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Control of Malaria in East Asia

*Report of the Bi-Regional Meeting
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Executive Summary

Epidemics of vivax malaria that occurred in 1998 in East Asia, especially at the border between the Democratic People's Republic of Korea (DPR Korea) and the Republic of Korea (ROK) are a serious concern. The disease does not claim any deaths but causes a lot of discomfort and socioeconomic loss. The resurgence of vivax malaria was caused by the long incubation period strains of *Plasmodium vivax* since the disease had been eliminated from the affected areas for years before the massive outbreaks. The WHO Western Pacific and the South-East Asia regions have been supporting Member States in East Asia in tackling the problem. Mass prophylaxis with primaquine among targeted population and promotion of the use of insecticide-treated nets are two main control measures. Efforts have been made to improve malaria diagnosis, the information system, information exchange and intersectoral collaboration.

An Interregional Informal Consultation on Vivax Malaria was convened by the WHO Western Pacific Regional Office in Shanghai from 17-20 November 2003. Significant progress has been made following intensive implementation of the recommendations of this meeting. The number of reported vivax cases is declining considerably. However, there is a need to follow up on the progress and address several technical issues in order to accelerate the efforts to control vivax malaria in East Asia. A bi-regional meeting on control of malaria in East Asia was convened by the WHO South-East Asia Regional Office in Shanghai from 30 November–3 December 2004. The objective of the meeting was to facilitate effective implementation of evidence-based malaria control programme in East Asia through intercountry and bi-regional collaboration, information exchange and networking.

Sixteen participants from PR China, DPR Korea and Republic of Korea, attended the meeting. The participants made a one-day field visit to the Jiangxu Institute of Parasitic Diseases (JIPD) to observe facilities in training and research, current case detection, treatment and personal protection and vector control.

The three countries reviewed the malaria situation and progress in the control of vivax malaria, with special attention to malaria diagnosis, implementation of mass prophylaxis with primaquine, insecticide-treated nets and malaria information. Establishment of the Asia Vivax Network, applications of DPR Korea and the Republic of Korea for membership of the Asian Collaborative Training Network on Malaria (ACTMalaria), research

needs and information exchange were extensively discussed. The meeting made several recommendations to WHO and Member States; i.e. strengthening of collaboration among the three countries and information exchange, especially information related to the border areas between the Republic of Korea and DPR Korea; structured training for programme managers, strengthening of laboratory diagnosis, mass prophylaxis with primaquine and ITNs as well as monitoring of these measures.

1. INTRODUCTION

The bi-regional (WPR-SEAR) meeting on control of Malaria in East Asia was held in Shanghai, PR China, from 29 November–2 December 2004. The participants included representatives from the Republic of Korea (ROK), Democratic Republic of Korea (DPRK), and People's Republic of China (PR China).

Dr Krongthong Thimasarn, Acting Regional Adviser (Malaria), SEARO, reported that the meeting was a follow-up of the interregional workshop on the control of vivax malaria in East Asia, held in Shanghai, PR China, from 17–20 November 2003.

2. OBJECTIVE

The general objective of the meeting was to facilitate effective implementation of evidence-based malaria control programme in East Asia through intercountry and bi-regional collaboration, information exchange and networking.

The specific objectives were:

- (1) To review the current malaria situation in East Asia and the progress of work in capacity development, epidemiological understanding, related research activities, as well as identification of challenges and constraints;
- (2) To identify strategies for operationalization, including monitoring and evaluation of *P vivax* malaria control in East Asia;
- (3) To define the need for research (including drug resistance) in malaria control, and
- (4) To promote information exchange and strengthen intercountry collaboration and networking of institutions.

Dr Egil Sorensen, WHO Representative to DPR Korea, read out the address by Dr Samlee Plianbangchang, Regional Director, South-East Asia Region. He conveyed greetings from Dr Samlee who could not come because of his commitments.

The resurgence of malaria in DPR Korea was caused by *P vivax* which has a long incubation period and frequent relapsing. It is a concern in East Asia. It is not responsible for deaths but causes a lot of discomfort and leads to socioeconomic losses. Reference was made to insecticide-treated nets for personal protection. Mass prophylaxis in limited population has been tried in DPR Korea successfully. Bi-regional collaboration between the South-East Asia and Western Pacific Regions, and collaboration between DPR Korea, Republic of Korea and PR China have served as an example of cooperation in addressing the common problem of control of malaria caused by *P vivax*. Intersectoral collaboration is needed to address the problem. Reference was made to intermittent rice cultivation in vector control. The meeting augurs well for the control of *P vivax*. He thanked to the Government of PR China and the Institute of Parasitic Diseases, Shanghai, for hosting the bi-regional meeting.

Dr Henk Bekedam, WHO Representative to PR China, read out the address by Dr Shigeru Omi, Regional Director for the Western Pacific. He welcomed the participants of the meeting on behalf of Dr Omi. The bi-regional meeting held in 2003 provided the basis for networking. There is a need to operationalize the recommendations of that meeting. *P vivax* in the Korean peninsula and Eastern Province of PR China can have a significant public health impact. The drugs available include chloroquine and primaquine. Reference was made to the recent potential evidence of possibility of artemisinin in the control of malaria. There is a need to control malaria epidemics in East Asia. Much can be learnt from the experience of PR China. He called upon the participants to take advantage of the experience and forge an alliance to develop new tools.

Prof Tang Lin-hua, Institute of Parasitic Diseases, Shanghai, welcomed the participants. He expressed his appreciation to the South-East Asia and Western Pacific regional offices and acknowledged the support of the Ministry of Health, PR China. He emphasized that *P vivax* is a major public health problem in East Asia. The meeting would help to identify the needs based on a review of the progress of work and the existing capacity, and promote exchange of information, networking and research for furtherance of knowledge. He hoped that it would help to formulate strategies for networking and to extend these strategies to other parts of the world.

Dr Xia Gang, (PR China) read out the welcome remarks of the Director-General, Department of Disease Control, Ministry of Health, PR China. Malaria does not only cause morbidity but affects socioeconomic

development adversely. PR China has assigned a high priority to malaria control. Surveillance has been strengthened and transmission control intensified during the last several decades. Unfortunately, despite these efforts, there was a reversal during the 1990s. Underreporting is widely prevalent and this is a constraint in effective implementation of the control programme. Although only 40 000 cases have been reported, the estimated cases run into several hundreds of thousands. Malaria is a disease that affects the rural, the poor and the people living in remote and inaccessible areas. Therefore the focus has to be on the poor and floating populations. He thanked all the international agencies, bilateral partners and NGOs who have contributed to the control of malaria. He hoped to get continued financial support as well as technical guidance from them.

3. PARTICIPANTS

There were 6 participants from the Republic of Korea, 3 participants from PR China and 5 participants from DPR Korea. The meeting was assisted by 4 Temporary Advisers besides WHO staff from the South-East Asia and Western Pacific regional offices. A list of the participants is at Annex I.

The Programme of the meeting is at Annex 2.

Prof. Tang Lin-hua (PR China) was nominated Chair person, Dr Kim Yun Chol (DPR Korea) and Dr Soo Chun Park (Republic of Korea) as vice-chairpersons and Dr Vijay Kumar as rapporteur for the meeting.

4. MALARIA SITUATION IN THE SOUTH-EAST ASIA REGION

Dr Krongthong Thimasarn (SEARO) presented the malaria situation in South-East Asia. In the SEA Region the population at risk of malaria is about 1.35 billion out of an estimated total population of 1.6 billion. Ten out of 11 countries are endemic for malaria (no indigenous cases of malaria has been reported from Maldives since 1984). There are problems of malaria outbreaks in all the endemic countries of the Region and of multi-drug resistance, especially in Myanmar and Thailand, which is spreading to other countries across the international borders. About 2.5 million cases are reported each year with an estimated 20 million cases. About 300 million cases are at risk of multi-drug resistance. India reportedly accounted for 73% of the cases in the Region, followed by Indonesia and Myanmar. Deaths are reported maximally from Myanmar (about 60% of the total deaths in the Region). This is followed

by India. Trends show some decline in reported cases of malaria during the past 3-4 years but there is an increase in the proportion of *P falciparum*, the dangerous form of malaria. Data show that there were 2.3 million reported cases in 2003 as compared to 2.6 million cases in 2001. While the number of reported cases of malaria has declined, reported deaths have remained static. The SEA Region follows the global malaria control strategy and seven countries have endorsed the WHO strategy of RBM recommended by WHO HQ. Vector distribution was described and the main vectors in the Region were identified. The coverage of insecticide-treated nets (ITNs) for personal protection and transmission reduction has increased. However, there has been a decline in the coverage of indoor residual spraying (IRS) and the use of DDT. The countries are encouraged to develop a national insecticide policy and to reduce their reliance on DDT. WHO will support the adoption and implementation of the integrated vector management (IVM) strategy.

