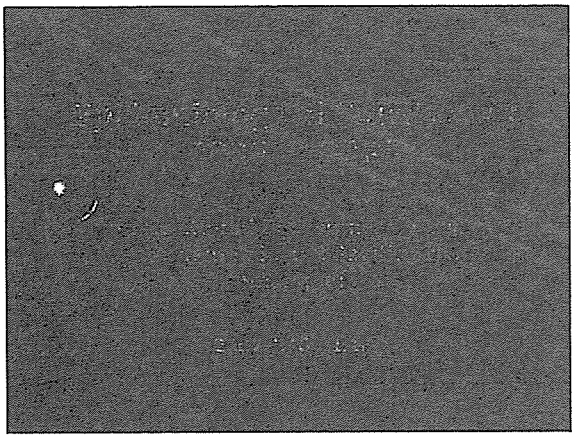


Malaria History in DPR Korea

- Malaria was eradicated 30 years back in DPRK.
- Reoccurred in 1998 with the peak of 300,000 cases in 2001.
- Showed decreasing trend since 2002.

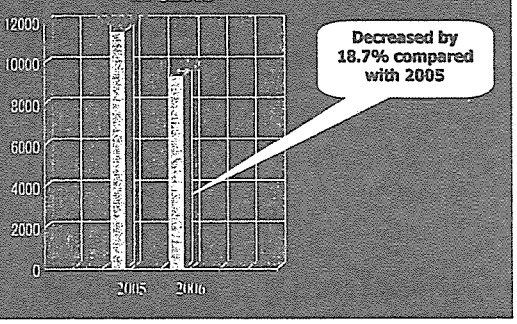
Malaria Epidemiological Situation in 2006

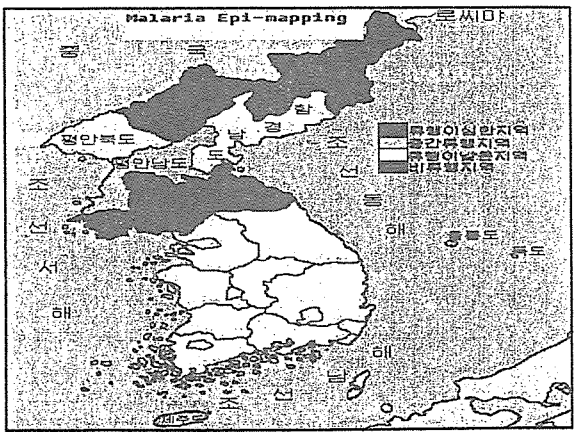
Blood smear 12,983 persons
Positive cases 6,913
Clinical diagnosed patients 2,440
Morbidiy in 2005 0.5‰
Morbidity in 2006 0.4‰

Province-wise Malaria Occurence

	2006	2005	Decreased rate(%)
n.Hwanghae:	1,498	5,844	74.4% decreased
s.Hamgyong:	267	574	53.5% decreased
n.Hamgyong:	88	248	64.6% decreased
Jagang:	18	25	28% decreased
Pyongyang :	105	135	22.3% decreased

2005-2006 Occurance in table

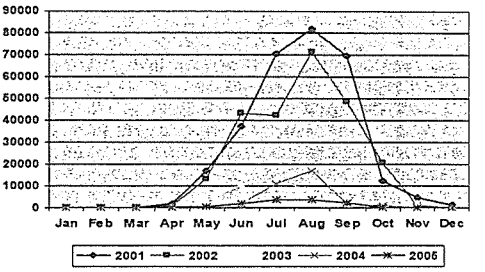




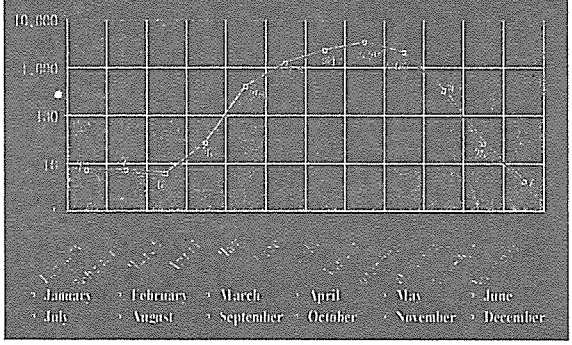
Province-wise Malaria Laboratory Tests and positive rate

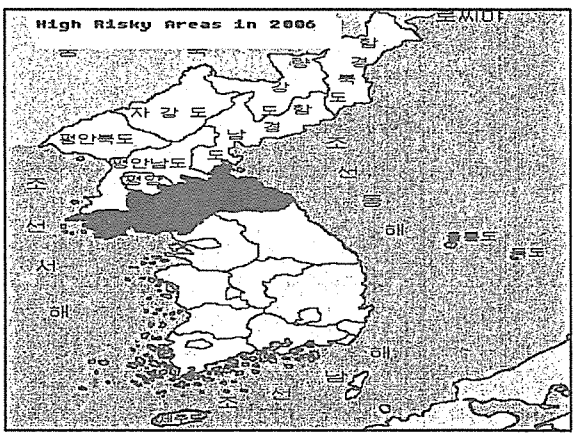
№	Infected areas	Confirmed infected cases	Blood smear test	Positive cases	Smear positive rate (%)	Vivax malaria	p. malaria	Clinical diagnosed cases	death
1	Pyongyang	105	159	69	43.4	69	-	36	-
2	s.Pyongan	1703	1863	1217	65.3	1217	-	486	-
3	n.Pyongan	1439	1539	894	58.1	894	-	545	-
4	Jagang	18	37	18	48.6	18	-	-	-
5	s.Hwanghae	2303	3733	1845	49.4	1845	-	458	-
6	n.Hwanghae	1498	2842	1312	46.2	1312	-	186	-
7	Kangwon	1925	2157	1253	58.1	1253	-	672	-
8	s.Hamgyong	267	496	229	46.2	229	-	38	-
9	n.Hamgyong	88	136	69	50.7	69	-	19	-
10	Ryanggang	7	21	7	33.3	7			
	Total	9,353	12983	6913	53.2	6913	-	2440	-

