquine and 97% of AMO, in S. Minahasa with ACPR of 81% of chloroquine, in

Mimika with ACPR of 79% of chloroquine, in Purworejo with ACPR of 90% of chloroquine, and in S. Lampung with ACPR of 33% of chloroquine.
The presentation on a small scale of study on resistance of *P. vivax* to chloroquine (day 1 and 2: 10 mg/kg BW/day, day 3: 5 mg/kg BW/day) and primaquine (7.5 mg of base/tablet, 0.25 mg/kg BW/day for 14 days) in Sumatera, Indonesia in 2004 showed that ACR was 94% and treatment failure rate was 6% with a follow-up of 28 days.

3. Thailand

Current standard regimen for treatment of vivax (including malariae and ovale) in Thailand is chloroquine 1.5 g 3 days and primaquine 15 mg 14 days (in malariae cases, no primaquine). For frequent relapse cases, primaquine will be shifted from 15 mg up to 20 mg/day 14 days. No evidence of resistance of *P. vivax* to chloroquine. The relapse rate of 15mg/day 14 days is 19% after 6 month's follow-up and 2% for 22.5 mg/day 14 days after 6 month follow-up.

Drugs in use for prophylaxis of malaria in Thailand are doxycycline, daily in general and mefloquine, weekly for specific groups.

4. Republic of Korea
In 1952 and 1999, studies on treatment of vivax malaria were conducted in Republic of Korea and the results showed that the relapse rates ranged from 0 to 1.4% for standard treatment of chloroquine and primaquine and 39% for chloroquine alone within a period of follow-up from 4 to 24 months.
From year 2000, two recent studies on efficacy of chloroquine and primaquine for 14 days were conducted。 First study was carried out in 92 patients hospitalized in Korea University Medical Center and Pajoo Medical Center after 2000 with a follow-up of 6 months. Second study was conducted in 689 patients in 6 malaria-risky areas. Patients were followed up for 28 days for observation of chloroquine failure and 2 years for observation of primaquine failure. No treatment failure and relapse were found in first study. For the second study, no treatment failure of chloroquine was found and the relapse rates were 0.7, 3.8 and 10.4% within a period of follow-up of less than 3, 6 and 24 months, respectively.

5. The Philippines
A re-assessment study of chloroquine on vivax malaria was conducted. Chloroquine (150 mg base/tablet) was administrated one dose of 10 mg base/kg BW on day 1 and 2 and 5 mg base/kg BW on day 3. *Primaquine (*15 mg/tablet) was given 14 single daily doses of 0.3 mg/kg BW after day 28. Analysis on the results of 36 cases showed that all the 27 cases with full follow-up showed adequate clinical and parasitological response and the gametocyte rates were 50%, 3.1% on day 0 and 1, and 0 from day 3 to 28.

6. The Solomon Islands
Since 1969 the treatment for *P. vivax* and *P. falciparum* was chloroquine plus primaquine. Primaquine then was given as a gametocytidal agent and was given as a single dose of

45mg. In 1991 primaquine was withdrawn because it was observed to cause haemolyses. In vivo studies done in Honiara, in 1995-1996, showed 30.43% resistance to chloroquine. At present, chloroquine is given at the dose of 10mg/kgBW/day on the first 3 days and primaquine is given at a dose of 0.25mg/kgBW/day for 14 days from Day 4. And for those patients with G6PD deficiency, a dose of 0.75mg/kg weekly for 8 weeks is administrated.

7. The Eastern Mediterranean Region
Primaquine is recommended for anti-relapse treatment (14 day course) in confirmed infection with *P. vivax. The c*hallenge on this regimen is poor compliance. Instead of this regimen, Pakistan is recommending primaquine for 5days. Primaquine is not to be used for children < 4 years and pregnant women. For those in G6PD deficiency areas, it is recommended that primaquine is used 0.75mg/kg weekly for 8 weeks to patients with G6PD deficiency in some countries. No information on CQ resistance for vivax malaria is reported. In Afghanistan and Pakistan, Diagnosis of malaria is poor and limited services for malaria microscopy. No pre-qualified RDT in vivax areas is applied in the region. Timely detection of vivax cases in malaria free countries is a concern due to vivax cases are mostly asymptomatic, occurrence of clinical relapses and poor epidemiological classification.

8. Japan
Mefloquine is administrated for prophylaxis
.
9. Democratic People's Republic of Korea
Primaquine are used for prophylaxis in malaria risk areas.