Malaria cases have shown a slightly declining trend in India over the last few years, but the proportion of *P falciparum* cases has increased significantly. The problem of chloroquine resistance in *P falciparum* has increased in some states, especially Orissa and the northeastern states of India. In Bangladesh, there is a problem of epidemics and increasing trend of *P falciparum* drug resistance, especially chloroquine and sulfadoxine/pyrimethamine. Failure of drugs has been demonstrated in the eastern districts bordering Myanmar. In Sri Lanka, the epidemics have declined and the malaria incidence has been brought down. *P vivax* accounts for 80-90% of the cases and malaria continues to be sensitive to chloroquine. The malaria situation has improved in all the countries of Region except Myanmar where the problem of *P falciparum* has increased. Drug resistance is high and epidemics continue in some certain areas. Myanmar has revised its national drug policy but it has not fully implemented it because of lack of funds for artemisinin. In Thailand, the problem of malaria has been reduced but the problem of drug resistance continues. There is countrywide resistance of *P falciparum* to chloroquine, sulfadoxine/pyrimethamine and resistance to mefloquine at international borders. There are specific areas in Thailand where the problem of multi-drug resistance is serious. Indonesia reported an outbreak of malaria in the Menoreh hills of Java.

Comments

Drug resistance to *P vivax* has been reported from Indonesia, Myanmar and some parts of India.

Amongst vector control strategies, the main emphasis continues to be on IRS even though the coverage has declined while ITN has been promoted since 1998. The beginning was small, but coverage is now expanding. Operational guidelines and strategic framework for ITNs have been developed. The increase in coverage is only a projection. The Region is now moving towards integrated vector management (IVM).

Several outbreaks of malaria have occurred in Myanmar, PR China and along the international border between the two countries. There are continuing problems with regular and timely sharing of information between the two countries. Difficulties in Myanmar relate to the difficult terrain and the lack of knowledge about epidemics during the early stages. However, the government recognizes that the areas on the border are highly endemic for malaria. Cooperation between the two countries has to be intensified. There is a lot of movement across the border which is contributing to the spread of malaria. WHO should consider further strengthening of the surveillance system and enhance the exchange of information. The principle of regular exchange of information should be extended to the control of other diseases as well.

5. MALARIA SITUATION IN THE WESTERN PACIFIC REGION

Dr Kevin Palmer (WPRO) presented the malaria situation in the Western Pacific Region. There are four malaria-affected areas in the Region. They are: the Mekong countries, the countries in the neighbourhood of Mekong called Mekong plus, the Pacific countries, and, finally East Asia including the eastern provinces of PR China and the Republic of Korea where the problem of malaria is distinct. The population at risk for malaria is 94 million which represents 7% of the population. There is a downward trend in malaria since the peak in 1992. The reported cases have decreased from 500 000 cases per year to about 350 000 cases. Malaria deaths have declined from over 6 000 per year to about 1 500 per year. The data are not very reliable but show a trend similar to that in the SEA Region. In some countries the entire population is at risk e.g. Pacific countries, Yunnan Province of PR China, Papua New Guinea, and Lao PDR. In Laos, maximum cases are of *P falciparum* while the proportion of the species is low in PR China. The proportion of *P vivax* is 100% in the Republic of Korea and 85% in PR China. In the Pacific countries like Papua New Guinea, the Solomon Islands and Vanuatu, the malaria problem is serious but it is low in Fiji. There are peaks of

the disease in February and October. Epidemics occur frequently. The overall ratio of *P falciparum* to *P vivax* is 60:40. Malaria in the Solomon Islands peaked in 1992 when there was one case of malaria per person per year. There was a 70% decline in malaria during the next 6-7 years to about 90 000 as a result of an intensive malaria control programme. However, the problem aggravated due to disruption of health services following ethnic violence. In Vanuatu, the cases declined from over 30 000 to less than 5 000 cases per year. The intensity of transmission is similar in Vanuatu and the Solomon Islands. In Papua New Guinea, the population is about 4 million and about 100 000 cases are reported per year. Both *P falciparum* and *P vivax* are resistant to chloroquine. ITNs and long-lasting insecticidal nets (LLINs) have been promoted in the Region. The Mekong plus countries include Malaysia, the Philippines, PR China, Viet Nam, Lao PDR, and Cambodia. Ethnic minorities, poor and difficult-to-reach populations are predominantly affected by malaria. In Viet Nam, 90% of the burden is in 5% of the population.

Malaria affects the indigenous population, migrants, poor people and those who work in the forests and forest fringes. In some of the countries of the Region, the problem of drug resistance is serious and the diagnostics are difficult to reach. There is a serious problem of fake and poor quality of drugs in some countries. In Cambodia, about 60% of the treatment is provided by the private sector. The drugs are often fake or of poor quality and, as a result, treatment fails. There is very little control on how the private sector treats these cases. The policy is to focus on the poor and the vulnerable population; promote rapid diagnostic tests and artemisinin drugs; monitor drug efficacy and drug quality; attempt to eliminate fake drugs; engage the private sector, and increase coverage with ITN. The strategy is to obtain high coverage. Most of the countries are supported by the Global Fund to Fight HIV/AIDS, TB and malaria (GFATM) and they are switching to the long-lasting insecticidal nets (LLINs). Each country has a different policy on the distribution of ITNs. There are very few countries in the Region that apply indoor residual spraying (IRS). The effectiveness of low coverage IRS is poor. This is partly related to poor construction of houses. The other problem is the quality of spray. In Cambodia, two brands of artemisinin-based combination drugs are promoted for use in public and private sectors. This is channelized through the routine distribution system and through commercial distribution system. The maximum cases occurred in early 1990s and they declined in about a decade. The malaria incidence in PR China has shown a decline from more than 200 000 cases to about 30 000 cases per year. The problem continues to affect the ethnic minorities who live in the southern areas bordering with

Myanmar and Lao PDR. Malaria in Lao PDR showed a peak in the mid-1990s and there has been a decline after about eight years of the control programme. Malaysia has shown a lot of success. Borneo showed the maximum problem (about 45 000 cases in the mid 1990s). As a result of intensified efforts malaria cases declined to about 3 000 by 2003. Viet Nam successfully brought down morbidity and mortality during the last eight-years from more than 200 000 cases to about 30 000 cases per year. In the Republic of Korea, the epidemic started in 1992 but there has been a substantial decline due to intensified control efforts.

Comments

There is no uniform reporting of malaria mortality and morbidity in the Western Pacific Region. There is no common definition of the population at risk for malaria. The criteria across the countries vary considerably, which makes comparisons difficult. The indicators are conventional annual parasite incidence (API), distribution of cases according to the parasite, geographical factors, presence of vectors, and reporting of cases from the area. WHO accepts the classification and the criteria used by the countries.

Estimations are not accurate due to gross underreporting of cases. Poor reporting contributes to the lack of visibility of the problem and serves as a poor advocacy for malaria. An example was given of HIV/AIDS as there is no way to determine the real burden. A survey on malaria is proposed to determine the extent of the burden of disease. The Global Malaria Report 2004 will serve as a starting point for addressing this issue. There is a need to validate the information from the countries. Household surveys may help to validate numbers. These tools have been developed and are proposed to be used in the countries of the Region.

6. RECENT DEVELOPMENTS IN VIVAX DIAGNOSIS

Dr David Bell (WPRO) made a presentation on recent developments in vivax diagnosis. Dr Bell stated that the recognition of malaria is based on microscopic diagnosis. The question is how useful it is to demonstrate parasitaemia before treating the patient. Prevalence of malaria varies a lot. In epidemics where the incidence is high, there may be no need to detect parasitaemia since many cases have *P. vivax*. Chloroquine is a cheap drug and the cost of diagnosis may be higher than the cost of treatment. Reliable microscopy needs technology, support and personnel.

Issues relating to sustainability and ability to monitor the quality of diagnosis are important. As regards clinical diagnosis, the incidence of malaria varies, malaria symptoms are non-specific and vary with the geographical area. There may be a delay between infection and clinical manifestation, especially if the disease has a long incubation period. Symptom-based clinical diagnosis has poor specificity. Accurate diagnosis helps to discriminate parasitaemia for treatment, leading to reduced patient cost and improved access and improved confidence, and provides better data for surveillance. The example of the Solomon Islands was mentioned to illustrate the value of diagnosis by microscopy. If case numbers are small, then rapid diagnostic tests (RDTs) may be more cost-effective; but if the caseloads are high, then the initial cost of microscopy is high but later on the cost comes down to a level that is lower than RDT. Microscopy in remote areas, such as villages can be difficult since there are problems in providing microscopes or preparing blood slides and transporting them to the microscopy centre. Village-based microscopy is difficult since it is not possible to ensure quality. No doubt there is greater reliability of diagnosis if blood films are sent to a centre, but there are delays in providing the results, which can lead to a delay in starting specific therapy.