Malaria Occurrence during 2001-2005 by month

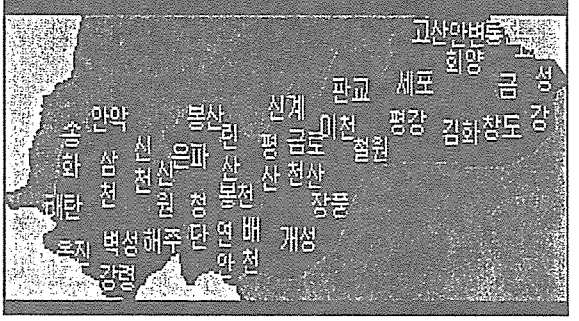


Monthly Malaria Occurrence in 2006

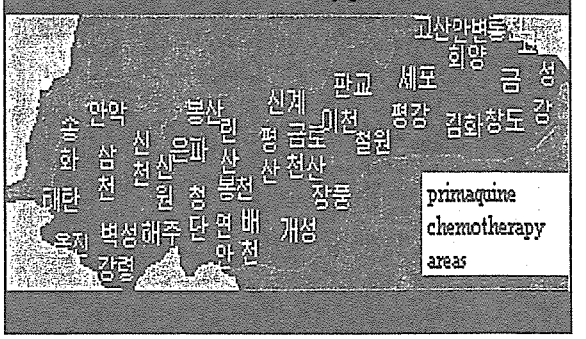


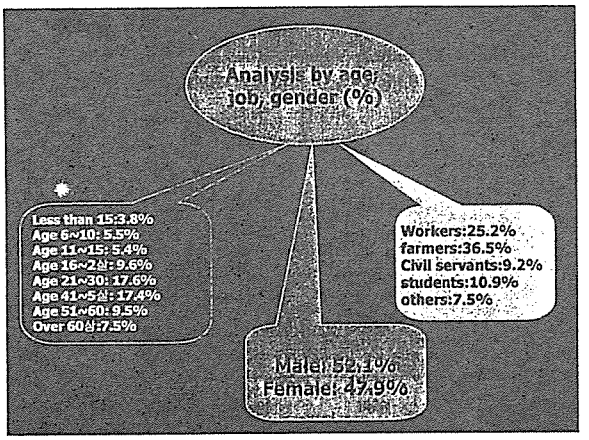


Areas with Increased Epidemiology in 2006



Target Areas of Primquine Chemotherapy so far





Outcome of study on ecological habit of malaria vector

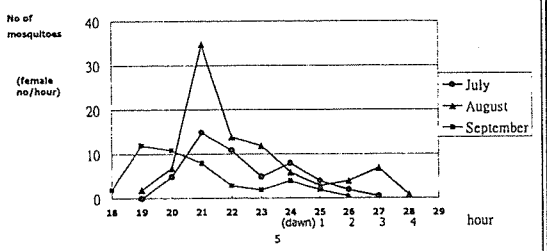
Table 3-1. blood-sucking habit (2006,Rinsan)

Species	Tested no of mosquitoes	Precipitation results						인월지수
		Human		Ox		Pigs, etc		
		Positive/	Rate	Positive/	Rate	Positive/	Rate	
An. Sinensis	116	45	38.79	59	50.86	12	10.34	0.3879
An. Lesteri ssp	41	28	68.29	8	19.51	5	12.19	0.6829
An. Yatsushiroensis	37	12	32.43	14	37.84	11	29.73	0.3243

Table 3-2. Resting habit (2006, Rinsan)

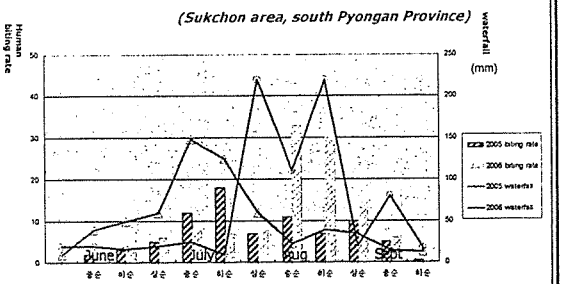
	Indoor			Cattle shed			Outdoor grass field		
	Total collected numbers	Malaria mosquitoes	Ratio (%)	1	2	3	1	2	3
Urban area	161	26	16.1	1455	871	59.8	372	108	29.0
Rural village	244	56	22.9	2866	1487	51.9	598	241	40.3

Character of one night blood-sucking activity of malaria mosquito (2006, Sukchon)



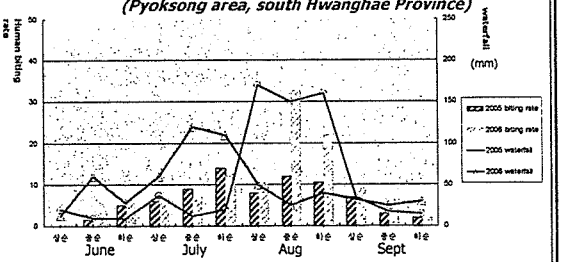
Relation between rainfall and malaria vector density

(Sukchon area, south Pyongan Province)



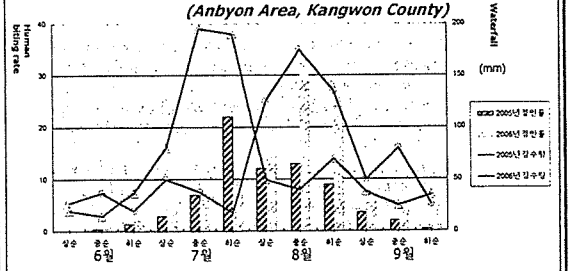
Relation between rainfall and malaria vector density

(Pyoksong area, south Hwanghae Province)

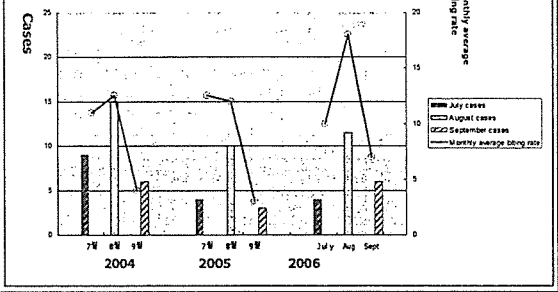


Relation between rainfall and malaria vector density

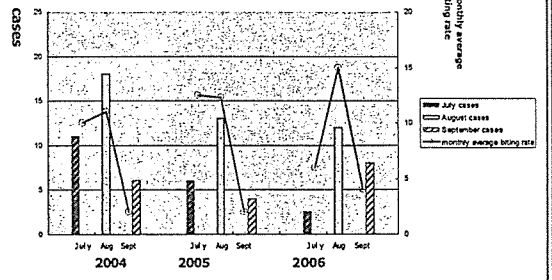
(Anbyon Area, Kangwon County)



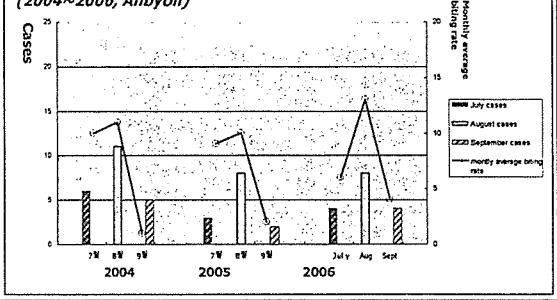
Relation between monthly malaria vector density and case outbreak ***(2004~2006, Sukchon)***



Relation between monthly malaria vector density and case outbreak
(2004~2006, Pyoksong)



Relation between monthly malaria vector density and case outbreak
(2004~2006, Anbyon)



Strategical Workplan for Malaria control in DPRK

Goal:

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.

1. **To strengthen national policy related to malaria control.**
2. **To improve the integrated survey, assessment on malaria and its vector, as well as the conditions to strengthen the capacity of the health personnel.**

3. **To conduct simultaneously the primquine chemotherapy targeting the malaria high risk areas and the neighbouring areas (all the southern part) in order to eradicate the sources of malaria outbreak.**
4. **To strengthen the medical services for the malaria patients.**
5. **To strengthen activities for collective protection and [illegible]tion in the high risk areas.**
6. **To provide health education on malaria to the population in the malaria-endemic areas for their continued vigilance and awareness.**
7. **To organize the training on vector control management and on improvement of laboratory capacity and planning/managerial capabilities.**
8. **To improve the surveillance and evaluation methodology and systems for malaria control program.**

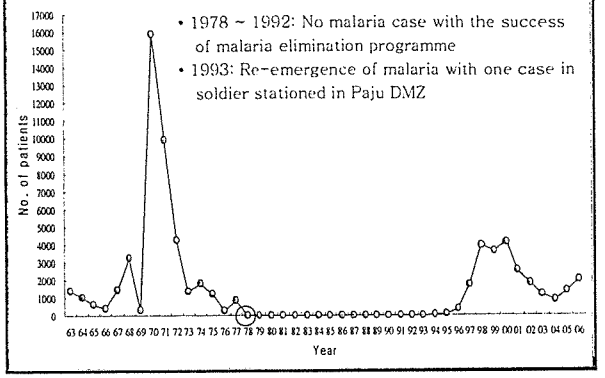
질병관리본부

Malaria Situation in the ROK

16th Jan. 2007

질병관리본부

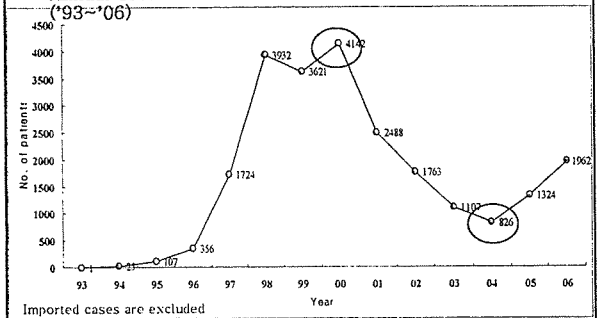
Annual Trend of Malaria Cases



- 1978 ~ 1992: No malaria case with the success of malaria elimination programme
- 1993: Re-emergence of malaria with one case in soldier stationed in Paju DMZ

질병관리본부

Annual Trend of Malaria Cases in the ROK ('93~'06)



- The total number of cases has decreased after reaching a peak of 4,142 cases in 2000 to 826 cases in 2004.

