

| 00.19            | IOV IO         | ocai sirains                                 | 1011FV (5011                  | nboon et al 1                                    |
|------------------|----------------|--|-------------------------------|--|
| Anopheles        | Carrier<br>110 | No. positive<br>with oveyst/no.<br>dissected | Mean no. of<br>oneyst (range) | Na: positive with<br>sporozaite/No.<br>dissected |
| Vagus            | PVI            | 5/5  | 6.6 (3-11)                    | J/B  |
| Kuchi            | PATE           | 100  | 4740(47)                      | NA   |
|                  | PV2            | 5/6  | 59.8 (2-135)                  | 2/3  |
| Annularis (Nepal | PV1            | UU   | 9.3 (2-30)                    | NA   |
| & Myanmari       | HV2            | 3/3  | 45.0 (21:65)                  | 517  |
| Minimus A        | 07/0           | 2/3  | 10.0 (9:11)                   | 1/0 .  |
|                  | 10/02          | 22   | 32:(1 (25:39))                | 385  |
| Sawadwangparni   | PVI            | + (A)  | 12(12)                        | 2/2  |
| Willmori (Nepal) | PVII           | 172  | 5(5)                          | 0/1  |
| Sinensis (China) | PV2            | :56  | 28.2 (1-101)                  | 8/13 .   |
| Barbirostotris   | PMI            | (r)  | 7(0)                          | NA   |
| (Indonesia)      | TIME           | 405  | (12-3)(5-522)                 | 285  |



Potential of An. barbirostris/campestris group

A two-year entomological study in Sa Kaeo Thailand (1998–1999) showed that a decrease in the abundance of *An dirus*, the main *Pf* vector, was accompanied by a concurrent increase in the abundance of members of the barbirostris/campestris group.

Might be important secondary vectors High fecundity = 173 - 311 eggs /female High indoor / outdoor biting = 9 / 4 bites/p-h High anthropophily = 78.6% (human); 7.1% (cow) Susceptibility to only P. vivax

Ref Apiwathnasorn et al 2002: J Med Ent 39: 583-586



#### Research gaps

Information required for strategic planning of control programs:
† Where does malaria transmission occur?
† When does malaria transmission occur (seasonal or year-round transmission)?
† What species of Plasmodium is the causative agent for malaria?
† What is the prevalence of Plasmodium vivax (VK210/247)?
† Who is the population at risk?
† What is the interaction between P vivax and vectors?
† Which mosquito species is the main vector(s) of malaria transmission?
† What is the insecticide sensitivity status of the malaria vector(s)?
† What is the distribution, ecology and human-vector contact of sibling species of Ap group in Solomon Is, Vanuatu, Irian Jaya and Moluccas?
† What is the role of minimus C in malaria transmission?
† What is the role of secondary vectors in changing or modified environments, eg deforestation

# Malaria Control in China 中国疟疾控制 Division of Schistosomiasis Prevention and Management Department of Disease Control Ministry of Health P. R. China 卫生部疾病预防控制局血防处

#### Contents 主要内容

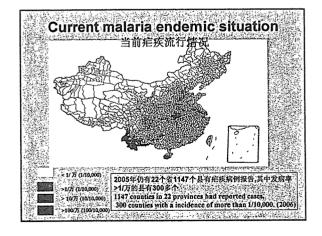
- e Historical Epidemic Situation历史流行情况
- Current Malaria Endemic Situation当前疟疾 流行形势
- Recent national control activities and Plans 国家疟疾防治规划

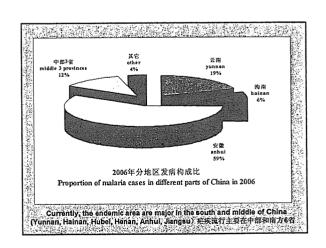
#### Historical Epidemic Situation 》 历史流行情况