Quality assurance issues include skills of microscopists, quality of blood films, quality of microscopes and quality of reagents, and this calls for training, proper maintenance of microscopes and provision of adequate reagents. Alternatives are RDTs and these include antigen detection tests. Antigen in blood binds with the antibody. There is a visible line as a result of the binding. The target antigens are pLDH, aldolase and others. The pLDH becomes rapidly negative after elimination of parasites. Aldolase is pan-specific and becomes positive in *P vivax* and *P falciparum* infections. Other antigen tests are under development. The cost of RDTs detecting both *P falciparum* and *P vivax* are under US\$ 1.30 per test. The cost can be less if only *P vivax* is proposed to be detected. However, a decision to use specific antigens can be made if the malaria epidemiology in localities is known. These tests detect the antigen and not the parasite. The RDTs are degraded by heat, and reliability depends on the technique and the quality of the products. Published results vary, possibly because of different study designs. The tests commonly detected 250-500 *P vivax* parasites/microlitre of blood. Storage conditions determine the shelf-life of the test. Temperature monitoring and control are important to maintain the quality of diagnosis by RDTs. Microscopy is not practical for screening parasites due to very low prevalence. In such a situation, antibody detection tests are more practical. Cell analysers can be

useful but are costly. There is a need for further work on RDTs and the test should be stable, cheap, sensitive and simple.

The options for *P vivax* are pLDH, aldolase and novel antigens. There are several options that include monoclonal antigens. These can be put on cassettes and used. It may be possible to indigenise production in East Asian countries. Antibody tests can also be considered for epidemiological surveys, for detection of liver stage for primaquine therapy, and for screening in blood banks. Antibody detection tests may not be useful for detecting early infection. Merozoite surface protein are specific in symptomatics while Circumsporozoite protein may be more useful prior to the development of symptoms. Circumsporozoite protein can be useful in predicting the occurrence of symptoms during the next transmission season although it has a low sensitivity. These studies have been done in the Republic of Korea.

Comments

The issue of correlation between antibody positivity and asymptomatic cases of *P vivax* malaria is important. Evidence shows that there is correlation between the presence of antibody and symptoms for about three months. The antibody of circumsporozoite protein (CSP) can be detected through the enzyme-linked immunosorbent assay (ELISA) technique. It is not clear as to how long positivity lasts, probably for a period of three months. Antibody detection by indirect fluorescent antibody test (IFAT) is done for surveillance in PR China. The important issues are the sensitivity of the test and its value as a clinical test. In the Republic of Korea, antibody tests have been used to detect symptomatic patients. These tests should not be used for routine surveillance due to the low sensitivity of tests and lack of information. The transmission season is only for 5-6 months. Currently, tests for detection of merozoite-surface protein (MSP) and circumsporozoite protein (CSP) are not available as commercial kits but are produced in laboratories.

7. TREATMENT OF *P VIVAX* AND MONITORING OF THERAPEUTIC EFFICACY OF CHLOROQUINE AND PRIMAQUINE

Dr Eva Christophel (WPRO) reviewed the treatment of *P vivax* malaria. Treatment with chloroquine and primaquine should be started together. The recommended dose for primaquine is 15 mg/day for 14 days. Exceptions are children below 3 years, pregnant women and cases with G6PD deficiency.

Treatment failures have been reported in Viet Nam and Myanmar. In the Pacific countries, chloroquine resistance is present in Papua New Guinea and the Solomon Islands. The failure rates vary between 10 and 30%. There is no systematic data on resistance to primaquine though anecdotal data are available. Primaquine targets the liver stages of *P vivax* which are responsible for relapses. Globally, 5-80% of malaria cases end in a relapse. The relapse rate depends on the total amount of primaquine given and not on the duration of treatment with the drug. The usual dose of primaquine is 210 mg. Now there is evidence that this dosage is may not be sufficient and should be increased to 315 mg. This would be 22.5 mg-30 mg daily for 14 days. Larger doses may be needed for people who weigh more than 70 kg body weight. In general, primaquine is well tolerated in persons who do not have any contraindications. Gastrointestinal tolerance is increased if the drug is taken with food. Methaemoglobinaemia that occurs usually is mild and self-limiting. It can be dangerous in patients with G6PD deficiency. This includes the use of primaquine in pregnancy when the status of the foetus is not known.

Primaquine has transmission blocking effect in mosquitoes. Its effect in *P falciparum* remains undetermined. There is clinical evidence of resistance but it is difficult to recognize. Patients do not take the drug for 14 days as prescribed. There is probably tolerance for the drug but this is not the same as resistance to the drug. There is suppressive effect of chloroquine for a period of seven weeks which can mask the effect. There can be a problem because of resistance to chloroquine and reinfection may complicate the picture. Alternatives to primaquine are tafenoquine but this is also an 8-aminoquinoline. This drug has a longer half life and therefore the compliance may be better. Toxicity and side-effects are similar. For chloroquine, the alternative drugs are artemisinin-based combination drugs and halofantrine. Artesunate alone has a failure rate of up to 50% but the efficacy is 100% when the drug is given as a combination therapy. The alternative is to give artesunate for five days and primaquine for fourteen days. This may be especially useful in patients who have mixed infections. This has been seen in Thailand where 30% of *P falciparum* patients also develop subsequent vivax infection. About 11% vivax patients develop *P falciparum* malaria. In cases of severe malaria, intravenous quinine or artemisinin or intramuscular artemether and artesunate suppositories are recommended. There is a need to determine the optimum doses of primaquine, simple and cheap methods of diagnosing G6PD deficiency, to explore alternative treatment of *P vivax* infections, to work out treatment for mixed infections, and to study alternative drugs to 8-aminoquinolines.

There are three tools available for recognizing resistance. These include therapeutic efficacy trials, *in vitro* tests and genetic tests including molecular markers. If symptoms reappear on day 27 it could be a recrudescence, relapse or reinfection. For these reasons monitoring of drug resistance in *P vivax* infection is much more difficult than *P falciparum* infection. Globally agreed protocols are not available to monitor drug resistance in *P vivax* malaria. Primaquine can hide chloroquine resistance. The sample size for monitoring is 50-100 patients. The inclusion and exclusion criteria are defined and there is a follow-up schedule. In *P vivax*, blood levels of chloroquine and its metabolite are also measured. The other markers that are monitored are molecular markers and blood haemoglobin. The outcome criteria are also different. No differentiation is made between early and late treatment failure. The WHO protocol should be considered as a draft protocol. At present, no tools are available for primaquine monitoring. It is important to know the strain before undertaking this exercise. *In vitro* tests do not guide national policy since these tests only show trends; the success rate of the test is much lower since it is not possible to culture *P vivax*. G6PD deficiency monitoring is also important.

The recent workshop on antimalarial drugs in Hanoi, Viet Nam in November 2004 recommended that therapeutic efficacy study should have follow-up data up to 28 days. The workshop also recommended the establishment of sentinel sites only if there is evidence of chloroquine failure, standardization of chloroquine and primaquine monitoring, development of genetic markers, and standardization of *in vitro* tests for monitoring of drug resistance in *P vivax* malaria.

Comments

The present protocols for monitoring therapeutic efficacy of drugs in the treatment of *P vivax* malaria may not be suitable for application in countries where temperate strains are responsible for malaria. This is because the present protocols monitor for only 28 days. For monitoring, even a follow-up for 28 days is difficult. These are important operational issues. *In vitro* tests should be considered as an alternative. This may serve as an early warning signal. Regarding the efficacy of primaquine, a seven-day trial with primaquine was given in the Republic of Korea in 1965 and the cure rate was 94%. This formed the basis for a shorter duration of the drug.

For the management of malaria in Eastern China, DPR Korea and the Republic of Korea, the complete treatment should be agreed upon and operationalised. There is a need for networking to monitor therapeutic efficacy of chloroquine. In the three countries of East Asia, *P vivax* is caused both by temperate and tropical strains. This complicates the issue further. Compliance with primaquine as such for 14 days is difficult and extending it to beyond that period will be extremely difficult. In China an eight-day regimen is used and it is effective. In DPR Korea, it was shown that 5 days treatment was not adequate.