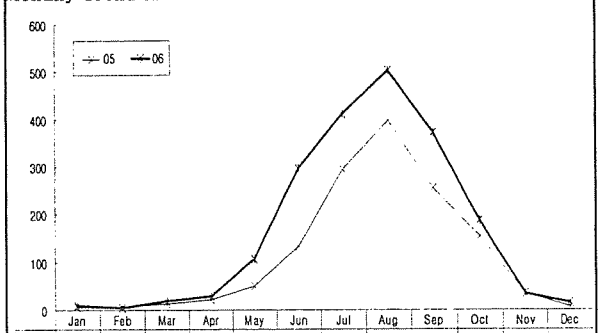
질병관리본부

Malaria Cases by Occupation (2005~2006)

Year	2005	2006
Civilians	769	1,229 (60)
Discharged Soldiers	322	432
Soldiers	233	301
Subtotal	555	733 (32)
Total	1,324	1,962 (48)
Imported	45	24

질병관리본부

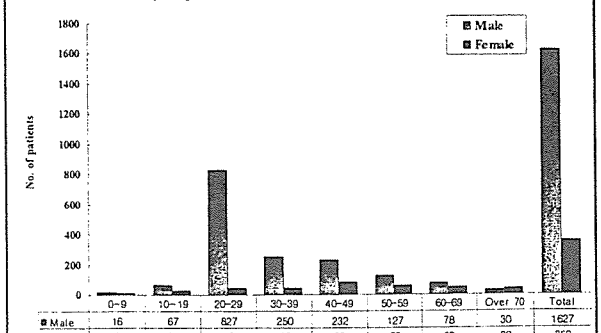
Monthly Trend of Malaria Cases in the ROK ('05~'06)



	Jan	Feb	Mar	Apr	May	Jun	Jul	Aug	Sep	Oct	Nov	Dec
05	6	5	12	21	49	133	295	398	256	154	34	6
06	9	3	18	29	106	296	412	503	373	188	34	15

질병관리본부

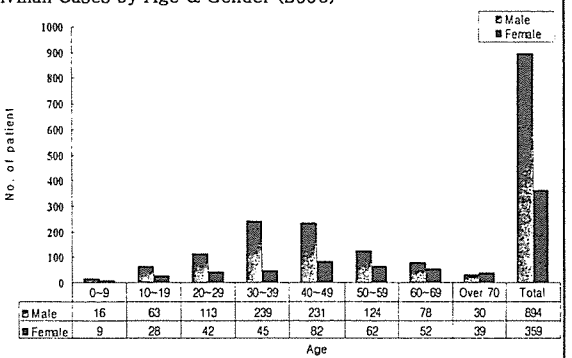
Malaria Cases by Age & Gender (2006)



	0-9	10-19	20-29	30-39	40-49	50-59	60-69	Over 70	Total
Male	16	67	827	250	232	127	78	30	1627
Female	9	28	43	45	82	62	52	38	359

24 imported cases

Civilian Cases by Age & Gender (2006)



	0~9	10~19	20~29	30~39	40~49	50~59	60~69	Over 70	Total
Male	16	63	113	239	231	124	78	30	894
Female	9	28	42	45	82	62	52	39	359

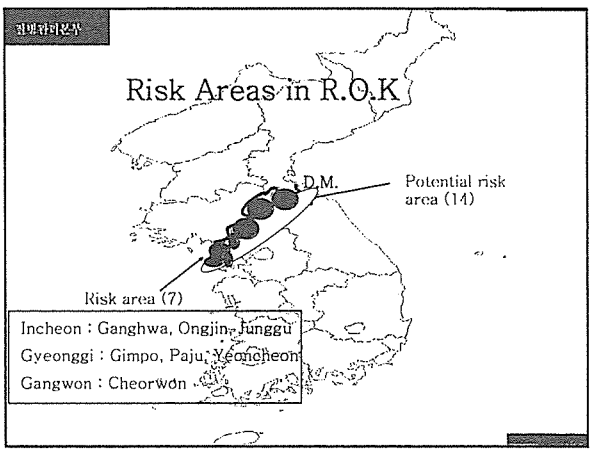
24 imported cases

Civilian Cases by Region (2005~2006)

Regions	2005	2006
Incheon	182	406 (123%)
Gyeonggi	397	535 (35%)
Gangwon	29	46 (59%)
Sub total	608 (79)	987 (80) (62%)
Seoul	120 (16)	180 (15)
Busan	2	5
Daegu	0	4
Gwangju	1	3
Daejeon	3	-
Ulsan	0	4
Chungbuk	4	8
Chungnam	5	6
Jeonbuk	8	7
Jeonnam	9	12
Gyeongbuk	6	4
Gyeongnam	3	7
Jeju	0	2
	161 (21%)	242 (19%)
Total	769	1,229 (60%)

* Provisional statistics for 2006

Risk Areas in R.O.K



Risk Areas in 2006

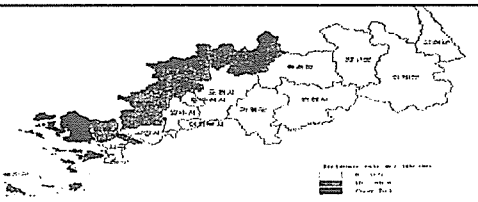
Division / Region	Risk Areas (Per 100,000 population)		
	High-risk area (Over 100)	Risk area (10~99)	Potential risk area (Less than 10)
Gyeonggi (10)	-	Gimpo, Paju, Yeoncheon	Yangju, Uijeongbu, Pocheon, Gapyeong, Goyang(Ilsan, Deogyang), Dongducheon
Incheon (5)	Ganghwa	Junggu, Ongjin	Incheon (Donggu, Seogu)
Gangwon (6)		Cheorwon	Chuncheon, Yanggu, Inje, Hwacheon, Goseong

Criteria for Stratification of Risk Areas

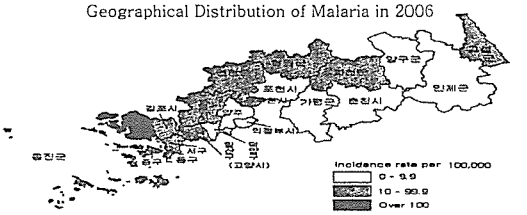
○ High-risk area
- more than 100 cases in 100,000 population