II. Detection of G6PD

There are 4 ajor screening methods for detection of G6PD deficiency, i.e., UV-spectrophotometric assay, Spot test, using UV light, Formazan-ring (Fujii) method (MTT/PMS) and Sephadex-gel (Hirono) method (MTT/PMS). UV-spectrophotometric assay is accurate and quantitative. However, this method requires an expensive spectro-photometer, so is inadequate for field assay. Spot test using UV light is simple, rapid and qualitative, but requires UV light and dark room or chamber. It can detect only severe deficiency. Formazan-ring (Fujii) method (MTT/PMS) is accurate, time-consuming to make kit, qualitative. However, his method is photo-sensitive, incubation at 37C for 8 hrs. Sephadex-gel (Hirono) method (MTT/PMS) is simple, rapid, qualitative, but strong photo-sensitive. It detects only severe deficiency and is difficult to identify heterozygous female.
Dr. Fumihiko Kawamoto at Institute of Medicine, Oita University invented a new method, WST-8 method, for detection of G6PD. It is a new method using WST-8 and 1-methoxy PMS and is photo-resistant, quantitative (ELISA reader) and the chemical reaction can be stopped by 1N-HCl. The reaction color is orange and persists for more than 120 minutes. Both fresh and -4°C-stored blood could be applied and there is no much difference between the colors of fresh and -4oC-stored blood samples. The preliminary study results showed that this method is quick and may applied in rural areas without supply of

electricity. It can detect both severe deficient individuals and heterozygous females qualitatively in the field. G6PD deficiency screening kit (Dojindo, Kumamoto, Japan) based on this method is developed and is or is going to be tested in Indonesia, Thailand and Anhui Province of China.
There are many gene variant types in the region such as Viangchan, Mahidol (Southeast Asia), Canton, Kaiping (China), Union, Vanua Lava (Oceania), Chatam (Middle East), Mediterranean and Coimtra. Although Viangchan and Mahidol are dominant types of G6PD on Southeast Asian countries, the distribution of G6PD variants differs in each country. Reaction of different variant types to primaquine is different.

III. Diagnosis
Diagnosis vivax malaria in Asia, Pacific and Eastern Mediterranean regions is mostly based on clinical manifestation and microscopy. Sensitivity and specificity of RDTs on diagnosis of vivax malaria is not as satisfied as that of falciparum malaria.
1. Japan: New method of ongoing study
Dr. Han Eun-Taek from Japan introduced a newly invention of nucleic acid amplification method, the Loop0deidated isothermal amplification (LAMP). The method can detect all the four species of human malaria parasites. The primary study indicated that the sensitivity and specificity of LAMP were 98.5% and 94.3% respectively compared with microscopy. The times from reaction to reading of results were 26 minutes on average of for detection of genus Plasmodium, 31 to 36 minutes for detection of *P. vivax*, falciparum, malariae and ovale. The times are shorter than nested PCR. No special equipments are needed and results are read by simple visual inspection or by turbidimeter. It provides rapid, simple and reliable results for routine screening of malaria parasite. However, at present the cost is high.
2. Republic of Korea: diagnosis through multiple methods
100% of malaria cases in Korea are vivax malaria cases. One of specific characteristics of it is the long incubation. Microscopy and PCR are applied to detect malaria parasites morphologically and antigen molecular-biologically. IFAT, ELISA are used to detect circumsporozoite protein (CSP) (Pv247, Pv210), merozoite surface protein (MSP, P. v) and liver stage specific antigen (LSA, P. f).

IV. Researches on vivax malaria
1. Plasmodium vivax vaccine development in AFIRM
Jetsumon Prachumsri from AFRIM introduced the development of *P. vivax* vaccine. At present, strategies to identify vivax vaccines are similar to that of *P. falciparum*. Studies of antigens cover all development stages of vivax parasites, including blood, pre-erythrocytic and mosquito stage. The 8 candidates of vivax vaccines include CTRP (circumsprorozoite protein/thrombospondin-related anonymous protein), PvAMA-1 (Apical membrane antigen-1), PvCSP (Circumsporozoite protein), DBP (Duffy binding protein), PvMSP (Merozoite surface protein), RAP-1 (Rhoptry-associated protein 1), PvSSP2/TRAP (Sporozoite surface protein 2/Trombospondin related adhesive protein family), Pv25/Pvs28 (ookinete surface antigens) and PvTRAg (Tryptophane-riched antigen). Antigen selection is dependent upon a variety of factors that include expression and purification success (for recombinant proteins), limited polymorphisms in amino acid

sequence in various P. vivax strains, ortholog antigen to clinical tested of P. falciparum vaccine candidates, immunogenicity and prime-boost effects.

2. Studies in NIH, CDC, Republic of Korea

Systematic studies are conducted in National Institute of Health, CDC, Republic of Korea.