8. OUTCOMES AND RECOMMENDATIONS OF BI-REGIONAL MEETING ON VIVAX MALARIA, SHANGHAI, NOVEMBER 2003

Dr David Bell (WPRO) dealt with this subject. He said that the meeting took note of several years of resurgent seasonal vivax malaria in PR China and its re-emergence in DPR Korea. The peak occurred in DPR Korea with more than 200 000 cases. The reasons for this resurgence were possibly climate and changed agricultural practices. There is uncertainty over primaquine treatment, vectors and the role of *Anopheles anthropophagus*. In the management of the disease, accuracy of clinical diagnosis, long incubation period and relapsing nature are issues that remain to be solved. Microscopy should remain the preferred diagnostic tool. These facilities should be established in all endemic areas or where epidemics are reported. Chloroquine 25 mg/kg over 3 days is the recommended drug. Artemisinin is useful in the treatment of severe vivax malaria. Primaquine should be used only in confirmed cases in a dose of 0.25 mg/kg for 14 days. The total dose of primaquine is more important than the duration of treatment. The regimen of primaquine for G6PD deficiency was agreed as 45 mg of primaquine once a week for 8 weeks. Testing of G6PD should be undertaken. Kits are available and can be used. In DPR Korea, mass chemoprophylaxis with primaquine was undertaken over a three-year period. There has been a decline in malaria cases. As such, mass chemoprophylaxis should be used in targeted areas and not used as a large-scale intervention strategy. PR China has good experience with this approach. To justify this, more information is required in reduced hypnozoites in the long incubation period vivax malaria. G6PD deficiency should be monitored and more data collected on compliance and effectiveness of primaquine prophylaxis. In operational research, intercountry

projects that involve sharing of samples and results to facilitate capacity development are important. Biology of long incubation *P vivax* including relapse rate and severity of the disease, drug efficacy monitoring with chloroquine, and application of chloroquine and primaquine combination are important to evaluate. The role of primaquine in preventing long incubation period relapse should be studied. A study of the distribution of G6PD deficiency by rapid assessment needs to be conducted. A rapid test indicating severity, sensitivity and specificity of clinical diagnosis needs to be evaluated. It is important to develop a test for detecting the disease before symptoms develop.

In vector control, the influence of human behaviour, particularly in the agricultural sector, personal protection measures for soldiers, farmers and other groups with high exposure, relating to change in domestic animals on vector behaviour, assessment of the significance of *Anopheles anthropophagus* in the Korean Peninsula are important issues to be addressed. Vector control and personal protection are the main strategy. High coverage with personal protection measures is useful but space spraying is not effective. Indoor residual spraying if done well is useful. Vector control and personal protection interventions need to be monitored. Surveillance and reporting should be strengthened, and the information obtained should be regularly shared. The Kunming indicators should be reviewed and revised for *P vivax*. Epidemic and early warning system should be used and stratification done to increase effectiveness of the interventions. WHO should help to coordinate timely exchange of information. Regional networks should be developed for strengthening technical support, encourage data exchange, undertake advocacy, operational coordination, information transfer, and for mobilizing more resources. Capacity building is the priority in DPR Korea and should be extended beyond malaria control. Enhanced training in microscopy and involvement of the Asian Collaborative Training Network on Malaria (ACTMalaria) should be considered. DPR Korea and the Republic of Korea have been invited to join the Network and the countries should join. Field epidemiology training programme (FETP) should be considered for DPR Korea.

The recommendations of the working groups included research on G6PD deficiency, studies on primaquine, benefits of spring treatment with primaquine before the transmission season, development of treatment flow charts and standard protocols, determination of major vector species, and assessment of the proportion of clinical diagnosis cases that are positive.

Comments

The chairperson suggested a discussion on the formation of these networks at the group discussion.

9. CURRENT MALARIA SITUATION AND PROGRESS ON IMPLEMENTATION OF MASS CHEMOPROPHYLAXIS AND ITNs IN DPR KOREA

Dr Kim Yun Chol (DPR Korea), who presented this item, stated that the peak of malaria transmission in DPR Korea occurred in 2001. More than 75% of fever cases tested were positive for *P vivax*. Since 2002 there has been a decline in the number of reported cases. A further decline has been noticed during 2003. Despite this, there are high endemic areas. The summer season witnessed the maximum number of cases of malaria. July and August are the peak months. More than 88% cases occur in adults above the age of 17 years. There is a higher proportion of malaria in males (53%) as compared to females (47%). This may be because males work outdoors and are exposed to mosquitoes. Malaria is equally distributed in the wetlands (29%), low hills (30%) and in the plains 29%. There are no cases in the hills and in northern parts of the country. *Anopheles sinensis* is the main vector, followed by *Anopheles lesteri*. The vector dominates in the south eastern parts of the country. The vector becomes active from early May and continues until October. Only *P vivax* is responsible for malaria. Typical features of malaria occur in 85% of cases while others have atypical symptoms of the disease. The relapse rate was 38% in 2000 but has been brought down to 3-4.5%. About 80% of the relapse cases have a long incubation period.

In 2004, the major strategies comprised early detection and laboratory diagnosis. Laboratory equipment has been provided in 100 counties in the 7 high-risk provinces. Medicine is started within 24 hours and primaquine is given for 14 days to confirmed cases. Vector control measures comprise smoking of tunnels, cellars, storehouses, animal shelters in January-February, removing places where larvae could live in June-September and supervision of activities. This has been difficult because of various constraints. Mass protection has been done by ITNs and insecticide screening. This year 400 000 population is targeted for mass chemoprophylaxis. Health education about malaria control is emphasized. Capacity building has been done in collaboration with WHO and comprised training of 25 epidemiologists and overseas training of 3 laboratory personnel. Studies in progress comprise

efficacy of mass chemotherapy and effectiveness of ITNs. Factors that have led to success were reviewed. The constraints and challenges of the programme include poor laboratory quality since a quality assurance system is not fully established. There is less social attention due to a decline in reported cases. Antimalarial drugs are not being produced in the country, capacity in programme management is poor and tools and equipment at the provincial level are not adequate. Two main strategies were described:

(a) Effectiveness and safety of primaquine in mass chemoprophylaxis

This approach was applied in 2002, 2003 and 2004. The population covered was 323 313 in 2002, 425 475 in 2003 and 393 732 in 2004. The reported side-effects were the highest in 2002 and they declined by 50% during subsequent years. Side-effects were observed in 1.5% cases in 2004. There was a very impressive decline in malaria in areas where mass chemoprophylaxis was used as compared to earlier year and as compared to the control area.

(b) Effectiveness of insecticide treated nets (ITNs)

The objective of the ITNs project was to identify susceptibility of mosquitoes to pyrethroids and evaluate the repellent effects of ITNs. The project was introduced in 8 target areas in the country. The adult mosquito is highly sensitive to insecticides. The repellent effect of permethrin declines after about 8-10 days of treatment. The dose of 200 mg/meter square was sustained for more than 75 days while the effect could not be sustained by the application of a lower dose. Human biting rates declined remarkably during and after transmission months. In 2004, as a result of intervention the biting rates declined to about 30%. There has been a reduction in incidence to 41%. The reduction after the use of ITNs will be discernible after 2-3 years.

Comments

Higher incidence is reported from areas that border with the Republic of Korea. This is why there is a need for increased collaboration between that country and DPR Korea. In the Republic of Korea, peak of malaria transmission occurred in soldiers during 1998. It was asked if soldiers be included as an occupational category affected by malaria. In DPR Korea, soldiers are not a part of the social sector. Therefore it is not possible to comment on the vulnerability of the soldiers in DPR Korea. In the Republic of

Korea the peak of malaria occurred in 2003-04. Therefore data will become available only after a few months.

Entomological studies are difficult because of inadequate capacity of the health system and the behaviour of vectors. An entomological survey was conducted and microscopy done to identify the vector. The areas most affected were west, south and eastern areas. Traps were used in the studies. Details of the study were presented by Dr Gao Qi in a subsequent session.

Dr Sorensen, WHO representative to DPR Korea summarized the good work done in the country. He acknowledged the financial support extended by the Republic of Korea. A lot of progress has been made in the past one year.

10. MALARIA SITUATION IN PR CHINA AND IMPLEMENTATION OF MALARIA CONTROL IN EASTERN PROVINCES

The presentation on this subject was made by Professor Tang Lin-hua (PR China). In 2003, the number of malaria cases increased to 40 681 which is 15.3% higher than that in 2002. *P falciparum* comprised 11% of cases. Indigenous cases were reported in 78 counties of Yunnan and Hainan Provinces while in 107 counties, there were imported malaria cases. Malaria has been controlled in most parts of China except Yunnan and Hainan Provinces. Malaria is unstable in eight provinces. Nearly 162 counties have an increased tendency towards malaria and 73 counties report focal epidemics of malaria. Malaria is re-emerging in the central and eastern provinces. The capacity in the periphery is low and there is the problem of long incubation period and relapsing vivax malaria. Because of the low prevalence of malaria, health workers are less serious about malaria control. The malaria early warning system is not well established in the country. Most cases occur in remote areas where the local capacity is poor. Baseline surveys showed that there was underreporting to the extent of 93.0%. The estimated figure is 18 times of what is reported (740 840 cases). Therefore missing cases are enormous. There is an increase in malaria cases year by year. In the 1980s and 1990s the eastern provinces had achieved elimination of malaria with less than 1 case per 10 000 population for three years. Elimination of *P falciparum* was achieved in four provinces in the 1990s. The tropical strains of *P vivax* occurs in southern China. The temperate strains are reported in eastern and central China. Until now no resistance to chloroquine or primaquine has been

reported. *Anopheles anthropophagus* is the main vector. Global warming affects vivax transmission. For diagnosis, microscopy is the standard method. Recently efforts have been made to develop rapid diagnostic tests for *P vivax* malaria. The use of chloroquine was abandoned in 1979 and the programme shifted to piperazine or pyronaridine monotherapy. Now artemisinin monotherapy is used although not, as a policy. Primaquine is used as an 8-day course, 4 days at a time, interspersed with one week's gap after the first course. Drug combination trials are in progress in *P falciparum* malaria. This includes artemether/lumefantrine (Coartem). Most surveillance is passive and only 10% of health facilities is active in reporting malaria.