○ Risk area
- more than 10 cases in 100,000 population

○ Potential risk area
- less than 10 cases in 100,000 population

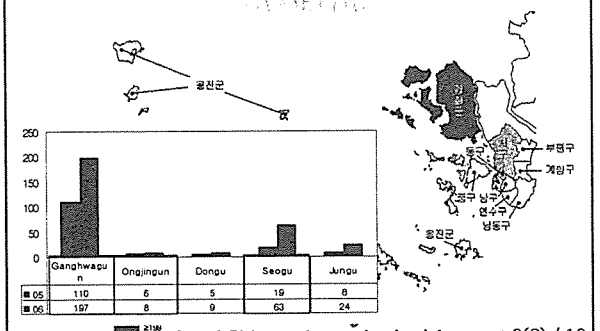


Geographical Distribution of Malaria in 2006



Geographical Distribution of Malaria in 2007

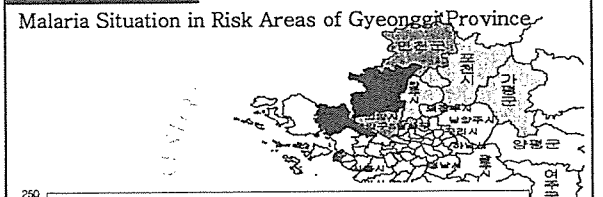
Malaria Situation in Risk Areas of Incheon



	Ganghwapu n	Ongjingun	Dongu	Seogu	Jungu
05	110	6	5	19	8
06	197	8	9	63	24

No. of Cities and counties in risk areas: 3(2) / 10

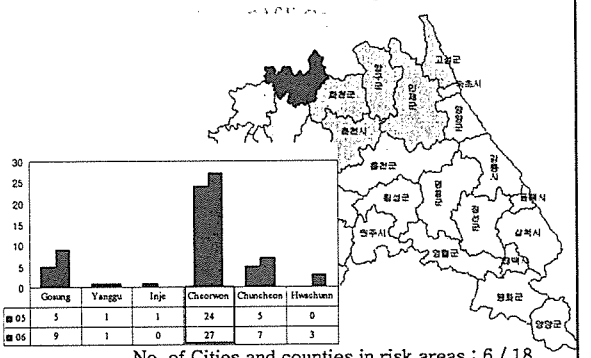
Malaria Situation in Risk Areas of Gyeonggi Province



	Gimpo	Yangju	Gapyung	Paju	Goyang Deogyan	Uijeongb u	Pocheon	Goyang Ilsan	Dongduc heon	Yeonche on
05	63	9	2	139	32	8	3	42	8	36
06	104	15	2	196	32	16	6	76	11	41

No. of Cities and counties in risk areas : 3 (7) / 12

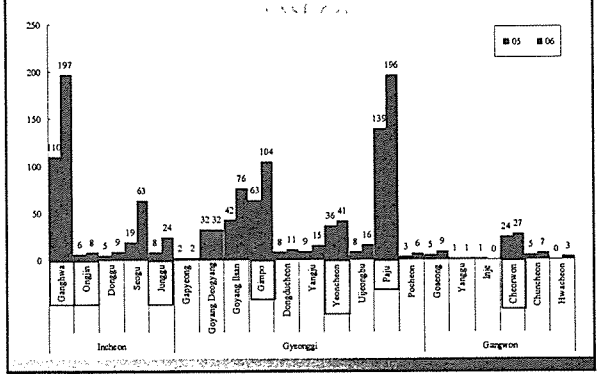
Malaria Situation in Risk Areas of Gangwon Province



	Goseng	Yanggu	Inje	Cheorwon	Chunchoen	Hwachunn
05	5	1	1	24	5	0
06	9	1	0	27	7	3

No. of Cities and counties in risk areas : 6 / 18

Year-on-Year Malaria Cases in Risk Areas



Malaria Cases among Kaesong Industrial Complex related Personnel

Year	2005	2006
No. of malaria cases / de jure population	11cases / 500 persons	18cases / 900 persons

Kaesong Industrial Complex in DPRK
2000 cases - 2200 cases/ 100,000 population
Ganghwa county in ROK
169 cases -298 cases / 100,000 population

Malaria Cases related to Mt.Kumkang Tour

Year	2005	2006
No. of malaria cases	3 cases	7 cases

Summary

1. Since its re-emergence in 1993, we have malaria incidence mostly in areas near the DMZ and gradual spread to neighboring areas.
   - 21 cities and counties in Incheon, Geonggi, Gangwon are designated as risk areas
2. Malaria incidence is high in western areas and low in eastern areas
3. Seoul Metropolitan area seems to function as a defensive shield against malaria, preventing its spread to areas south of the metropolitan area
4. Jjoint activities involving both ROK and DPRK are going on with a significant success.

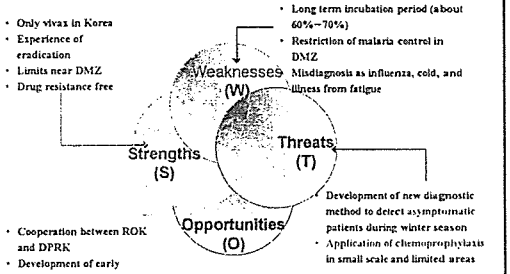
Malaria Researches

Researches on biological strategies against *Plasmodium vivax* in Republic of Korea

National Institute of Health
CDC, Republic of Korea

Malaria Researches

SWOT (Korean malaria)



Malaria Researches

Works on Malaria

Div. of Malaria and Parasitic Diseases, NIH(CDC)

Diagnosis | Control | Researches

- Confirm suspected malaria
  - Final institute to confirm
  - Provide acute and rapid diagnosis service
- Cooperation of diagnosis in public or private hospitals
  : Antibody detecting Method (IFAT and ELISA)

Early diagnosis and prevention of the long time latency patient by antibody detection

Biological strategies on Malaria and vector control
- Vaccine development
- Diagnostic Kit Development (Dip stick)
- Genetic diversity etc

Malaria Researches

Works on Malaria

Div. of Malaria and Parasitic Diseases

Diagnosis | Control | Researches

- Confirm suspected malaria
  - Final institute to confirm
  - Provide acute and rapid diagnosis service
- Cooperation of diagnosis in public or private hospitals
  : Antibody detecting Method (IFAT and ELISA)

Malaria Researches

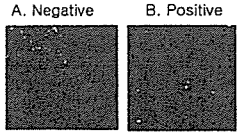
Antigen detection method

Microscopic examination | Polymeric chain reaction (PCR)

Antibody detection method

1) IFAT

A. Negative | B. Positive



2) Enzyme linked immunosorbent assay (ELISA)

1. Circumsporozotite protein (CSP) – Pv247, Pv210 detection
2. Merozoite surface protein (MSP) – Pv detection
3. Liver stage specific antigen (LSA) – Pf detection

Malaria Researches

Works on Malaria

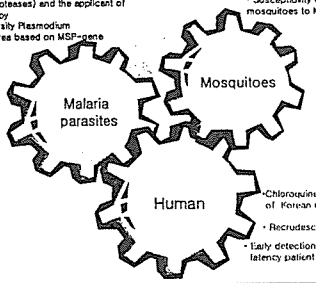
Div. of Malaria and Parasitic Diseases

Diagnosis | Control | Researches

- Biological strategies against *Plasmodium vivax* malaria and vector control in Korea
- Vaccine development
- Malaria Diagnostic Kit Development (Dip stick): Antigen Detection
- Genetic diversity

Strategies of Research

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



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

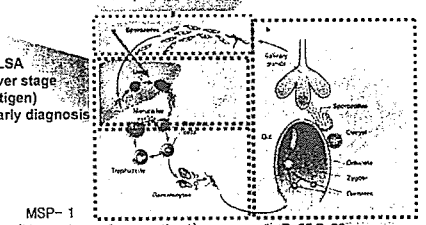
Direction of our Malaria Researches

Mosquito	Human
Anti-Transmission	Anti-Infection
-TBV (Transmission Blocking Vaccine) Development	-Predict and Prevention
	Hypnozoite → Long and Short Incubation period
	-Early diagnosis in the latent period
	Anti-Disease
	-More effective treatment -Monitoring of resistant -Gene diversity

On-going researches

CSP
(Circumsporozoite Protein)
: Dipstick Kit

PvLSA
(Liver stage antigen)
: Early diagnosis



MSP- 1
(Merozoite surface protien1)
:Gene diversity
: Diagnosis system

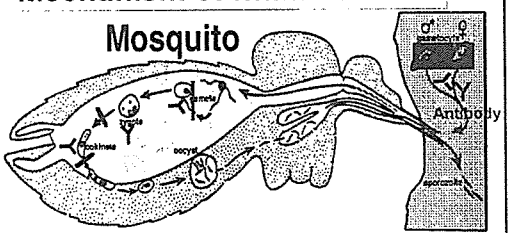
Pv25,Pv28
(Ookinete surface protein)
CDPK
(Calcium Dependent Protein Kinase)
: Transmission Blocking vaccine

Transmission Blocking Vaccine (TBV)

Characterization of Calcium Dependent Protein Kinase (Pv-CDPK) of *Plasmodium vivax*

Mechanism of malaria TBV

Mosquito



Possible outcome

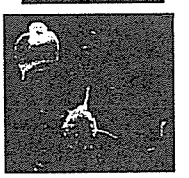
1) Regional elimination of malaria
2) Protect the spread of drug/vaccine resistant parasites

○ Calcium Dependent Protein Kinase (CDPK)....?