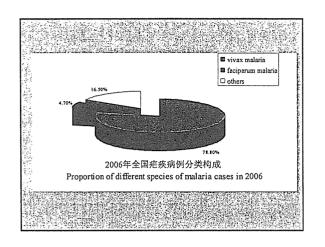
- e in 1940's, more than 30 million people were infected by malaria. The mortality rate is 1% for each year, 20世纪40年代, 我国每年至少有3000万以上患者。病死率约为1%
- In early 1950's , there were 1829 endemic counties in China, accounting for 80% of the total counties. 20世纪50年代初期,全 国有1829个县疟疾流行的。约占全国总县数的80%。
- in 1960's and 1970's, two malaria pandemics occurred in the central part of China (plains of Yellow river and Hualhe river). The number of infected people reached 17 million and 21 million respectively, 20世纪六十和七十年代,黄河和淮河平原曾经 两次发生疟疾大流行;发病人数分别高达1700万和2100万。

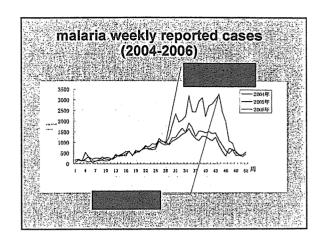
## Three stages of malaria control in China 中国疟疾控制的3个阶段。

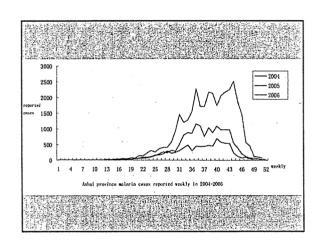
- 1950's Base-line investigation. To investigate the endemic degree, endemic area, character of vectors, carry out pilot study for the control activities.调查摸底阶段:摸清流行程度、范
- Study for the Common Study for the Study f to different vectors and prevalence in different period.全面开
- uniterent vectors and prevalence in different period.
  展疟疾的治阶段:各地因地闭直地采取综合性防治措施。
  After 1990's Surveillance:监测阶段:
  South provinces; continue implement materia control, programme 相力各合维铁强化症疾防治。
  Other provinces; strengthen surveillance 非任合转入监测

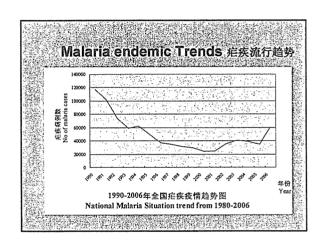












### Current malaria endemic situation(2) 当前疟疾形势

Reasons for the increase 疟疾回升的主要原因 ·National infection diseased reporting system have been strengthened国家疫情报告系统的加强 ·Malaria imported cases increased by people's migration (especially along the bordering areas of Yunnan province)流动人口疟疾问题 •Malaria reemerging in the central part of Anhul and Henan provinces 中部以安徽为重点的沿 淮河流域疟疾回升

#### Main Problems (1) 存在的主要问题

- Poor access to accurate diagnosis and appropriate treatment 不能获得正确的诊断和治疗。

  - Pone-third of the township hospitals in malaria endemic areas,
     cannot perform blood examination 1/3的乡領卫生隊不修开展直位
     No more than 10% of patients receive prompt idagnosis and propertreatment at village clinics 在月上生皮状段及时诊断和正确治疗的病人不到10%
- 2. Low coverage of anti-relapse and pre-transmission season treatment 休止期治疗覆益率低
- 3. Drug resistance 耐药性......
- → Paiciparum malaria exhibit resistance to a broad range of antimalarials including chloroquine, amodiaquine, piperaquine and pyrimethamine. 恶性症対限多名物財苗

#### Main Problems (2) 存在的主要问题

- 4. Low coverage of vector control measures 控制媒介措施覆盖率很低
  - → Bednets ownership: about 50% 蚊帐覆盖串在50%左右
  - → ITN ownership: below 5% 药没文章覆盖率低于5%
- Weak surveillance and inadequate capacity for outbreak response 监测和应急处理能力弱
  - → Less than 5% of outbreaks are properly controlled within 2 weeks of onset 暴发疫情在2周内及时处理率不到5%
- 6. Low malaria awareness 疟疾知识知晓率低
  - → Awareness related malaria in residents: only 16%; 居民知识 知晓率只有16%
  - → Awareness related malaria in students: 36% 学生知识知晓率 36%

