Meeting Report

MEETING ON REVISED WHO MALARIA TREATMENT GUIDELINES FOR MALARIA-ENDEMIC COUNTRIES OF THE WESTERN PACIFIC REGION

30–31 August 2017
Hanoi, Viet Nam

World Health Organization
Western Pacific Region

WORLD HEALTH ORGANIZATION

REGIONAL OFFICE FOR THE WESTERN PACIFIC

RS/2017/GE/57(VNM) English only

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Convened by:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

Hanoi, Viet Nam
30–31 August 2017

Not for sale

Printed and distributed by:

World Health Organization
Regional Office for the Western Pacific
Manila, Philippines

February 2018

NOTE

The views expressed in this report are those of the participants of the Meeting on Revised WHO Malaria Treatment Guidelines for Malaria-Endemic Countries of the Western Pacific Region and do not necessarily reflect the policies of the World Health Organization.

This report was prepared by the World Health Organization Regional Office for the Western Pacific for governments of Member States in the Region and for those who participated in the Meeting on Revised WHO Malaria Treatment Guidelines for Malaria-Endemic Countries of the Western Pacific Region, which was held in Hanoi, Viet Nam from 30 to 31 August 2017.

CONTENTS

Keywords:

Malaria – epidemiology, prevention and control / Disease vectors / Therapeutic – standards / Regional health planning / Guideline / Antimalarials

ABBREVIATIONS

AHA	acute haemolytic anaemia
ACPR	adequate clinical and parasitological response
AL	artemether + lumefantrine
ACT	artemisinin-based combination therapy
ASMQ	artesunate + mefloquine
bw	body weight
CDC	Centers for Disease Control and Prevention
CCM	community case management
CQ	chloroquine
DHA-PIP	dihydroartemisinin + piperaquine
DRS	drug resistance surveillance
GMS	Greater Mekong Subregion
G6PD	glucose-6-phosphate dehydrogenase
IM	intramuscular
IV	intravenous
RDT	rapid diagnostic test
PCR	polymerase chain reaction
P.	*Plasmodium*
POC	point-of-care
PQ	primaquine
SP	artesunate + sulfadoxine + pyrimethamine
TES	therapeutic efficacy study

SUMMARY

The Meeting on the Revised WHO Malaria Treatment Guidelines for Malaria-Endemic Countries of the Western Pacific was convened from 30 to 31 August 2017 in Hanoi, Viet Nam. Malaria programme managers and case management focal points from the endemic countries in the Western Pacific – China, Cambodia, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, the Republic of Korea, Solomon Islands, Vanuatu and Viet Nam – attended the meeting.

The meeting objectives were:

- to address challenges faced while implementing their current national malaria treatment guidelines and update them as necessary;
- to rapidly facilitate expansion of universal access to quality-assured malaria diagnostics and treatment, especially to high-risk populations; and
- to adopt a practice of using quality-assured diagnostics for parasitological confirmation of malaria in all settings before use of antimalarial treatment.

Malaria-endemic countries in the Western Pacific Region have revised their national malaria treatment guidelines following WHO's recommendation on the use of artemisinin-based combination therapy (ACT). However, some countries have not yet introduced in their national treatment guidelines the use of single low-dose primaquine (0.25 mg/kg bw) with ACT to patients with *Plasmodium falciparum* malaria as a gametocytocidal to reduce transmission. In other countries, full and effective implementation of this policy is delayed.

Participants discussed issues and challenges faced in updating, revising and implementing national treatment guidelines that include regulatory, procurement and treatment guidelines dissemination with follow-up training of health-care providers. The need for updating national treatment guidelines based on results from therapeutic efficacy surveillance activities and full implementation of the WHO recommendations on the use of primaquine for *P. falciparum* and *P. vivax* was emphasized. Countries were encouraged to start full implementation of the use of low-dose primaquine as early as possible to arrest the further spread of falciparum malaria (especially important in the Greater Mekong Subregion, in the context of multidrug-resistant falciparum malaria) and the problem of relapses in vivax malaria. It was reiterated that low-dose primaquine was safe for use in *P. falciparum*-infected patients without screening for glucose-6-phosphate dehydrogenase (G6PD) deficiency status. It was emphasized that WHO recommends the use of primaquine for treatment of confirmed *P. vivax* infections irrespective of transmission intensity and that such use for *P. vivax*-infected patients should be guided by the G6PD status of infected patients.