Gametogenes

CDPK Bind to Ca^{2+}
↓
Signal transmission of CDPK
↓
Signal enters in the body of Mosquitoes
↓
Stimulation of Xa in Mosquito
↓
Exflagellation in Macrogamete
↓
Microgamete bind with macrogamete
↓
Zygote formation

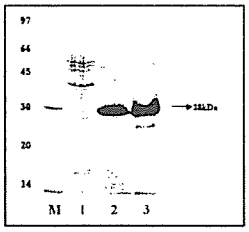
Exflagellation



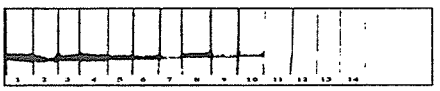
CDPK structure

×Xanthurenic acid(Xa) : a small mosquito molecule (Billker et al., 1998)

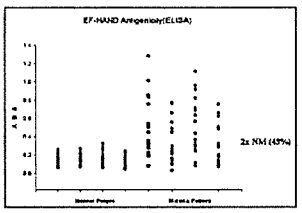
EF-region of CDPK from *P. vivax* was cloned expressed



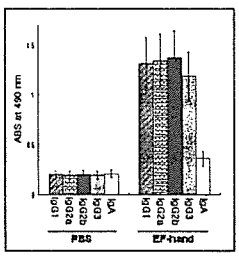
Expression and purification of the recombinant protein. Lane 1, non - induced *E. coli*; Lane 2, IPTG - induced *E. coli*; Lane 3, purified thioredoxin fusion EF - hand protein. The expression of the cloned EF - hand gene was induced by adding IPTG to a final concentration of 0.5 mM and analyzed on SDS - PAGE followed by Coomassie blue staining. The recombinant protein was clearly detected when the cells were lysed under denaturing condition. The size of expression protein was approximately 28 kDa which corresponded with the predicted molecular weight the protein by DNASIS.



Western blot analysis of the expressed protein with patient serum infected with malaria. Lane1 - 10, sera of malaria patient; Lane 11 - 14, Normal sera.

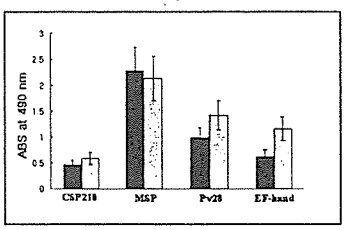


Scattergram group of absorbance by ELISA using EF-HAND recombinant protein. The serum of Normal People and Malaria Patients : used in ELISA which were confirmed as malaria patients under microscopic examination with blood smears.



Analysis of IgG levels in the polyclonal serum with rEF-Hand by ELISA. Total IgG and each subclass IgG levels were analyzed. rEF-hand, polyclonal antibody; PBS, serum from Balb/c infected with PBS.

Analysis of expression antigen in lately infected malaria patient

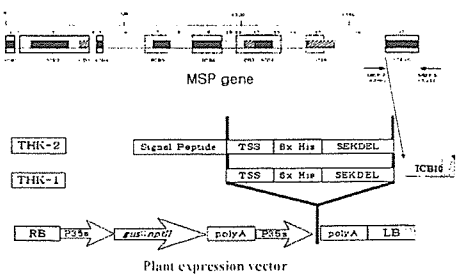


CSP210 is expressed in circumsporozoite, MSP is expressed in merozoite, Pv28 is expressed in gametocyte, and EF-hand is expressed in gametocyte. Black square is used IgM secondary antibody. Gray square is used IgG secondary antibody.

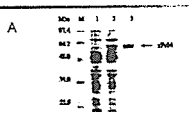
Edible vaccine trial

Transgenic plant (Edible vaccine trial)

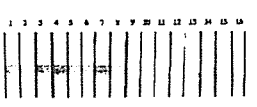
Merozoite Surface Protein gene (ICB10 region)



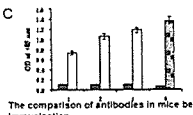
Transgenic plant (edible vaccine trial)



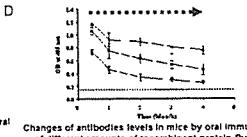
Purification of the expressed recombinant protein Pv20054. Lane M, Protein size marker; Lane 1, uninduced E.coli; Lane 2, IPTG-induced *E. coli*; Lane 3, purified recombinant protein Pv20054.



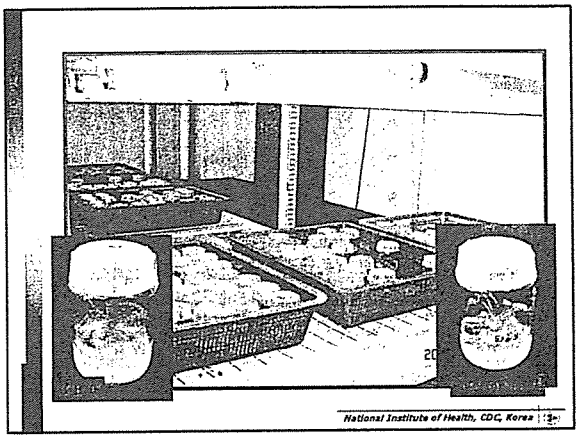
Western blot analysis if the recombinant Pv20054 with sera of *P. vivax* patients and normal human.



The comparison of antibodies in mice between oral immunization and interperitoneal immunization by ELISA using recombinant protein Pv20054.
1: oral immunization with 200㎍ of Pv20054
2: oral immunization with 400㎍ of Pv20054
3: oral immunization with 800㎍ of Pv20054
4: parenteral immunization with 200㎍ Pv20054
Black bar: oral immunization with PBS
Hatch bar: parenteral immunization with PBS

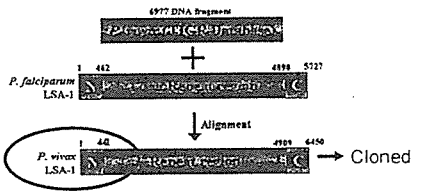


Changes of antibodies levels in mice by oral immunization of different amounts of recombinant protein Pv20054.
: oral immunization with 200㎍ of recombinant protein Pv20054.
: oral immunization with 400㎍ of recombinant protein Pv20054.
: oral immunization with 800㎍ of recombinant protein Pv20054.



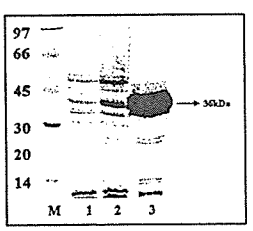
Liver stage antigen 1 (Pv-LSA1) of vivax malaria in Korea

Cloning of *P. vivax* LSA-1 gene



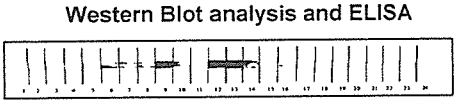
Diagrammatic representation of the construction of *P. vivax* LSA1. Numbers are given to denote N - terminal, repeat, and C - terminal regions in the DNA. All DNAs are based on the LSA - 1 (P. falciparum: NF54, P. vivax: TIGR database) sequence in GenBank.