To improve reporting, active surveillance and epidemiological surveys are recommended. Routine surveillance covers 1316 counties covering a population of 760 million. Blood examination is done for 5.6 million fever cases. Indoor residual spraying or insecticide-treated nets covered 4.2 million population; 25 200 workers were trained for this work. Several operational research areas have been identified. These include the role of *Anopheles anthropophagus*, study of early warning system through monitoring of fever cases, and strengthening reporting of malaria cases.

Comments

Surveillance has been strengthened since 1998 by establishing a network involving counties up to the provincial level. Microscopic diagnosis has also been strengthened. Fever cases are subdivided into four different categories to be able to conform to typical and atypical presentation. Blood slides in respect of cases are examined. Surveillance data are supported by a mathematical model. For vector surveillance, entomological units have been established at peripheral level. Support is provided by the government to counties, townships and provinces which are linked through computers. The reliability of the diagnosis depends on the infrastructure and it varies from county to county. The Solomon Islands show a high incidence because of good facilities and diagnosis by microscopy. Malaria is not a reportable disease in PR China. Studies to determine the true burden of malaria cannot be undertaken too frequently because they are expensive and labour-intensive. Therefore it is important to monitor the trends. If the programme reports more cases in the system, it means the programme is improving and does not necessarily mean a worsening of the malaria situation. If there is a suspicion of an increase, then a survey should be done. If there is a breakdown in the health system or if there is population migration or vector

surveillance is showing worsening of the parameters, then probably there is a real worsening in the malaria situation.

11 MALARIA CONTROL PROGRAMME IN THE REPUBLIC OF KOREA

The presentation on this subject was made by Dr Kidong Park (Republic of Korea). The goal of the malaria control programme is to eradicate malaria by 2010. It is proposed to reduce the incidence of malaria by 30% every year. The focus of the programme is on malaria-risk areas, and cooperation amongst all the sectors is encouraged. There are no high malaria-risk areas in the country but there are some moderate malaria-risk areas. It is proposed to turn these into low malaria-risk areas. The classification of malaria-risk is based on the number of cases per 100 000 population. In 1997 there was only one high-risk area in the country. By 2000, the high risk areas extended to the south and eastern parts of the country. After 2000 the number of high-risk areas has declined again. The control programme in the risk areas includes disease surveillance which, in turn, includes monitoring mosquito density and the number of reported cases. This is combined with epidemiological survey. Diagnosis is made early. Treatment is provided free of charge. The access to treatment is increased up to the health sub-centre. Fever cases are monitored as a priority. Health education is intensified in two medium-risk areas. The rate of household participation in these areas varies between 14.4% and 17%. The reduction rate of malaria cases was 47.6-61.3%. Educational activities were intensified. Amongst soldiers, the strategy is chemoprophylaxis comprising chloroquine once a week for 20 weeks and primaquine for 14 days, mosquito control by larval control measures, provision of permethrin-treated clothing and early diagnosis and prompt treatment (EDPT).

Imported cases of malaria have been monitored since 1994. The peak of imported cases (68) was in 2001. About 64 cases were imported in 2003. The imported cases had travelled to or were coming from African and Asian countries such as Nigeria, India and Indonesia. The Republic of Korea has supported malaria control of border counties in DPR Korea through WHO. As a result the problem of malaria has declined.

Research studies comprised detection of parasites by molecular biology. These included Acridine orange staining, DNA hybridisation and the polymerase chain reaction (PCR) technique. Antibody detection techniques

comprised IFAT, ELISA, and Western blot. A vaccine development project has been initiated. The candidate vaccines are liver stage-specific vaccine, transmission-blocking vaccine, sporozoite vaccine, and merozoite surface protein vaccine. Other research includes vector species complex, vector competence and vector control that include new methods of control and insecticide resistance tests. Guidelines for vector control were developed in 1999. Larvivorous fish to control mosquito larvae were adopted. Indoor residual spraying was used for control of adult mosquitoes. *Bacillus Turingensis Israeli* (BTI) was also used for larval control. The country follows the principle of integrated vector management (IVM).

Strategies include cooperation with other countries for effective malaria control at the international border, maximizing the performance of public health centres, increasing cooperation between civilians, the military and the government, and enlarging the scope of research on newer diagnostic tests.

Comments

During the transmission season, primaquine is used for 14 days as prophylaxis to decrease the transmission of long incubation period *P vivax* (to eliminate hepatic phase). Chloroquine is used during the transmission season to reduce the transmission potential. One of the problems is that chloroquine is believed to reduce vigour in men in the army. The problem of malaria is higher in males as compared to females because men spend more time outdoors, and soldiers are mostly men.

The outbreak in DPRK started in 1995 and in the Republic of Korea in 1997. The epidemics might have started among soldiers and subsequently spread to civilians. There is intensive surveillance of discharged soldiers. If they have fever, they get free diagnosis and treatment. Facilities are provided even outside the border areas.

The major vector is *Anopheles sinensis*. There is no transmission outside the border areas. Intensive surveillance is very important and this must be combined with prompt treatment of disease amongst soldiers. This is necessary since the vector is widely distributed and if soldiers who are infected travel to other areas, then there is increased risk of disease transmission.

In DPR Korea paddy fields are the breeding ground for mosquitoes. Projects are being developed in Kaesong which is a high-risk border area. There is a need to intensify cross-border collaboration. The Republic of Korea

would like increased cross-border collaboration to effectively control not only malaria but all communicable diseases.

Residential designing has window screens and clothing has permethrin treatment. Ponds and puddles are tackled by larvivorous fishes to control mosquito larvae. Although they are difficult to implement, the Republic of Korea has implemented programmes of larvivorous fish effectively for control malaria.

12. ENTOMOLOGICAL STUDIES IN DPR KOREA

Dr Gao Qi (PR China) in his presentation on the subject, the malaria situation is showing an improvement in DPR Korea as compared to earlier years, though the problem persists in some areas of the country, particularly in southern and eastern provinces. *Anopheles sinensis* accounts for 80-93% of all the vector population collected. The others are *Anopheles anthropophagus* (6-15%), and *Anopheles yatsushiroensis* (0.5%). Morphological differences among these species are minor. Therefore, the PCR technique was used for classification based on genetic and molecular characteristics. The vector capacity of *Anopheles sinensis* is very low. The sporozoite rate is very low (0.1-0.2%). The infection rate is less than 10%. The vector has indoor and outdoor biting habit. They feed on human and animal blood and breed mostly in rice fields. In contrast, the biting rate is predominantly indoor in *Anopheles anthropophagus*. As a result of food shortage there is not enough animal population to bite on so they resort to biting humans. There are high larval and adult mosquito densities in the rice fields because of low coverage by insecticides. The bednet coverage is low, the population protection is poor and the biting rate is high. By using multiple methods it was possible to collect more than 4000 mosquitoes in one night of which *Anopheles sinensis* was 88%. The strategy is to reduce the human biting rate through vector control and to reduce the parasite carrier rate through early diagnosis and prompt treatment.

An additional strategy is to reduce mosquito breeding in rice fields and improve personal protection through bednets. A field trial was described at the meeting. The trial comprised distribution of bednets to 346 families and indoor residual spraying with permethrin. The results were good before July but control measures were not effective there-after. Overall, the reduction was not significant. Permethrin spraying is ineffective. Another reason was the low coverage of ITN (only 56%). Laboratory tests have shown that the vector is

susceptible to permethrin. Wall spraying with permethrin is effective for about 7-10 days. No effect is perceptible at the end of 20 days. In contrast, the effect of ITN lasted more than 75 days. The concentration of permethrin is about 10 times higher than deltamethrin that was used in PR China. A field trial was carried out in one county in DPR Korea. Nearly 98% of the population was covered by ITNs. There was a 70% reduction in malaria in ITN covered county as compared to 33-45% reduction in non-ITN counties. This work was supported by WHO. In a study in 2004, a research institute was involved in the evaluation of ITNs. The ITN coverage was 95%. There was vector surveillance every 10 days. The limitation was the poor selection of the area. The incidence rate was very low to start with and the vector density was also low; consequently the human biting rate was also low. Despite these constraints, the results were good. BTI was also used but there is lack of adequate information on its impact. There is a need for larval control studies in paddy fields in DPR Korea. There is also a need for collaboration between WHO and FAO. There are constraints in the use of chemical insecticides and bio techniques for larval control in the country. Wet irrigation can be used for effective larval control. It has been used effectively in PR China in the 1980s. It will also help to increase the production of paddy and save costs since water required for irrigation can be saved. ITNs should be further evaluated since it is proposed to use them as part of the GFATM project. Entomological surveillance should be strengthened and upgraded. The role of *Anopheles anthropophagus* should be clarified. It is also important to better describe the malaria vector behaviour in the country.