The need to ensure universal access to quality-assured malaria diagnosis and treatment was emphasized to accelerate malaria control and elimination. The meeting discussed options and opportunities to accelerate achievement of universal access, including strengthening health systems, community-based case management, and involvement of the private sector in malaria service provision to high-risk populations with limited or no access to commodities and services. Strengthening surveillance including regular conduct of therapeutic efficacy studies (TES) on antimalarials that guide the revision of national treatment guidelines and ensure effective treatment of malaria patients was also discussed.

WHO will continue to provide technical assistance to Member States in reviewing, updating and implementing their national malaria treatment guidelines and in improving access to quality-assured malaria diagnostics and treatment by strengthening disease surveillance.

1. INTRODUCTION

1.1 Background

Malaria case management, consisting of early diagnosis and prompt effective treatment, remains a vital component of malaria control and elimination strategies. Malaria-endemic countries in the Western Pacific Region – China, Cambodia, the Lao People's Democratic Republic, Malaysia, Papua New Guinea, the Philippines, the Republic of Korea, Solomon Islands, Vanuatu and Viet Nam – have progressively updated their treatment policy from the use of monotherapy to the currently recommended artemisinin-based combination therapies (ACTs). ACTs have generally remained highly effective and well tolerated, and, when coupled with other preventive interventions, have contributed to substantial reductions in morbidity and mortality from malaria. Building on this success and the achievement of Millennium Development Goal (MDG) targets in the Region, the recently endorsed *Regional Action Framework for Malaria Control and Elimination in the Western Pacific (2016-2020)* aims to further reduce malaria mortality by 50% by 2020 and morbidity by 30%, relative to the 2015 baselines.

The Meeting on the Revised WHO Malaria Treatment Guidelines for Malaria-Endemic Countries of the Western Pacific Region informed countries of the need to scale up universal availability of quality-assured malaria diagnostic services and full implementation of the revised WHO malaria treatment guidelines within countries to facilitate achievement of national targets and collectively this regional goal.

See Annex 1 for the meeting agenda and Annex 2 for the list of participants.

1.2 Objectives

The objectives of the meeting were to:

- to inform malaria-endemic countries of the revised WHO malaria treatment guidelines;
- to review and compare national and WHO treatment guidelines; and
- to identify next steps for the implementation of the revised treatment guidelines in countries.

1.3 Opening remarks

Associate Professor Tran Thanh Duong, Director of the National Institute of Malariology, Parasitology and Entomology, gave the opening remarks on behalf of the Viet Nam Ministry of Health.
Dr Rabindra Abeyasinghe, Coordinator of the Malaria, other Vectorborne and Parasitic Diseases (MVP) Unit in the WHO Regional Office for the Western Pacific, delivered the welcome address on behalf of Dr Shin Young-soo, WHO Regional Director for the Western Pacific.

2. PROCEEDINGS

2.1 Technical session 1: Global and regional updates

2.1.1 Regional action framework for malaria control and elimination in the Western Pacific 2016-2020, and the need for implementation of updated national treatment guidelines – *Dr R. Abeyasinghe*

The overall vision of the Regional Framework is a region free of malaria and it has three goals: (1) reduce mortality due to malaria in the Region by 50% and morbidity by at least 30% by 2020, relative to 2015 baselines; (2) achieve malaria elimination in three countries by 2020; and (3) establish and maintain elimination-capable surveillance systems in all malaria-affected countries of the Western

Pacific Region by 2020. The Regional Framework is modelled on the three pillars and two supporting elements of the WHO *Global Technical Strategy for Malaria 2016–2030,* which are:

- Pillar 1: Ensure universal access to malaria, prevention, diagnosis and treatment
- Pillar 2: Accelerate efforts towards elimination and attainment of malaria-free status
- Pillar 3: Transform malaria surveillance into a key intervention
- Supporting element 1: Strengthening the underlying health system and the enabling environment
- Supporting element 2: Expanding four themes of research in support of improved delivery of services and innovation