Expression of recombinant LSA-1 protein

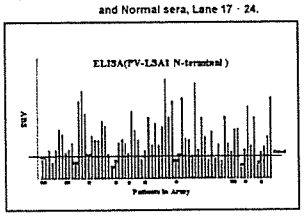


Lane 1, non - induced *E. coli*; Lane 2, IPTG - induced *E. coli*; Lane 3, purified Pv - LSA1(N) protein. The size of expression protein was approximately 36 kDa which corresponded with the predicted molecular weight the protein by DNASIS.

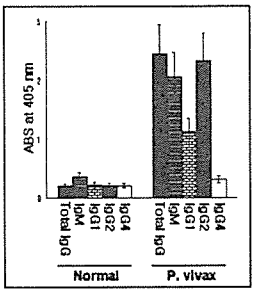
Western Blot analysis and ELISA



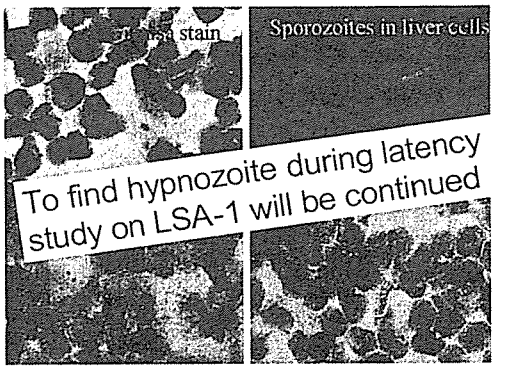
Western blot analysis of the expressed protein with serum of human malaria patient, Lane 1 - 16 and Normal sera, Lane 17 - 24.



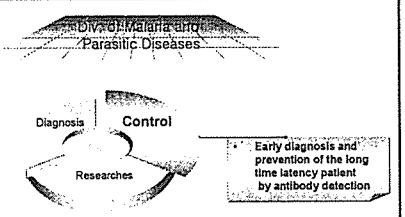
Scattergram group of absorbance by ELISA using Pv - LSA1 (N - terminal) recombinant protein. The serum of Army malaria patients: used in ELISA which were confirmed using IFAT (upper number is IFAT data, bottom square is CSP ELISA data).



Analysis of IgG levels in the malaria patient sera with rPv-LSA(N) by ELISA. Total IgG and each subclass IgG levels were analyzed. *P. vivax*, malaria patient sera; Normal, Normal persons sera.



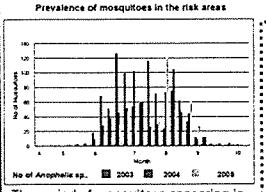
Works on Malaria



The points to control vivax malaria in Korean

- Korean vivax malaria (*P. vivax*) was characterized by its extraordinarily prolonged period in certain circumstance (Shute et al., 1977)
- Vivax malaria in Korea shows clear seasonality because there are 4 clear seasons Spring-Summer-Autumn- Winter) in Korea and mosquitoes hibernate during winter time, indicating that no transmission in winter
- Many infections acquired in summer and autumn do not become patent until the following spring
- CSP antigen is a useful tool to know the exposure to mosquitoes

Prevalence of mosquitoes in the risk areas



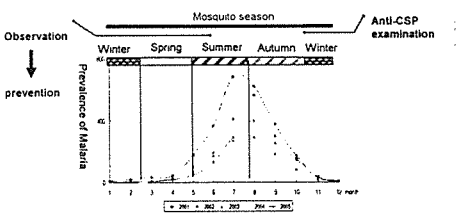
The period of mosquitoes appearing is getting longer

Incubation period

- In the previous study, around 70% of malaria patient had a long latency in Korea (Tiburskaja and Vullevskaja,1977)
- In our recent study (Nishiura et al., 2006),
  - Mean short -term incubation : 26.6days
  - Mean long -term incubation : 48.2 weeks (maximum period was 90 weeks)
- Incubation time is the important factor for control of malaria prevalence
- Regards with prevention of malaria, winter season is good chance to control malaria

Project on anti-CSP antibody examination to find long-latency patient

1. Purposes
   - To find the patient exposed to malaria infected mosquitoes and might have malaria
   - To prevent malaria prevalence in advance
2. Materials : Blood from the residence living in high risk area, around 40,000
3. Method:
   - Blood collection from November to February
   - ELISA based on CSP and PCR
   - Observation the people who become patient until June



Thanks for kind attention!!!!

T d

Dynamic Korea

Antimalarial drug response of *Plasmodium vivax* in ROK

Department of Laboratory Medicine,

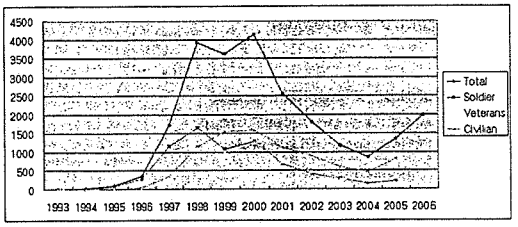
College of Medicine, Korea University Ansan Hospital

Chae Seung Lim

Introduction

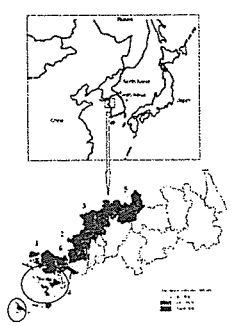
Malaria in Korea

- Hakjil, Haruguli - ancient term in Korea
- *Plasmodium vivax* accounts for 100% of indigenous malaria cases in ROK
- Indigenous Malaria status in Korea
  - 1960th 1,500-2,000 cases per year
  - In 1984, last report in Korea
- Resurgent malaria in Korea
  - In 1993, 1 case and gradually increased
  - In 2000, 4142 cases (1960th level)
  - In 2005, 1336 cases



- Increased period 93 – 00
- Decreased period 01– 04
- 2005 increase again (56%)
  - •Civilian 74%
  - •Solder 45%
  - •Veterans 31%

Classification of malaria risky region in ROK (2006)



Category 1
- 1 region
- 100 > cases / 100,000 resident

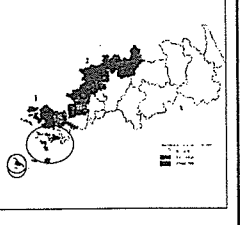
Category 2
- 5 region
- 10 to 99 cases/100,000 resident

Category 3
- 12 region
- less than 10 cases/100,000 resident

2006 Malaria RiskyRegion

Category	Region	Incidence rate *	Category	Region	Incidence rate *
			3	HwaCheon	6.39
	CheolWon	43.45		GoYoung	3.62
	KimPo	29.19		GoYang 1	7.79
2	YeonCheon	65.91		GoYang 2	8.24
	Paju	53.05		DongDooCheon	7.24
	Ongjin	39.30		Yangju	5.50
	Incheon Joong	10.83		Pyeongtaek	2.24
	GoSung	-		PoChoen	1.35
	YangGoo	-		InCheon Dong	6.35
3	Inje	3.05		InCheon Seo	5.05
	ChoonCheon	1.55			

* Malaria incidence per 100,000 resident without soldiers



- **Chloroquine 1500 mg base in 3day**
  - **Day 0 - 600mg**
  - **8hr 300mg**
  - **8hr 300mg**
  - **8hr 300mg**
- **Followed by primaquine**

  15 mg x 14day

Summary of reports of relapse of *Plasmodium vivax* after treatment with a standard regimen