Comments

WHO has been assisting in capacity development for vector control in the country. This should be expanded and sustained. ITN is one of the best control measures. As regards larva control in paddy fields, it may be possible to reduce the vector density by changing the irrigation pattern. The country did not have experience with ITNs. The distribution was too thin i.e. about 2-3 nets per village. Now the strategy is to concentrate on net distribution where the problem of malaria is maximal or the vector density is high. This requires the adoption of a stratified approach. The number of nets has to be increased considerably and distributed in a strategic manner. Permethrin can be used for treating bednets. However, it is not recommended for house spraying. The efficacy depends on the material that the walls to be sprayed are made of. The period of protection of three months is not good enough since the

transmission is for a period of 5-6 months. Since IRS is not likely to be useful, the ITN strategy has to be improved. The use of long-lasting insecticidal nets (LLINs) should be considered.

It would be worthwhile to document how malaria could be eliminated in the Republic of Korea. The anopheles survives during the cold season even though it is hibernating. Fumigation and smoking have been used successfully in the past. It is not clear whether these measures have any relevance in the programme now. Houses are mosquito-safe in DPR Korea. Documentation has improved considerably. The contribution to entomology is very good and this should be published. The technical capacity to conduct operational research is limited but what is available should be optimally utilized. Training has been undertaken during the last few years. Research capacity also needs to be increased. The Republic of Korea could help in enhancing technical capacity.

13. INTEGRATED VECTOR MANAGEMENT AND INTERSECTORAL COLLABORATION

Dr Chusak Prasittisuk (SEARO) said that WHO has prepared a draft integrated vector management (IVM) strategy and urged Member States to take steps to reduce reliance on insecticides (DDT) in accordance with the Stockholm Convention on Persistent Organic Pollutants (POPS) of 1998. The Regional Office had started capacity development through international courses in 1998. Since 2003, IVM has been taken up by the Region. IVM is a process to reduce or interrupt transmission of disease by effective vector control measures while reducing adverse environmental impact of insecticides. It includes methods based on knowledge of factors influencing the local vector biology, disease transmission and morbidity. Under IVM it is proposed to use a range of interventions in combination and synergistically, through collaboration with the health sector and public and private sectors, engage local communities and other stakeholders and take into consideration public health regulatory and logistic framework. It is a strategy and a programme that can be applied for vector-borne disease control programmes.

Agriculture and malaria are intricately related. Agricultural income influences living conditions in rural areas. Crop cultivation influences vector breeding and crop production. Central control is possible in main irrigation canals while at the local level, irrigated agriculture and vector control is in the hands of farmers. Therefore the capacity of farmers should be enhanced. The

important question is how to do this. A variety of participatory methods is available where farmers become owners of vector control efforts. This will help sustainability. It is important to enhance their expertise through adult learning. Farmer field schools (FFS) have helped the agricultural sector and promise sustainability. The management must be timely and locally adapted. There is a need to decentralize the expertise to farmers. A reference was made to the progress in Sri Lanka. The farmers observe and organize group discussions to effectively control pests and, at the same time, preserve the good insects. They organize topics and undertake field experimentation. Training of trainers is organized. The educational approach can be used for vector-borne diseases control using paddy fields as the entry point. Agricultural insects and mosquitoes live in the same paddy fields. There are synergies between pest and vector management and there is widespread use of agro pesticides. There are five project sites in Sri Lanka. The project was started in 2002 and training curricula have been developed. The training incorporates the popular perception of farmers. Simple methods are devised and used. The curriculum is quite comprehensive. An evaluation of the project demonstrated an increase in the knowledge of farmers. An important outcome is the change in practices of farmers. This has helped to develop farmer-to-farmer interactions and involvement of schools in the sanitation programme. The use of this approach promises to reduce the incidence of the disease. The outcomes are reduced transmission of vector-borne diseases, reduced use of insecticides, increase in awareness and the possibility of increased income generation. There are good prospects of using this experience in East Asia. It is possible to improve vector control, increase the yield of paddy and generate more income. The farmers can be used to promote the programme amongst themselves through peer education.

Comments

Pilot studies may be considered by the countries on water management and improved agricultural practices for effective vector control and increased income. This can be undertaken with support from WHO, FAO and UNEP.

14. NETWORKS FOR *P VIVAX* IN ASIA

Dr Kevin Palmer introduced the subject. As proposed in the 2003 meeting, Asia vivax network originally includes DPR Korea, PR China, Republic of Korea and Viet Nam. The terms of reference would be capacity development,

sharing of information, experiences, and surveillance data, and conducting operational research in priority areas. DFID research consortium proposal has been put forward after the last meeting in Shanghai. This would fit in well with the plans for establishing an Asia vivax network. It would be important to identify a number of institutions who can participate in the DFID consortium. Many institutions in Australia are willing to participate. Later, the network can also include institutions in Papua New Guinea, DPR Korea and the Republic of Korea. The consortium promises to provide about US\$ 1 million dollars per year. The deadline for submitting the proposals would be January 2005. The objectives are to redefine tropical and temperate forms of malaria, develop human resources for further research, develop molecular markers for use by participating countries, study the sociology of treatment-seeking behaviour, and ensure compliance with treatment and other sociological aspects of vivax malaria that are different from falciparum malaria. The proposed terms of reference for the East Asia network were presented. These are similar to the objectives identified for the Pacific. The suggested countries for the expanded network would be PR China, DPR Korea, Republic of Korea, Papua New Guinea, the Solomon Islands and Vanuatu although a beginning may be made with the participation of DPR Korea, Republic of Korea and PR China. The proposed network will be useful for the development of human resources, molecular markers, sociological aspects of vivax and develop a reference centre. The structure would comprise research supported by DFID, training through ACTMalaria, China CDC and Australian universities. The networking should include sharing of surveillance information, coordination of control activities, quality assurance for diagnosis, drug efficacy monitoring, drug use monitoring, and IVM. The Board of Directors can be on the pattern of the ACTMalaria Executive Board. The network would need a coordination mechanism and a secretariat. It is important to explore possibilities of funding for the network besides DFID fund.

Comments

There is a lot of vivax malaria in India, Sri Lanka and Indonesia. It is suggested to expand the proposed network to these countries later on or as a separate entity. Any country can join the network but the number of institutions should remain restricted at least in the beginning. For the establishment of the network recommendation was made at the Shanghai meeting in 2003. The network should be focused in its terms of reference and work on the resources that can be mobilized. It may be useful to start with a few countries

and once the network begins to function, it can be expanded to other countries which face the problem of vivax malaria. The proposal was endorsed by DPR Korea, Republic of Korea and PR China. The network will be an excellent opportunity for the three countries and the two WHO regions to work together.

15. ASIAN COLLABORATIVE TRAINING NETWORK ON MALARIA (ACTMALARIA)

Professor Tang Lin Hua presented this item. There are 11 countries participating in this network. At present the headquarters of ACTMalaria is in the Philippines. It is an intergovernmental network of malaria control programmes in South-East Asia and the Greater Mekong Sub-region. ACTMalaria promotes working together in a sustained manner, with equal partnership and with the objective of eliminating malaria as a major public health problem in the region. The focus is to facilitate capacity development, advance international cooperation, encourage information dissemination and exchange, and seek partnerships. It was established eight years ago. Dr Krongthong Thimasarn was the first Coordinating Country Director (CCD) of the network. Capacity development, technical support, communication and information exchange and partnerships and promotion have been the focus of ACTMalaria since its inception.

Communication and information exchange is for enhancing the relationship amongst Member States and partners through continuous knowledge and experience sharing. The other activities are training, operational research, and technical support. International training courses conducted include courses on management of malaria field operations, broadening involvement of malaria through team training workshop, drug policy development, transferring training technology, operational research, training and management of severe malaria. Funds are drawn from international agencies. It is proposed to establish networking on expertise. It is also proposed to improve the quality of microscopy through training. ACTMalaria also promotes partnerships through strengthening of existing partnerships with Member States, invites non-member countries to participate in the network and its activities, and engage other institutions. It invites non-member institutions to enlarge the scope of work of ACTMalaria. The Chairman invited DPR Korea and the Republic of Korea to join the membership of ACTMalaria.