#### National Malaria Control Plan (NMCP) 国家疟疾控制规划

The National Malaria Control Plan (2006-2015) " started in 2006 (2006-2015年全国在疾防治规划》于2006年开始实施 Goal: by 2015

Control malaria in Yunnan Province (incidence <0.1/1000) Eliminate falciparum malaria in Hainan province (incidence <0.01/1000)

Eliminate malaria in other areas of China

日标: 到2015年

云南省控制疟疾流行(发病率<0.1/1000) 海南省消除恶性疟(发病率<0.01/1000) 全国其它地区基本消除疟疾

#### Strategy 控制策略

- People in remote areas have better access to malaria preventive measures. 使边远地区居民得到更有效的疟疾预防措施
  - → Free provision of LLIN (long-lasting bednets)免费提供长效药物浸泡蚊帐
     →ITNs (retreatment for existing conventional nets) 现有蚊帐免费药物浸泡

#### Strategy 控制策略

- People in remote areas have better access to timely diagnosis and appropriate treatment in the public and private sectors. 使边远地区居民得到及时诊断与规范治疗
  - →Strengthen microscopy system in township hospitals 加强乡镇卫生院显微镜镜检
  - →Free provision of RDTs in remote P.f endemic areas 在偏远恶性疟流行区提供快速诊断试纸条
  - ⇒Provision of appropriate anti-malarials treatment 提供免费抗疟药进行规范治疗

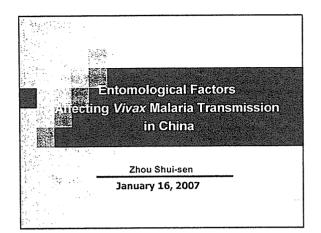
#### Strategy 控制策略

- Strengthen malaria surveillance and epidemic preparedness and response 加强疟疾监测,提高暴发流行应急反应能力
  - →Strengthen surveillance and routine case reporting 加强疟疾监测和疾病报告
  - →Provide equipment, RDTs and insecticide for outbreak control 加强暴发流行应急反应处理能力
  - →Strengthen border checks and improve cooperation with neighboring countries 加强 毗邻国家的合作交流

#### Strategy 控制策略

- Increase community awareness and demands for effective malaria treatment and prevention. 提高社区居民有效预防和治疗疟疾的意识和需求
  - →Develop IEC/BCC methodologies and materials 根据不同对象设计开发健康教育材料
  - →Implement IEC/BCC activities through a broad range of players 针对不同人群,通过各种渠道、多部门参与进行健康教育





#### Vivax malaria in China

Plasmodium vivax is the predominant species in China, all the malaria areas have vivax transmission. Only Yunnan and Hainan provinces have falciparum malaria transmission locally, even in these two provinces the proportion of vivax malaria is also up to 80%.

#### Vivax malaria in China

In recent years the re-emergence and epidemic of vivax malaria is the crucial problem in China especially in central provinces. The reasons of malaria coming- back are complicated, besides the existence of Plasmodium vivax with long incubation period, vectors play very important roles in malaria transmission.

## Main vectors transmitting *vivax* malaria in China

Currently 4 species of mosquitoes are the major transmitting vectors in China, they are:

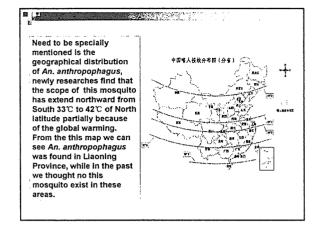
- ---Anopheles sinensis
- ---Anopheles anthropophagus (lesteri)
- ---Anopheles minimus
- ---Anopheles dirus

## Geographical distribution of different vectors in China

■ Generally An. anthropophagus and An. sinensis are the major transmitting vectors in the central provinces, while An. minimus and An. dirus are key malaria vectors in Yunnan and Hainan provinces.

## Geographical distribution of different vectors in China

- An. sinensis extensively distribute in the country except for a few provinces such as Xinjiang Autonomous Region and Qinghai Province.
- An. minimus mainly distribute in Southern parts of 33°C North latitude, especial in parts of 25°C North latitude, it is the major vector in Southern provinces.
- An. dirus limitedly distribute in hilly and forest areas in Hainan and Yunnan Provinces.