Year	Treatment	No of Patients	Duration of follow up	% of Relapse
1952*	None	1021	>4mo	32 %
1952**	CQ only	355	24 mo	39%
1952**	CQ+PQ14d	914	4-20 mo	0 %
1952**	CQ+PQ14d	348	2 year	0%
1999***	CQ+PQ14d	81	2 year	1.4%

* Exposure cases in Korean War, Baird 2004 review
** US Army patients cases during Korean war, Alving 1953
*** Resurgent Korean P.vivax cases in 1997, Lim 1999

Current Problems

- Increase of Relapse cases
  - About 40 cases recent 3 years
  - D/Dx Relapse or reinfection
  - Primaquine failure
- Malaria risky region expand to city limit
  - Pajoo to Ilsan
  - Kimpo to Incheon
- Increase of total cases again after 2005

Objectives

- To evaluates current
  - after 2000
  - Chloroquine response
  - Primaquine response
    - Relapse rate (%) of Korean P.vivax

Material and Method

- Subject
  - Group I
  - Malaria patients after 2000
    - Hospitalized in Korea University Medical center
    - Pajoo medical center
    - 92 cases
  - CQ+PQ14d standard therapy
  - Followed 6 month
  - Measured G6PD level

Group II

- Malaria patients after 2000
  - 689 patient
  - In six risky area
- Epidemiolgic data analysis
  - Face to face Patients interview in bed side
  - Suspicious case - interview again by Phone call
    - Chloroquine failure- within 28 day
    - Primaquine failure – follow up to two years

Result

Baseline data

Treatment group	Group I (n=92)	Group II (n=589)
Sex (male/female)	148/58	394/195
Mean age in years (SD)	28.6(12.1)	54.2(17.9)
Patients with G6PD def. (IU/ 10^{12} RBC)	None (n=63) (164.5 ± 128.9)	

Group I Korea university medical center cases
Group II All collected cases in risky area

Therapeutic responses of Chloroquine

Treatment group	Group I (n=92)	Group II (n=689)
No. of patients completing with 28 days follow-up	92	689
Cure rate at 28 days (%)	100	100
Failure rate during 28 days (%)	0	0

Group I Korea university medical center cases
Group II All collected cases in risky area

Efficacy of primaquine regimens for *P. vivax* in Korea (Group I)

Treatment group	Group I (n=92)
No. of pts	92
Total reapearence	0
Relapse (%)	0

Group I Korea university medical center cases
Follow-up by Phone
* < 6 month

Group II result

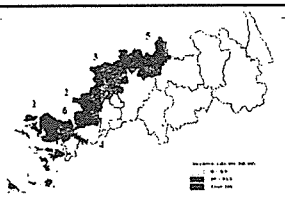
	2003	Relapse 2004	2004	Relapse 2005	2005	Relapse 2006	Total
GangHwa			76	13	120	13	196
Pajoo	116	6	89	6	133	7	338
GoYang			48	3			48
YeonCheon			24	2			24
Cheolwon	23	0	13	0			36
Kimpo			47	1			47
Total	139		297		253		689

Efficacy of primaquine regimens for *P. vivax* in Korea (Group II)

Treatment group	≤6 month	≤ 12 month	≤ 2 year
No. of pts	454	454	192
Total reapearence	3	17	20
Relapse (%)	0.7	3.8	10.4

Group II All collected cases in risky area

Relapse rate
Vs
Incidence rate



Region	Incidence rate per100,000 residents(2005)	Relapse ≤ 6mo(%)	Relapse ≤ 12mo(%)	Relapse ≤ 2 year (%)
1 GangHwa	168.2	2.6	9.2	14.5
3 Yoncheon	65.9	0	0	
5 CheolWon	29.2	0	0	
6 KimPo	48.5	0.9	1.8	
Total		0.6	3.9	10.4

Mean Relapse time vs Incidence rate of Geographic region

Region	Incidence rate per100,000 residents(2005)	Total Relapse No	Mean relapse month
1 GangHwa	168.2	13	15.1
	53.1	13	22.8
3 Yoncheon	65.9	2	44
	7.78	3	47
5 CheolWon	29.2	0	-
6 KimPo	48.5	2	11
Total		33	17.4

Comparison of relapse rate after standard primaquine therapy

Type of therapy, geographic location	Year	No. of patients	Duration of follow-up, months	Percentage of patients with relapse	References[s]
Supervised					
Vietnam	1974	218	12	4	Kaplan 1974
Thailand	1994	141	1–18	18	Bunnag 1994
Solomon Islands	1977	10	12	0	Saint Yves 1977
Korea	1953	914	4–20	<1	Alving 1953
Korea	1999	81	24	1.4	Lim 1999
Nicaragua	1953	115	4	0	Theiler 1953
Central America	1974	57	9–36	4	Miller 1974
Unsupervised					
Vietnam	1970	251	12	18	Fisher 1970
Brazil	1991	1347	3–12	25	Boulos 1991
Somalia	1997	60	NR	43	Snoeck 1997
Global	1995	57	>18	13	Jelinek 1995
Global	1987	175	NR	10	Ohtomo 1987
Global	1990	122	NR	9	Tenebe 1990
Korea	2000	192	24	10.4	This study
	2003	454	12	3.8	

NOTE. Mo, months; NR, not reported.

Summary

- Chloroquine response of P.vivax of ROK
  - ~ Respond well
- Relapse rate of vivax malaria after primaquine in ROK
  - ~ 0.6% ≤ 6 month
  - ~ 3.9% ≤ 12 month
  - ~ 10.4% ≤ 2 year
  - Increasing tendency compared to previous report and similar to global report
  - Higher dose of primaquine
    - Suggested only relapsed case

Thank You

Chloroquine Resistance in Plasmodium vivax (CRPV)

in Langkat District, North Sumatera, Indonesia

by
Nurfida KA*, Lambok S*, Umar Z**

*Parasitology Department, Medical Faculty, University of North Sumatera
**Internal Medicine Department, Medical Faculty, University of North Sumatera

1

Introduction

- *P. vivax* causes a clinical benign illness but relapses frequently
- Chloroquine has been the first-line therapy for vivax malaria since 1946
- Emerging resistance to chloroquine by *Plasmodium vivax* threatens the health of hundred millions people routinely exposed to the risk of infection with these parasites

2

Background

- Resistance to chloroquine by *P. vivax* was first confirmed among Australians repatriated from Papua New Guinea
- Followed by several countries including Indonesia
- In 4 Subdistricts October 2002 : 154 cases
  December 2002 : 149 cases
- During October – December 2002 showed that management of vivax malaria in Tanjung Pura Subdistrict not properly controlled the cases
- Chloroquine resistance ???????

3

Main Objectives

- To find Chloroquine-Resistant Plasmodium Vivax (CRPV)
- Socialize malaria and bad effect of CRPV

4

Study Area

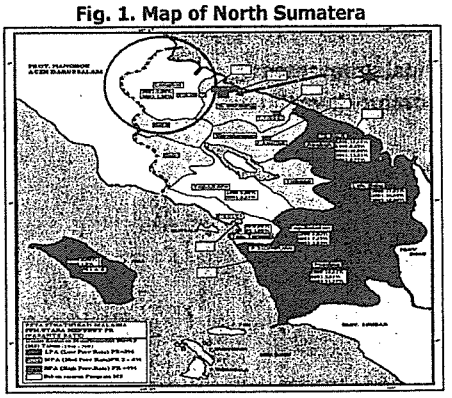
- Several villages in Tanjung Pura Subdistrict, Langkat District, North Sumatera, Indonesia
- The study was conducted from March to July 2004