Comments

The role of ACTMalaria continues to expand. Most of the initial technical and financial support for ACTMalaria has come from WHO, especially development of course curriculum, initial governance and fellowships. The Organization should try to mobilize additional resources. Countries should plan to secure fund for ACTMalaria activities ahead of time to incorporate it within the budget that is likely to be available.

16. GROUP WORK

The participants were divided into three groups and provided with guidelines and terms of reference for the group work (Annex 3).

Each group discussed the core issues in detail and proposed recommendations which were then discussed at the plenary session.

Comments

Group 1: Capacity development, training, logistics and networking of institutions

The proposed quarterly report on malaria is different from the annual report. It should deal with urgent issues which need immediate attention. The reporting formats should be designed accordingly. It should be simple. The channel is through WHO and therefore it should not be a problem in the country. The information shared should be kept confidential. However, practical aspects have to be kept in mind. There was a lot of discussion on whether the sharing of information should be done on a quarterly or six-monthly basis. The consensus was that information in the event of an outbreak should be prompt. The programme should not be burdened with having to report too frequently when the information is not likely to be of use. For quarterly reporting, a common format may be designed by WHO.

The modalities for establishing a network should be discussed. To begin with, a formal structure may not be necessary. There may be a one-week training in a centre of excellence which should be followed by an observational visit to countries. Training of senior programme managers should be structured. This will also help them to develop a common understanding amongst themselves and contribute to networking.

Group 2: Strategy for operationalization of malaria control and monitoring of therapeutic efficacy of chloroquine

A strategy for operationalization of malaria control and monitoring of therapeutic efficacy of antimalarials needs to be developed.

The experience in the three countries should be documented and shared since each country has adopted different strategies for malaria control. Each country should strengthen its laboratory services and surveillance system including quality control to improve and stratify surveillance of at-risk areas. Studies on G6PD deficiency should be carried out in each country to provide evidence for safety of mass prophylaxis used for prevention of outbreaks. Each country should carry out at least one therapeutic efficacy study on chloroquine and follow the WHO standard protocol.

The ITN programme should be scaled up in all the high-risk areas aiming at more than 80% coverage for transmission reduction. Monitoring and evaluation of ITN should be strengthened. A small technical intercountry working group should be formed to develop and coordinate studies that assess ITNs which include LLINs. A pilot study of IVM should be conducted in one site. Information, education and communication should be an integral part of vivax malaria control in order to improve adherence to 14 days primaquine and bed net usage protection against malaria during late night activities.

An intercountry research programme should be considered. Strengthening of the health system should be regarded as a sustainable approach and should be an integral part of operationalization. Piloting of IVM may be considered for DPR Korea. The country needs to stratify malaria risk for effective mass drug administration, for use in outbreak preparedness and control, and to identify high-risk areas for better targetting of the ITNs. Stratification may be done through laboratory services and by other means.

There is a need to define cases that should be given complete treatment. Whether only microscopically-confirmed cases should be treated or treatment should be given to fever cases who conform to the case definition is an important issue. Clinical cases should be given complete treatment, especially when cases of malaria are on the decline. A case definition should be developed for treating cases when it is not possible to recognize malaria by microscopy or RDT. The group discussed the issue of public attention during post epidemics: when there is an outbreak, there is a lot of concern and resources get mobilized but when there is success the resources decline.

Decision-makers should be convinced that they should not reduce budget but keep the resource provision at a high level to maintain the capacity of the system even when malaria incidence has declined.

Group 3: Review of current research and identification of operational research needs and networking of research on vivax malaria in East Asia

Development of more sensitive RDTs is important. At the same time, the programme should continue to focus on microscopy and this should be extended to the ri level in DPR Korea and backed up by RDTs. This may also be relevant to PR China.

There is a need for a large-scale field trial on ITNs to determine how these can be scaled up rapidly and what is the impact of large-scale implementation. Vector control is a priority and there is a need to develop a strategy on IVM. Each country should develop its own strategy. Protection from vectors by the use of protective clothing should be evaluated. Vector hibernation should also be evaluated. The strategy should be to reduce the load of vectors in winter.

The group discussed the issue of discrepancy between reported and estimated cases and how best to assess the real incidence of vivax in PR China. If the gap is big, then larger investments are justified. Based on estimated cases there should be some studies on the socioeconomic impact of vivax malaria.

The results of the trials in DPR Korea should be published and widely disseminated. The methodology should be improved further in future trials. Alternative and better primaquine regimens should be explored. G6PD deficiency has not been studied but then large-scale clinical trials indicate that this is not a major problem in countries and therefore it has not been studied.

There is a need to mobilize additional resources for research. DPR Korea needs support for developing and sustaining laboratory diagnosis. There is a need for training in epidemiology for personnel from DPR Korea.

Exchange of fellows and visits to research institutions in the three countries could help in developing research capacity.

Primaquine is widely used but there is no study to show its efficacy. The study should be carried on for a long enough time period and should evaluate the total dose.

ITN is an operation as well as a research issue. There should be support to entomological research to identify the role of vectors and the vectorial capacity in continuing vivax malaria transmission in East Asia.

Studies in collaboration with the department of agriculture should be considered as a priority. Intermittent irrigation studies have been done but there is not enough experience. This will be discussed with the government which should conduct trials on the efficacy of the intermittent irrigation system in malaria control.

Research on the role of providing re-treatment in spring cases that were reported during the past two years, as has been done in PR China, is required.

For vivax control in the three countries, there is a need to prioritise research issues that need to be addressed during the next 2-3 years. There should be a mechanism to regularly share the findings of research. DPR Korea can also apply for a small research grant from TDR.

There is a big difference in the sensitivity of clinical diagnosis in an outbreak situation and in a situation when disease incidence is low. Should the clinically-suspected cases of malaria get full dose treatment? The Republic of Korea has intensified training and improved access to microscopy. RDT is used in the remote and difficult-to-reach areas. The Republic of Korea has a policy to give primaquine only to those who are microscopically or RDT-positive.

17. RECOMMENDATIONS

- (1) To strengthen collaboration in the control of vivax malaria amongst the countries in East Asia, regular exchange of information on the malaria situation, especially in relation to the border between DPR Korea and the Republic of Korea, at least at six-monthly interval, is recommended. Outbreaks should be reported promptly to initiate timely control measures across the border. WHO should facilitate information exchange and prepare a format that is agreed upon by the participating countries (Action: WHO, Member States).
- (2) A study-cum-observation tour for programme managers in the three countries should be organized. This should comprise structured training on various managerial and technical issues in an institution for about one week followed by visits to selected country sites to observe malaria control programmes in action. It is recommended that the structured training part take place in Shanghai. (Action: WHO).

- (3) ACTMalaria should officially extend invitation to DPR Korea and the Republic of Korea to join the network. Focal points for ACTMalaria in each country should be identified (Action: ACTMalaria, DPR Korea and Republic of Korea).
- (4) Asia vivax network should be established to help the countries (DPR Korea, Republic of Korea and PR China initially) to intensify collaboration in the control of vivax malaria. Start-up funds should be mobilized with the help of WHO to support the network (Action: WHO and Member States).
- (5) As the number of malaria cases decreases, there is increased need to strengthen the laboratory diagnosis including quality assurance. Microscopy is a priority but RDTs may have a place in the remote areas of PR China and in DPR Korea (Action: Member States in East Asia).
- (6) Stratification for better targeting of malaria control interventions, such as ITNs, MDA, and for defining high-risk areas should be based on information from smaller units which may be townships in PR China and ri in Republic of Korea and DPR Korea (Action: Member States in East Asia).
- (7) ITNs or other appropriate vector control measures should be scaled up in high-risk areas. For ITNs the objective should be to attain a coverage of at least 80% in the area selected. Monitoring and evaluation of ITNs should be further strengthened (Action: Member States in East Asia).
- (8) Therapeutic efficacy studies of chloroquine for the treatment of vivax malaria should be carried out in each country following the draft WHO protocol (Action: Member States in East Asia).
- (9) Countries are now using a number of different primaquine treatment regimens based on a total dose concept. Countries should monitor the effectiveness of these regimens as relevant to long incubation period relapsing malaria (Action: Member States in East Asia).
- (10) Operational research should be conducted to assess shorter effective regimens to improve compliance with an in-built system to monitor the completeness of treatment (Action: WHO and Member States).
- (11) Based on the experience of DPR Korea, mass prophylaxis with primaquine seems to be safe. However, a low frequency of serious side-effects including haemolytic side-effects has been reported. Therefore, necessary precautions should be taken when prescribing primaquine, particularly during mass prophylaxis, and to deal with the side effects promptly (Action: Member States concerned).

- (12) A small technical working group should be formed to assess the current knowledge and identify operational research and capacity needs related to vectors of vivax malaria (Action: WHO and Member States).
- (13) Methodologies need to be developed and studies carried out to assess vivax disease burden including case numbers and socioeconomic impact (Action: WHO and Member States).
- (14) Following the decline in the incidence of vivax malaria in the affected countries in East Asia, resources for malaria control should not be reduced. In order to effectively deal with resurgence and spread of malaria, efforts to strengthen the health system including monitoring and surveillance of malaria should be continued (Action: Member States and partners).