The Regional Framework has listed several objectives under each pillar and several regional and country priorities. Some of these priorities that relate to treatment of malaria are: (1) responding aggressively to and eliminate malaria in areas with multidrug resistance (including ACT resistance) in Cambodia, the Lao People's Democratic Republic and Viet Nam; (2) respond aggressively to and reduce transmission in Papua New Guinea and in high transmission areas of the Lao People's Democratic Republic, the Philippines and Solomon Islands; (3) address the challenges posed by *Plasmodium vivax* and *P. knowlesi*; (4) determine malaria burden among mobile, migrant and marginalized population groups and ensure equity in access to services; (5) achieve rapid reduction of transmission in highly endemic areas through targeted delivery of both proven and innovative intervention; and (6) ensure adequate uptake and effectiveness of interventions through sound monitoring and evaluation.

2.1.2 Revised WHO treatment guidelines for malaria particularly its application to the Asia Pacific perspective – *Dr P. Olumese*

Malaria case management, consisting of early diagnosis and prompt effective treatment, remains a vital component of malaria control and elimination strategies. The third edition of the WHO *Guidelines for the Treatment of Malaria* (2015) contains updated recommendations based on new evidence particularly related to dosing in children, and it also includes recommendations on the use of drugs to prevent malaria in high-risk groups. The core principles underpinning this edition include: early diagnosis and prompt, effective treatment; rational use of antimalarial treatment to ensure that only confirmed malaria cases receive antimalarials; the use of combination therapy in preventing or delaying development of resistance; and appropriate weight-based dosing of antimalarials to ensure prolonged useful therapeutic life of products and an equal chance of being cured for all patients.

Key recommendations include that all cases of suspected malaria should have a parasitological test, either through quality-assured microscopy or rapid diagnostic test (RDT), to confirm the diagnosis. Results of such parasitological diagnosis should be available within less than 2 hours to health-care providers to ensure correct choice of antimalarial treatment and dosing. However, in the absence or delay of parasitological diagnosis, patients with suspected severe malaria, and other high-risk groups should be treated on clinical grounds.

<u>Treating uncomplicated falciparum malaria</u>

The therapeutic objective of treating uncomplicated falciparum malaria are to cure the infection as early and rapidly as possible, thus preventing progression to severe disease and reducing opportunities for onward secondary transmission. Early and effective treatment in foci of drug resistance will also contribute to preventing the further emergence and spread of antimalarial drug resistance.

Treatment of uncomplicated *P. falciparum* malaria in children and adults (except pregnant women in their first trimester) can be one of the following recommended ACTs:

- artemether + lumefantrine (AL)
- artesunate + amodiaquine
- artesunate + mefloquine (ASMQ)
- dihydroartemisinin + piperaquine (DHA-PIP)
- artesunate + sulfadoxine + pyrimethamine (SP)

ACT regimens should provide three days' treatment with an artemisinin derivative. In low-transmission areas, a single dose of 0.25 mg/kg bw primaquine (PQ) should be provided with the ACT to patients with *P. falciparum* malaria (except pregnant women, infants aged < 6 months, and women breastfeeding infants aged < 6 months) to reduce transmission, and testing for glucose-6-phosphate dehydrogenase (G6PD) deficiency is not required.

Recurrence of *P. falciparum* malaria can result from reinfection or recrudescence (treatment failure). Treatment failure may result from drug resistance or inadequate exposure of parasites to the drug due to suboptimal dosing, poor adherence, vomiting, unusual pharmacokinetics in an individual or substandard medicines. Treatment failures must be confirmed with appropriate parasitological tests. In case there is failure within 28 days of treatment, an alternative ACT (second-line treatment) known to be effective in the region must be provided. If there is a failure after 28 days, this could be considered a new infection and first-line treatment may be repeated. The distinction between recrudescence or a new infection can only be made by polymerase chain reaction (PCR) parasite genotyping of the initial and recurrent infections.

For a pregnant woman in her first trimester with uncomplicated *P. falciparum* malaria, seven days of quinine + clindamycin should be given. Infants less than 5 kg bw with uncomplicated *P. falciparum* malaria should be treated with an ACT at the same target dose (in mg/kg bw) as children weighing 5 kg. Non-immune travellers with uncomplicated *P. falciparum* malaria returning to non-endemic settings should also be given ACTs.

Treating uncomplicated vivax malaria

The therapeutic objective of treating uncomplicated vivax malaria is to cure both blood-stage and liver-stage infections (called radical cure), thereby preventing recrudescence and relapse, respectively.