Study Design

Monitoring of antimalarial drug efficacy

5

Fig. 1. Map of North Sumatera



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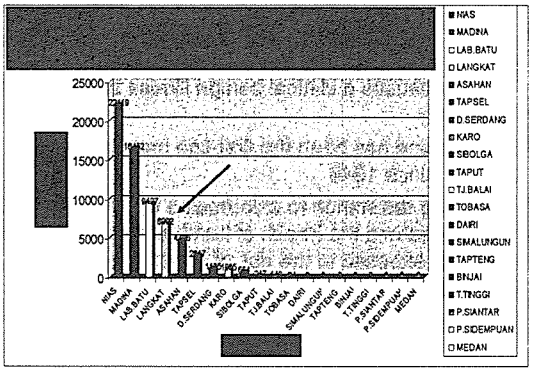

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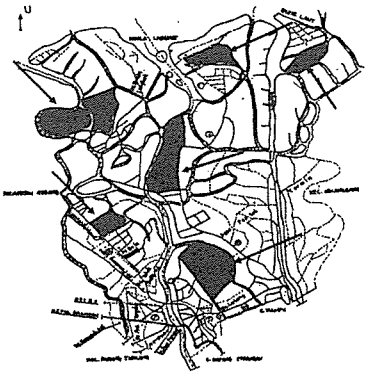


8

Methods

Inclusion Criteria

- Age > 1 year
- P vivax monoinfection in blood smears
- History of fever during 48 hours prior to time of recruitment
- Willingness to give Informed consent

9

Exclusion Criteria

- Taking antimalarial drug during the two weeks period prior to admission
- Urine was positive by screening test Dill-Glazko
- Pregnant or breast-feeding
- Sign and symptoms of severe malaria
- The presence of any other severe underlying diseases
- History of drug hypersensitivity

10

Diagnosis was confirmed by

- **Clinical assessment**
- **Laboratory Investigation**

Treatment :

- **Chloroquine**
- **Primaquine**

11

Table 1.
Treatment of Vivax Malaria

Day	Drug	Number of tablet based on age group				
		<1 years	1-4 years	5-9 years	10-14years	>15 years
1	Chlor	½	1	2	3	3-4
	Prim	-	¼	½	¾	1
2	Chlor	½	1	2	3	3-4
	Prim	-	¼	½	¾	1
3	Chlor	¼	½	1	1 ½	2
	Prim	-	¼	½	¾	1
4 - 14	Prim	-	¼	½	¾	1

Dosages based on body weight for Plasmodium vivax :
- Chloroquine : day I & II = 10 mg/kgBW/day III = 5 mg/kg BW
- Primaquine : 0.25 mg/kgBW /day for 14 days.

12

Therapy for Treatment Failure

Alternative therapy established for *P. vivax* treatment failure

- Re-treatment with chloroquine and primaquine combination as from Day 0
- Quinine according to conditions
- Amodiaquine

13

Table 2.
Treatment of malaria vivax (Chloroquine resistant)

Day	Name of drug	Number of tablet based on age group					
		0–1 month	2-11 months	1 - 4 months	5 - 9 years	10–14 years	≥ 15 years
1 - 7	Quinine	*)	*)	3 x ½	3 x 1	3 x 1 ½	3 x 2
1 - 14	Primaquine	-	-	¼	½	¾	1

Dose based on body weight : - Quinine30 mg/kgBW/day (divided into 3 doses)

- Primaquine 0,25 mg/kgBW.

14

Classification of Treatment Outcomes

- **Early Treatment Failure (ETF)**
- **Late Clinical Failure (LCF)**
- **Late Parasitological Failure (LPF)**
- **Adequate Clinical and Parasitological Response (ACPR)**

15

Result

350 persons

- Clinical Assesment
- Blood smear

28 P. falc
2 Mix
282 Negatif

32 persons P.vivax

Exclusion
- Dill-Glazko test positive
- Breast feeding

30 persons

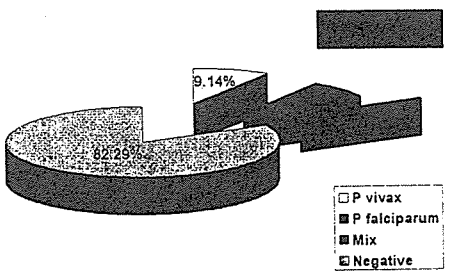
16

Table 3. Distribution of Malaria Infection

No	Village	Blood Sample (%)			
		P.vivax	P.falc	Mix	Total
1	Tapak Kuda	5.71	3.71	0	9.42
2	Bubun	2	1.43	0.29	3.72
3	P Cengal	0.86	0.57	0	1.43
4	Pekubuan	0	0.86	0	0.86
5	P Banyak	0	0.86	0.29	1.15
6	K Serapuh	0.57	0.57	0	1.14
		9.14	8	0.58	17.72

17

Fig. 6. Distribution of Malaria Infection



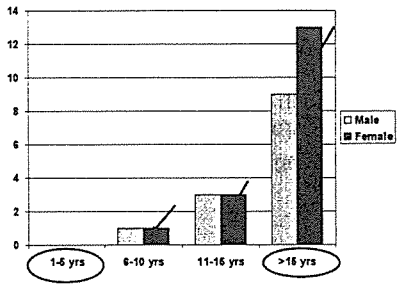
18

Table 4.
Distribution of Vivax Malaria Infection

Age (yrs)	Gender		Total (%)
	Male	Female	
1-5	0	0	0
6-10	3.33	3.33	6.7
11-15	10	10	20
> 15	30	43.3	73.3
Total (%)	43.33	56.67	100

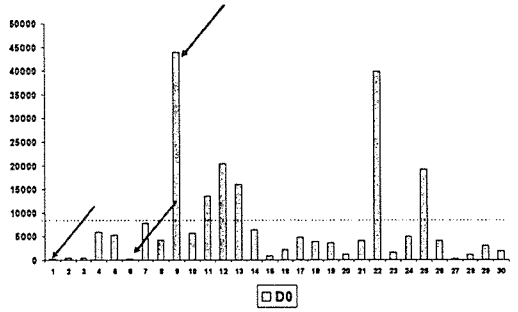
19

Fig. 7.
Distribution of Vivax Malaria Infection



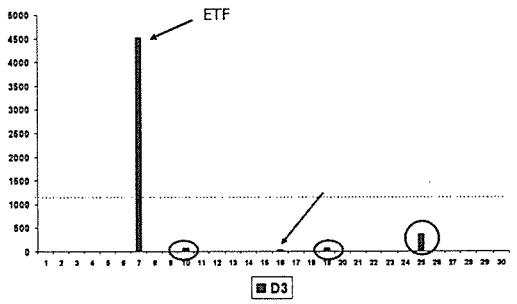
20

Fig. 8. Parasite Density on D0



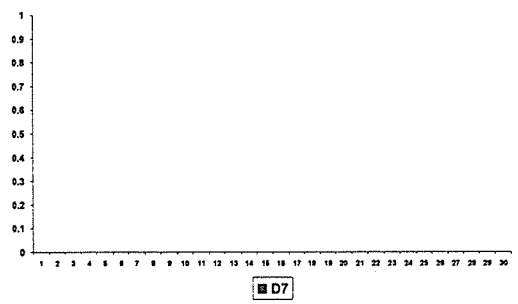
21

Fig. 8a. Parasite Density on D3



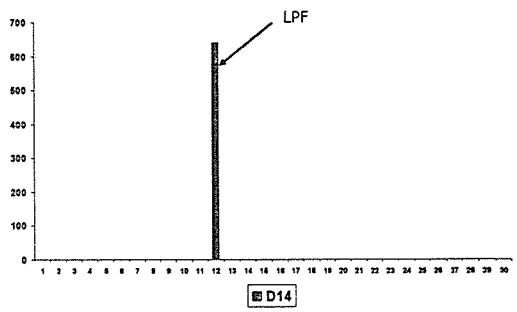
22

Fig. 8b. Parasite Density on D7



23

Fig. 8c. Parasite Density on D14



24