18. CONCLUSION

Prof. Tang Lin-Hua, Dr Krongthong Thimasarn, Dr Kevin Palmer and Dr Eigil Sorensen thanked the organizers of the meeting, the hosts and the staff in the local facilities. A lot of progress has been made and collaboration is increasing. The subject is important to all the three countries and is well supported by the two Regional Directors. The support provided by Professor Tang Lin-hua and Dr Gao Qi's team was acknowledged by all the speakers. Prof Tang Lin-hua stated that all the objectives of the meeting had been met.

Annex 1

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Annex 2 PROGRAMME

Day 1, 29 November 2004

08.30 – 09.00 hrs	Registration	
09.00 – 09.30 hrs	Opening Ceremony	
	– Background of the meeting	Dr Krongthong Thimasarn
	– Address by RD SEARO (to be read out by WR, DPRK)	Dr Eigil Sorensen
	– Address by RD WPRO (to be read by WR, CHN)	Dr Bekedam
	– Welcome remarks	Prof Tang Lin-hua
	– Self Introduction of participants	Participants
	– Appointment of Chair and Rapporteur	Dr Kevin Palmer
	– Administrative announcements	Dr Krongthong Thimasarn
	– Group photograph	

Review of malaria situation at regional level

10.00 – 10.30 hrs	Review of malaria situation in WPRO	Dr Palmer
10.30 – 11.00 hrs	Review of malaria situation in SEARO	Dr Krongthong

Technical updates

11.00 – 11.30 hrs	Recent development in vivax diagnosis	Dr David Bell
11.30 – 12.00 hrs	Treatment of <i>P. vivax</i> and monitoring of therapeutic efficacy of chloroquine and primaquine	Dr Eva Christophel

Current situation and progress on malaria control

13.00 – 13.30 hrs	Outcomes and recommendations of the bi-regional meeting on vivax malaria 2003	Dr Bell
13.30 – 14.15 hrs	Current malaria situation and progress on implementation of mass chemoprophylaxis and ITN in DPR Korea	Malaria Programme Manager DPR Korea

14.15 – 15.00 hrs	Malaria situation in PR China and implementation of malaria control in eastern provinces, PR China	Prof Tang Lin-hua
15.30 – 16.00 hrs	Implementation of malaria control in Republic of Korea with special attention to border areas	Malaria Programme Manager Republic of Korea
16.00 – 17.00 hrs	General discussion	

Day 2, 30 November 2004

Technical updates (continued)

08.30 – 09.00 hrs	Entomological studies in DPR Korea	Dr Gao Qi
09.00 – 09.30 hrs	Integrated vector management on control of vivax malaria	Dr Chusak Prasittisuk
09.30 – 11.30 hrs	Water management and intermittent control of water in rice paddy field to control <i>Anopheles sinensis</i>	Dr Chusak
	Experience in water management in malaria control in Sri Lanka	Dr Chusak
11.30 – 12.30 hrs	Intersectoral collaboration (Panel discussion)	Malaria Programme Manager DPR Korea, Republic of Korea and PR China
13.30 – 14.00 hrs	Asia Vivax Network	Dr Palmer
14.00 – 14.30 hrs	ACTMalaria: Role of the network in malaria control and extension of membership to Republic of Korea and DPR Korea	Prof Tang Lin-hua
14.30 – 15.30 hrs	Group work (3 groups) (to review progress in implementation of recommendations of the bi-regional meeting in November 2003)	
	Group 1 Capacity development, training, logistics and networking of institutions Group 2 Strategy for operationalization of malaria control and monitoring of therapeutic efficacy of chloroquine	(Participants will work in 3 groups. Core issues to be discussed will be provided)

Group 3 Review of current research and identify research needs, and networking of research on vivax malaria in East Asia

15.45 – 17.30 hrs **Group discussion** (continued) and preparation of brief presentations

Day 3, 1 December 2004

Field visit to Jiangxu Institute of Parasitic Diseases (JIPD) PR China

Day 4, 2 December 2004 Plenary Session

08.30 – 9.15 hrs Presentation of Group 1
Discussion

09.15 – 10.00 hrs Presentation of Group 2
Discussion

10.00 – 10.30 hrs Presentation of Group 3
Discussion

11.00 – 11.30 hrs Summary of lessons learned from field visit
Representatives of
Republic of Korea and
DPR Korea

11.30 – 12.00 hrs General Discussion

12.00 – 13.00 hrs **Recommendations**
Chairman and
Rapporteur

13.00 – 13.30 hrs **Conclusion**

14.30 – 17.00 hrs Informal discussion (Optional)

Annex 3

**OBJECTIVES OF FIELD VISIT TO JIANGXU INSTITUTE OF
PARASITIC DISEASES (JIPD) PR CHINA
1 DECEMBER 2004**

- (1) To observe facilities in research, training and implementation of malaria control
- (2) To observe field activity at county level
- (3) To observe current case detection, treatment and personal protection and vector control
- (4) To review malaria information system

Annex 4

GUIDELINES FOR GROUP WORK

- Select a chairperson and a rapporteur
- Briefly review the topics to be covered and **prioritise** those that your group would like to discuss.
- Allocate time that your group would like to spend on each of the items proposed to be discussed.
- Discuss what is implementable and, if possible, issues where there is a need for collaboration between two or more countries for the solution of a common problem.
- The group should focus on operationalization of the strategies. Separate the issues for implementation from those where research and evidence may be needed.
- If possible, a rough time plan for the next one year may be outlined.
- Discuss what resources may be required and from where these resources might become available.
- Discuss what support WHO might be requested to provide.
- Identify the bi-regional collaboration required to facilitate the work.
- The rapporteur should make notes and, if possible, the important conclusions and recommendations should be noted for presentation in the plenary.
- Discuss the main recommendations and obtain the approval of the chairperson.
- If possible make a power point presentation in the plenary

Group 1

Capacity development, training, logistics and networking of institutions

Suggested issues for discussion

- What is needed for development of capacity in the participating countries.
- What are the needs for development of capacity in diagnosis and treatment, integrated vector management, surveillance (disease and vector), early warning and response to epidemics/outbreaks.
- Training needs to enhance management skills at different levels of the control programme.
- What are the steps to be taken for DPR Korea and the Republic of Korea to become members of ACTMalaria.
- Who should become the focal point for coordinating capacity development in malaria control in East Asia.
- What steps are needed to enhance information exchange on surveillance- outbreaks and epidemics (surveillance network).
- How can border collaboration be established?
- Facilitation of drug efficacy monitoring through networking.
- Establishing IVM and ITN network.
- Training needs and identification of institutions to be responsible for training of staff.
- Procurement of drugs according to the national policy and collaboration in effective management of logistics.

Group 2

Strategy for operationalization of malaria control and monitoring of therapeutic efficacy of chloroquine

- Identification of first and second line treatment of *P vivax* malaria (long incubation period and relapsing type).
- Implementation guidelines to ensure complete treatment of vivax.

- Monitoring therapeutic efficacy of antimalarials in *P vivax* malaria.
- (sentinel sites, protocols to be used, what drugs should be included, should the studies be hospital-based or community-based, how to ensure follow-up of patients included.)
- Operationalization of mass chemoprophylaxis. In what situations should mass chemoprophylaxis be used.
- Quality control of diagnosis (Microscopy + Rapid Diagnostic Test)
- Improving reporting system/surveillance of disease and the vectors.
- Operationalization of IVM including scaling-up of ITN.
- Intersectoral collaboration.
- Monitoring of malaria control programme.
- Guidelines and standard operating procedures to prevent spreading of malaria from Demilitarized Zone to other areas.
- Stratification for implementation of operational strategies.

Group 3

Review of current research and identifying operational research needs and networking of research on vivax malaria in East Asia

- Identify researchable issues that were discussed during the meeting.
- Prioritize operational research projects.
 - Development and testing of suitable RDT for *P vivax*.
 - Dose regime of primaquine .
 - G6PD deficiency test.
 - Vector studies (e.g. vector biology, incrimination of vectors).
 - Replacement of chloroquine by suitable alternatives.
 - Primaquine on hibernation of *P vivax*.
 - Impact of mass chemoprophylaxis with primaquine.
 - Determining the gap between reported cases and the estimated cases. (validation of information)
 - Socioeconomic impact of malaria.
 - Vector control strategies (evaluation of ITN programme, pilot project on IVM in East Asia countries).

- Cost-effectiveness of diagnosis as a prerequisite for treatment.
- Increasing access to marginalized and difficult-to-reach populations.
- Developing protocols for operational research.
- Increasing capacity for operational research.
- Sharing of research findings.