In treating blood-stage uncomplicated non-falciparum malaria, either ACT (excluding pregnant women in their first trimester) or chloroquine (CQ) should be given in areas with CQ-susceptible *P. vivax*. In areas with CQ-resistant *P. vivax*, treatment should be with an ACT (excluding pregnant women in their first trimester). Treatment of pregnant women in their first trimester with CQ-resistant *P. vivax* malaria should be with quinine.

In all transmission settings, to prevent relapse, treatment of *P. vivax* or *P. ovale* malaria should be with PQ unless contraindicated.[1] The G6PD status of patients should be used to guide administration of PQ for preventing relapse. In G6PD normal individuals, use a 14-day course (0.25–0.5 mg/kg bw daily) of PQ. In people with G6PD deficiency, consider using PQ base at 0.75 mg/kg bw once a week for eight weeks, with close medical supervision for potential PQ-induced haemolysis. When G6PD status is unknown and G6PD testing is not available, the decision to prescribe PQ must be based on assessment of the risks and benefits of adding PQ. In women who are pregnant or breastfeeding, consider weekly chemoprophylaxis with CQ until delivery and breastfeeding is complete, then treat with 14 days of PQ to prevent future relapse.

[1] Primaquine is contraindicated in pregnant women, infants aged less than 6 months, and women breastfeeding infants less than 6 months of age.

Treatment of severe malaria

Treatment of adults and children (including infants, pregnant women in all trimesters, and lactating women) with severe malaria should be with intravenous or intramuscular artesunate for at least 24 hours or until able to tolerate oral medication. After at least 24 hours of parenteral therapy and being able to tolerate oral therapy, treatment should be completed with three days of oral ACT. Artesunate is given at a dose of 2.4 mg/kg/dose, but to ensure an equivalent drug exposure, children weighing less than 20 kg should receive a higher dose of artesunate (3 mg/kg/dose). If artesunate is not available, use artemether in preference to quinine.

Where complete treatment of severe malaria is not possible but injections are available, a single dose of intramuscular artesunate is given as pre-referral medication followed by referral to an appropriate facility for further management. Where intramuscular artesunate is not available, use intramuscular artemether or, if that is not available, use intramuscular quinine. Where intramuscular injections are unavailable, treat children less than 6 years of age with a single rectal dose (10 mg/kg) of artesunate and refer immediately to an appropriate facility for further management.

Management of malaria in special situations

In epidemics and humanitarian emergencies, there will be challenges in healthcare services delivery especially when there is an increase in malaria cases. Attempts should be made to improve diagnostic capacity rapidly, including provision of RDTs. If diagnostic testing is not feasible, the most practical approach is to treat all febrile patients as suspected malaria cases (“mass fever treatment”), with the inevitable consequences of over-treatment of malaria and potentially poor management of other febrile conditions. If this approach is used, it is imperative to monitor intermittently the prevalence of malaria as a true cause of fever and revise the policy appropriately.

In elimination settings, WHO recommends the addition of a single dose of PQ (0.25 mg base/kg bw) to ACT for uncomplicated falciparum malaria as a gametocytocidal medicine.

In artemisinin-resistant falciparum malaria, an effective ACT should still be used. Single-dose PQ (as a gametocytocide) should be added to all falciparum malaria treatment regimens. For the treatment of severe malaria in areas with established artemisinin resistance, it is recommended that parenteral artesunate and parenteral quinine be given together in full doses, followed by ACT.

Community case management (CCM) of malaria is recommended to improve access to prompt effective treatment of malaria episodes by trained community members living as close as possible to the patients. CCM of malaria is delivered as part of integrated CCM (iCCM), which includes treatment of pneumonia and diarrheal diseases. Trained community providers (community health workers, medicine sellers or retailers) should be provided with RDTs; ACTs for treatment of uncomplicated malaria; rectal artemisinin suppositories for pre-referral treatment of severe malaria; information, education and communication materials; and simple patient registers and reporting forms.

In some countries, private sector involvement in the provision of diagnosis and treatment in a public-private mix maybe explored. Training and supervision must, however, be provided and should comply with national treatment guidelines. Availability of quality-assured commodities, especially RDTs and ACTs, must be ensured, while surveillance and reporting to national authorities should continue.