#### Feeding and resting behavior

- It has been found that An.sinensis can rest in both animal sheds and human house. Regarding feeding and resting behaviour, it seems that An.sinensis is neither a typical exophagic and exophilic nor typical endophagic and endophilic malaria vector.
- Indoor and outdoor human biting rate of An.sinensis is about equal in China.

#### Feeding and resting behavior

- The endophilic and anthropophilic habits of An. anthropophagus are very typical in the past, but latest findings showed that the resting behaviors of An. anthropophagus in different areas are distinctly different. In the Southern and central parts they are endophilic, while in the Western and North parts they are exophilic.
- The human blood index is up to 0.677~0.892 in Southern and central parts while only 0.125 in the North provinces (such as Liaoning).

## Feeding and resting behavior

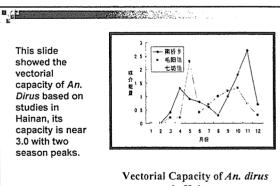
An.minimus is considered to be highly anthropophilic. From this map we can see the proportion of biting human is much higher than that of biting cattle, but in recent years it was found that the proportion of biting cattle increased.



An. dirus is also anthropophilic but typical exophagic, it normally be found in stone holes and small forest.

#### Vectorial capacity

■ It has been proven that the vectorial capacity of An. anthropophagus is 11-20 times higher than that of An. sinensis. Need to be mentioned, although the vectorial capacity of An. sinensis is relatively low, they still play an important roles in recent re-emergence of vivax malaria in central provinces because of its big population.



#### 

#### Entomological factors affecting vivax malaria transmission

- Different malaria vectors distributing in the similar areas made vector control measures more difficult and less effective.
- a An. sinensis is still a very important vector transmitting vivax malaria in central provinces because of its extensive distribution and big population. In recent years according to annual reporting system, most of malaria cases are found in areas where An. sinensis is only vector.

## Entomological factors affecting vivax

malaria transmission

■ Change of ecological environment and global warming made northward spread of An. anthropophagus, the density of the vector mosquito increased obviously and the mosquito was found in many new areas (such as Liaoning, Shandong), which posed higher risk for malaria transmission and epidemic.

#### Entomological factors affecting vivax malaria transmission

■ Genetic variation of mosquitoes made malaria vector more complicated. Studies have confirmed that a particular malaria vector is not a single species but a complex or group with different biological characters and behaviors. For example:

#### Entomological factors affecting vivax malaria transmission

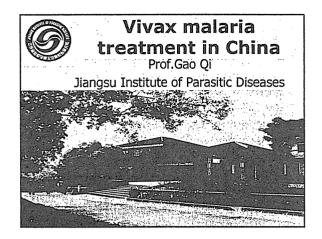
- Molecular biology researches have found that An. ninimus is a complex consists of sibling species A and C in China, and their importance and differentiations in malaria transmission need further studies.
- An. dirus was also found different supspecies including species A, B,C, D.

#### Entomological factors affecting vivax malaria transmission

- Changes in feeding and resting behavior make some measures such as indoor residual spray less effective in some areas.
- Although no enough evidence showed resistance of malaria vectors to existing insecticides, small scale investigation found An. sinensis exist resistant to permithrin.



Thank you for your attention





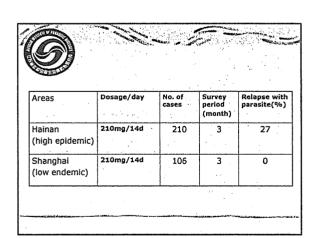
## 1. The operational test for vivax malaria treatment...