2.1 Strategies of researches are as the following:

2.1.1 towards malaria parasites

- Immune enhancement of malaria parasites by using immune cells and the development of DNA vaccines
- Characterization of malaria antigens (cystein proteases) and the applicant of new therapy
- Gene diversity Plasmodium
- Vivax in Korea based on MSP-gene

2.1.2 towards mosquitoes

- Molecular study for Korean Mosquitoes and the development species-specific molecular marker
- Colonization of malaria vector mosquitoes
- Susceptibility of Korean Anophelines mosquitoes to Malaria

2.1.3 towards human

- Chloroquine sensitivity analysis of Korean malaria patients
- Recrudescence and Relapse
- Early detection of the long time latency patient

2.2 Direction of our Malaria Researches is tow folds

2.2.1 Anti-Transmission: to develop Transmission blocking vaccine (TBV) in order to block the transmission from mosquitoes to human.

2.2.2 Anti-Infection: to study on blocking sporozoites entering liver or become hynozoites of long and short incubation in liver and on early diagnosis in the patent period

2.2.3 Anti-Disease: study on the blood stage with the purpose of more effective treatment and monitoring of resistant.

The ongoing studies are CSP (Circumsporozoite Protein) study towards dipstick kit development, PvLSA (Liver stage antigen) study towards early diagnosis, MSP- 1 (Merozoite surface protien1) study towards gene diversity analysis and establishment of diagnosis system, and Pv25, Pv28 (Ookinete surface protein) and CDPK (Calcium Dependent Protein Kinase) study towards development of transmission Blocking vaccine.

V. Surveillance and early detection warning system for vivax malaria

Malaria surveillance program is one of the important parts of "National Program on Malaria Control in 1991-1995"and National Program on Malaria Control 1996- 2000" National Program on Malaria Control 2001- 2015" in China. The purpose of surveillance is to know where malaria is endemic and how serious it is, to identify high-risk areas, to monitor progress towards the interruption of malaria transmission, to predict malaria trend, outbreak, incidence etc. It coves case detection, focus intervention, management on mobile population, drug resistance and vector monitoring it uses annual parasite incidence (API), annual blood examination rate (ABER), annual vivax incidence (AVI) and slide positive rate (SPR) as the main parameters. And feeding and resting behavior,

human biting rate, human blood index and vectorial capacity are use as main indicators to monitor vectors. The case reporting system including village doctors/private doctors/clinics, township hospital/other hospitals, county CDCs, prefecture/city CDCs, provincial CDCs and China CDC is to be strengthened. Three main groups of indictors to predict the timing and severity of a malaria epidemic, i.e., vulnerability indicators, transmission risk indicators and early detection indicators from health facility malaria morbidity data. Surveillance data, data of sentinel sites, laboratory-diagnosed malaria data will be applied to conduct analysis using temporal analytical techniques, time-series cross correlation and linear regression.

Surveillance and early warning system

During this section, the moderator was Dr. Krongthong Thimasam and there were three presenters, Dr. Tang Linhua presented the surveillance and early warning system for vivax malaria in China, Dr. Hiroshi Ohmae presented the limitation of present surveillance system to detect vivax malaria in the Solomon Islands, and Dr. Hoda Youssel Atta presented the overview of vivax malaria in EMRO. The presentations were followed by the discussions and comments among participants and could be summarized as follows:

The surveillance and early warning system for vivax malaria in China

- In China, malaria is confined to some parts of the country with range of incidence rate and classified the magnitude of API as less than 1 case per 100,000; between 1 to less than 10 per 100,000; between 10 to less than 100 per 100,000; and more than 100 per 100,000.
- The periods of malaria transmission vary and depend on many factors. In the South of 25^{O}NL, the period of vivax malaria transmission is between 9 to 12 months and An. minimus and dirus are the main discriminated vectors. In region between 25 to 33 ^{O}NL, the period of vivax malaria transmission is between 6 to 8 months and An. sinensis is the main discriminated vector. In region of North of 33 ^{O}NL, the period of vivax malaria transmission is between 3 to 6 months and An. sinensis and An. messeae are the main discriminated vectors.
- According to the statistics, it indicated that the total number of malaria cases was significantly reduced from more than 600,000 cases in mid-1980s to less than 100,000 cases after 1990s. The majority of cases was vivax malaria and according to the statistics in 2006, vivax malaria accounted for 78.8% of the total reported cases in the country. However, the number of cases had been slightly increased since 2000 and visibly increased in 2003. In 2003, there were 162 counties in 16 endemic provinces re-immerging and among them 73 had outbreaks.
- The CDC in China has established comprehensive network for diseases surveillance including malaria. The flow of information, particularly the reported cases, are from the lower level, e.g. village, to intermediate levels, e.g. township, hospitals, county CDC, prefecture/city CDC, up to the highest levels, e.g. provincial and China CDC. From intermediate levels to central levels, the communications are through electronic networks.