The choice of ACT in a country or region should be based on optimal efficacy, safety and adherence. Where possible, use fixed-dose combinations rather than co-blistered or loose single agent formulations; and for young children and infants, use pediatric formulations, with preference for solid formulations rather than liquid formulations. Artemisinin and its derivatives should not be used as oral monotherapy for treatment of uncomplicated malaria. National drug and regulatory authorities should ensure that antimalarial medicines provided through both the public and private sectors are of

acceptable quality, through regulation, inspection and law enforcement. All programmes should regularly monitor therapeutic efficacy using the standard WHO protocols for assessing antimalarial drug efficacy.

2.1.3 Update on antimalarial drug resistance status in the Western Pacific Region – *Dr D. Bustos*

The updated WHO standardized *in vivo* protocol for the assessment of therapeutic efficacy (2016) is the standard guide to monitor drug efficacy and determine the need for updating or changing drug policy. Two drug resistance surveillance networks cover the countries in the WHO Western Pacific Region: (1) the Mekong Network covers Cambodia, China, the Lao People's Democratic Republic, Viet Nam and other countries in the WHO South-East Asia Region (Myanmar and Thailand), and (2) the Pacific Network covers Malaysia, Papua New Guinea, the Philippines, Solomon Islands, Vanuatu and other countries in the WHO South-East Asia Region (Timor-Leste and Indonesia). Every six months, the WHO Global Malaria Programme releases an update on artemisinin and ACT resistance with a specific focus on the latest validated TES results and genotypes for molecular markers. In the Greater Mekong Subregion (GMS), ACT failure rates increased between 2016 and 2017. There are four artemisinin-based combination therapies (ACTs) failing in Cambodia, and increasing evidence of partner drug failures in more provinces of the Lao People's Democratic Republic, Thailand and Viet Nam including confirmed presence of Kelch 13 (K13) mutations and other resistance markers. In Myanmar, the situation remains stable with ACT partner drugs, as well as in Yunnan, China, with high efficacy of first-line DHA-PIP among the few local and all imported cases

As countries move into elimination or pre-elimination, they need to ensure that a functional microscopy quality assurance system is a part of their case management, while routine assessment of the efficacy of first-line antimalarial drugs should be available to detect early signs of drug resistance.

2.1.4 Ensuring universal access to quality assured diagnosis and effective malaria treatment in the Western Pacific Region – *Dr R. Abeyasinghe* and *Ms G. Gonzales*

WHO recommends parasitological confirmation of malaria in all settings by quality-assured diagnosis before treatment is started. Treatment solely on the basis of clinical suspicion should be considered only when a parasitological diagnosis is not available within two hours of presentation of a patient for treatment. For malaria diagnostic tests, all sick people who fulfil the definition of a suspected malaria case should have access to a reliable malaria test, administered by a trained health worker at a health facility or community health centre. However, this does not include asymptomatic people in the context of strategies for eliminating malaria. The use of RDTs or microscopy should not be planned as a separate activity run by the National Malaria Control Programme but should be integrated into case management programmes as part of overall efforts to strengthen laboratory services and case management. Universal access to diagnostic and treatment services will be different in the burden reduction phase and elimination phase. This not only implies availability but they should also be: acceptable to the community; available throughout the year, especially in high-transmission seasons, with no stock-outs; be free or of affordable prices; and quality-assured.

Challenges in providing universal access to malaria diagnostic services and effective antimalarials may be due to: poor understanding of disease distribution in time and space; inaccurate quantification; maldistributions; limited physical access due to terrain and topography; cultural beliefs and practices; and availability of poor quality alternatives.

The availability of early and accurate parasitological diagnosis ensures proper care of parasite-positive patients and has been proven to result in better compliance with antimalarial treatment regimens and better management of non-malarial febrile illness. It also ensures that antimalarial medicines are not used inappropriately and that surveillance data are reliable. Prompt and effective treatment is also important as it: prevents progression of uncomplicated falciparum malaria to severe forms, especially in people with no or low immunity; prevents recrudescence and relapses; and prevents malaria

transmission and spread of drug resistance. Universal access to prompt and early diagnosis and treatment also allows for better management of severe falciparum malaria with reduced fatality rates.