There were many operational tests for vivax malaria treatment with C/P carried out during 1970's and 1980's and different dosages of Primaquine were tested at that time.

| Areas    | Dosage/day  | No. of<br>cases | Survey.<br>period<br>(month) | Clinical<br>relapse |     | Relapse with parasite |     |
|----------|-------------|-----------------|------------------------------|---------------------|-----|-----------------------|-----|
|          |             | 11              |                              | cases               | %   | No. of                | %   |
| Shanghai | 210mg/14d   | 58              | 9                            | 0                   | . 0 | 0                     | 0   |
| Shanghai | 157.75mg/7d | 31              | 8                            | 0                   | 0   | 0                     | 0   |
| Shanghai | 112.5 mg/5d | 39              | 8                            | 0                   | 0   | 1                     | 3   |
| Shanghai | 105mg/7d    | 38              | 8                            | . 0                 | 0   | 0                     | 0   |
| Shanghai | 90mg/3d     | . 15            | 8                            | 1                   | 7., | 1                     | 7   |
| Shanghai | 75mg/5d     | 8               | 8                            | 1                   | 13  | 1                     | 13  |
| Hainan   | 210mg/6d    | 63              | 4                            | 0                   | Ò   | 2                     | • 3 |
| Guizhou  | 210mg/14d . | 13              | 12                           | 0                   | 0   | 2                     | 15  |
| Guiyzhou | 100mg/5d    | 102             | 12                           | 1                   | . 1 | 15                    | 15  |
| Henan    | 67.5mg/3d   | 14              | 11                           | 3                   | 21  |                       | 36  |



- 1.1 The results shown that the treated time was not less than 5 day and the total dosages of Primaquine was not less than 135 mg.
- 1.2 However, even the same dosage (210mg/14d) used in different malaria endemic areas the results were different.





# 2. Operational test for reducing relapse of vivax malaria with different dosage of Primaquine

| Dosage/d                | Interval | No. of            | Survey . | Relapse | Side-reaction |    |
|-------------------------|----------|-------------------|----------|---------|---------------|----|
|                         |          | period<br>(month) | (%)      | Normal  | Cyanosis      |    |
| 210mg/7d<br>2 times     | 4        | 71                | 3        | 0       | 19            | 26 |
| 180mg/8d<br>2 times     | 1        | 192               | 3        | 0.5     | 1             | 15 |
| 120mg/4d<br>2 times     | 0.5      | 91                | 5        | 3.3     | 0             | 2  |
| 210mg/7d<br>Single time | /        | 83                | 4.5      | 6.0     | 1.3           | 17 |

Normal side-reaction: Anorexia, Nausea, Vomiting et al.



- 2.1 The results shown that the 2 times treatment of Primaquine were better than single treatment.
- 2.2 Comparison with relapse and side-reaction, 180mg/8 days and 120 mg/4 days 2 times treatment were better than others. It would be suitable for a large scales performance in endemic areas.



#### 

The operational test carried out in Jiangsu province from 1990 –1993.

The C/P 8 days treatment: Chloroquine: 1.2 g( 3 days) Primaquine: 180mg(8 days)

The double C/P 4 days treatment:

Chloroquine: 1.2 g( 3 days)

Primaquine: 90mg(4 days) plus 90mg(4

days) within 1 month



| Double C/P 4 days |                  |                    | Single C/P 8 days |                  |                    |  |
|-------------------|------------------|--------------------|-------------------|------------------|--------------------|--|
| No.of<br>cases    | No.of<br>relapse | Relapse<br>rate(%) | No.of<br>cases    | No.of<br>relapse | Relapse<br>rate(%) |  |
| 125               | 4                | 3.2                | 88                | 3                | 3.4                |  |
|                   |                  |                    |                   |                  | <u> </u>           |  |



- 3.1 There were no different for relapse rate between the C/ P 8 days treatment and C/ P double 4 days treatment.
- The side-reaction of C/ P double 4 days treatment were less than C/ P 8 days treatment.



# 4. The Principle and Scheme for vivax malaria treatment in China

- 4.1 Eight days regimen of chloroquine plus primaquine
  - Total dosage of 1.2g Chloroquine plus 180mg Primaquine:
  - 0.6g chloroquine for the first day,
  - 0.3g chloroquine daily for the next 2 days.
  - 22.5mg Primaquine daily for 8 consecutive days administered with chloroquine simultaneously from the first day.



4.2Different dosage of chloroquine between China and WHO recommendation

| WHO (150mg/table) |        |        |        | China  | (150   | mg/t   | able)  |
|-------------------|--------|--------|--------|--------|--------|--------|--------|
| Total             | D1     | D2     | D3     | Total  | D1     | D2     | D3     |
| 10                | 4      | 4      | 2      | 8      | 4      | 2      | 2      |
| (1.50)            | (0.6a) | (0.6a) | (0.3a) | (1.2a) | (0.6q) | (0.3g) | (0.3g) |



4.3Different dosage of primaquine between China and WHO recommendation

| WHO                 | (7.5mg/table)                            | China (7.5mg/table      |   |  |  |
|---------------------|--|-------------------------|---|--|--|
| Total Days (14)     |  | Total                   | Days(8)                                   |  |  |
| 28tables<br>(210mg) | 2 tablets (15mg) /<br>day<br>for 14 days | 24table<br>s<br>(180mg) | 3 tablets (22.5mg)<br>/ day<br>for 8 days |  |  |



5. Radical cure of vivax malaria

Due to the frequent relapse of vivax malaria, there are a Radical cure( 8 days of primaquine) for vivax malaria cases in next spring season (notransmission period) in China.

The dosage of Radical cure in next spring season is primaquine 22.5mg/day for 8 days.



7. Chemoprophylaxis in transmission season

Piperaquine has been used for Chemoprophylaxis in target group or target areas in transmission season

Piperaquine: 4 tables for one month



6. The needed operational research

6.1 chloroguine resistant on vivax malaria

There is no laboratory data of vivax malaria resistant with chloroquine in China before 2005.

One research carried out in 2005-2006 and some suspected chloroquine resistant vivax malaria were found in middle part of China



6.2 Appropriate dosage and time for vivas malaria treatment in temperate areas

Although 8 days c/p treatment carried out in China for many years, there is no scientific documentation to compare 8 days c/p treatment with 14 days C/P for efficacy and side-effects of primaquine



6.3 New RDT suitable for vivax malaria diagnosis

Also many RDT products on the market most of them for falciparum malaria

Few of RDT products is suitable for vivax

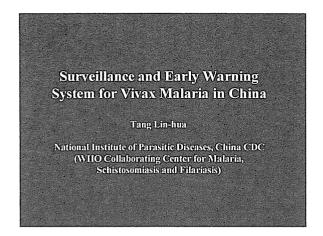
It is need for develop the New RDT suitable for vivax malaria diagnosis



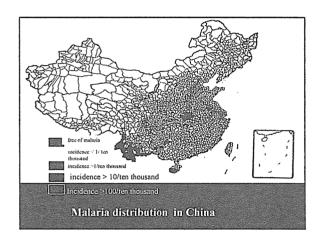
## 6.4 New technique for detection of G6PD absence

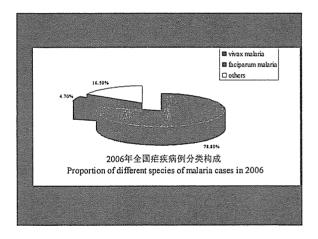
- G6PD absence is the major problem for implement mass chemoprophylaxis with primaquine in vivax malaria areas
- The ratio of G6PD absence is very low in major vivax malaria areas in China as well as in POK and DPRK
- So, It is needed to develop the new technique for detection of G6PD absence

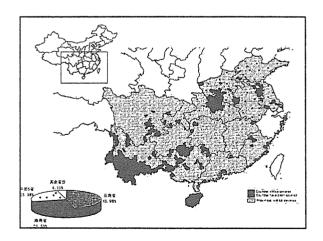


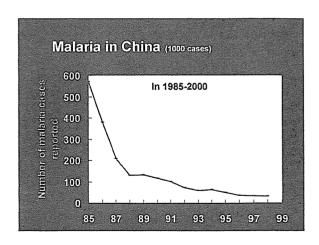


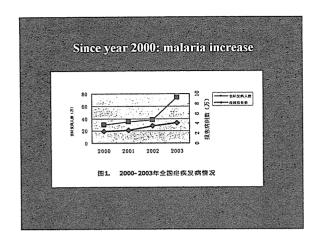


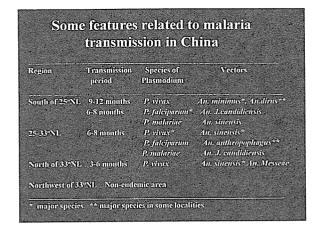






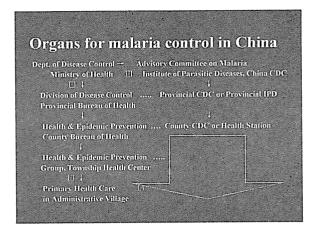






#### Malaria surveillance program

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.

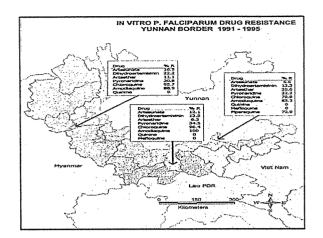


#### Strengthen vivax malaria surveillance

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.

#### Vivax malaria surveillance covers

Case detection
Focus intervention
Management on mobile population
Drug resistance
Vector monitoring



## Main parameters used in vivax malaria surveillance

- Annual parasite incidence (API);
- Annual blood examination rate (ABER)
- Annual vivax incidence (AVI)
- Slide positivity rate (SPR)

#### Main indicator for vector surveillance

feeding and resting behaviour human biting rate human blood index vectorial capacity

#### **Monitoring**

Environment rainfall, in some cases local surface waters depend on rainfall- or snowfall- upstream; temperature; humidity;

#### Medium- or long-term risk

Long term changes, e.g. in housing, relative numbers and accessibility of domestic animals, management of surface waters may eventually prevent malaria epidemics, but are unlikely to be planned for that purpose.

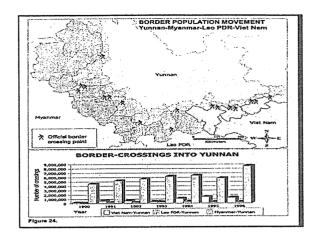
Monitoring the risk; build up the capacity to investigate suspected epidemics and to plan and implement emergency measures.

#### Strengthening case report system

Village doctors/private doctors/clinics
Township hospital/other hospitals
County CDC
Prefecture/city CDC
Provincial CDC
China CDC

## Control of malaria in migrant population

Malaria intervention work should be appointed to special personnel in relevant units situated at construction site or economic developing region in endemic areas. Under the guidance of local anti-epidemic station or department, elucidated information about the extent of prevalence and the major vector should be achieved after on-site survey.



#### Malaria early warning system

Three main group of indictors to predict the timing and severity of a malaria epidemic:

Vulnerability indicators

Transmission risk indicators

Early detection indicators from health facility malaria morbidity data

#### Malaria early detection

Surveillance data

Use of sentinel sites

Use of laboratory-diagnosed malaria data

Temporal analytical techniques

Analysis of time series data

Fime-series cross correlation and linear

regression

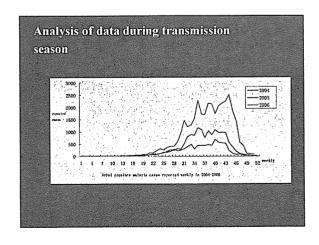
Conclusion

## Based on the formula of basic reproductive rate

Study on transmission density-threshold of  $An.\ sinensis$  for malaria in the Northern Anhui Province

Results The human blood index for *An. sinensis* was 0.1771 and the mean multiparous ratio was 0.51. In study spot, the adjusted human-biting rate for *An. sinensis* was 11.1877 and the critical human-biting rate was 7.6340, the adjusted human-biting rate was 1.47 times of its critical human-biting rate.

Conclusion A reduction of the adjusted human-biting rate of An. Sinensis by 47% is needed for interrupting malaria transmission by this vector in the study area.



An. sinensis is still a very important vector transmitting vivax malaria in central provinces because of its extensive distribution and big population. In recent years according to annual reporting system, most of malaria cases are found in areas where An. sinensis is only vector.

#### Prospective

Malaria control and surveillance will be strengthened, and drug policy will be further developed in China

Further decrease the incidence in most of endemic areas in central part of China
For malaria control in Yunnan and other border provinces, it is necessary to cooperation with WHO Roll Back Malaria, other international organization and the neigh bordering countries