To ensure quality of microscopy, WHO implements several activities such as: malaria microscopy trainings; establishment and maintenance of regional and national malaria slide banks for training and quality assurance; external quality assessment of national malaria laboratories; and external competency assessment of malaria microscopists. Additionally, WHO provides assistance to countries in establishing, reviewing and/or updating their national malaria microscopy quality assurance systems. For quality assurance of RDTs, WHO implements product and lot testing and from 2018 will adopt pre-qualification of malaria RDTs for quality assurance purposes.

To ensure antimalarial drug quality, WHO supports national drug and regulatory authorities in ensuring antimalarial medicines provided in both private and public sectors are of acceptable quality through regulation, inspection and law enforcement. WHO also recommends pre- and post-shipment testing of antimalarials to ensure compliance with quality standards. WHO also supports the regular conduct of therapeutic efficacy studies (TES) of antimalarial drugs using standard WHO protocols; and promotes rational use of antimalarial medicines

2.2 Technical session 2: Country presentations from the Greater Mekong Subregion

2.2.1 Cambodia national malaria treatment guidelines

Current treatments for uncomplicated *P. falciparum* malaria are guided by treatment responses as measured by TES. In 2000, ASMQ was used as first-line treatment and in 2008 DHA-PIP was introduced for use only in Pailin. In 2010, the treatment guideline was revised and the use of DHA-PIP was introduced in all provinces, with full implementation in 2011. In 2014, the treatment guideline was again revised but was only implemented in 2016 where ASMQ fixed-dose combination was used in five provinces. However, starting 2017, ASMQ was introduced in all provinces based on the results of TES conducted in 2015 and 2016, where ASMQ was shown to have a 100% adequate clinical and parasitological response (ACPR). Second-line treatment for all species of uncomplicated malaria is quinine + doxycycline/tetracycline, given for seven days. However, single low dose PQ use has only started to be piloted in sites (ASMQ + one single dose of PQ) where TES is being implemented. After the revision of the national treatment guideline this year and after training of health facilities on use of PQ, Cambodia hopes to implement addition of one single doze PQ + ACT in all provinces next year.

First-line treatment for *P. vivax* is same as for *P. falciparum* (i.e. ASMQ) plus PQ for 14 days or 8 weeks for radical cure. For *P. vivax*, use of PQ for radical cure has not yet started because of concerns about G6PD deficiency. It is proposed to introduce point-of-care (POC) G6PD kits in 2018.

2.2.2 Lao People's Democratic Republic national malaria treatment guidelines

From 2005 to 2015, AL was used as first-line treatment for malaria in the Lao People's Democratic Republic. The national malaria treatment guideline was revised in 2016, with the introduction of single low-dose PQ , where first-line treatment for uncomplicated *P. falciparum* malaria is AL (three days) + single dose PQ (0.25 mg/kg bw) to kill the gametocytes. Second-line treatment is quinine (30 mg/kg bw/day for seven days) + doxycycline 3.5 mg/kg bw/day for seven days + single dose of PQ 0.25 mg/kg bw. For pregnant women, oral quinine is recommended in the first trimester and AL in the second and third trimester. For severe falciparum malaria, artesunate injectable is recommended as first-line treatment and quinine infusion + AL for three days. For pregnant women, quinine infusion is recommended in the first trimester and artesunate injection in the second and third trimester.

For uncomplicated *P. vivax* malaria, first-line treatment is AL (3 days) + PQ (14 days) with G6PD test, while second-line treatment is CQ (3 days) + PQ (14 days) with G6PD test. For pregnant women, however, CQ is recommended for the first trimester and AL for the second and third trimester. If the G6PD test is normal, 0.25 mg/kg bw/day for 14 days is recommended, while for G6PD deficiency 0.75 mg/kg bw/week for 8 weeks is recommended. In the Lao People's Democratic Republic, CQ is

still used for *P. vivax* as second-line treatment because CQ resistance has only been confirmed in *P. falciparum.*

However, this new regimen was piloted in only five southern provinces in 2016 and hopefully will be fully implemented in 2018 after training of health facility workers.

Between 2005 and 2012, the therapeutic efficacy of AL, the first-line antimalarial treatment of *P. falciparum* at that time was still good with a cure rate of over 97%. However, the results of TES in 2013–2015 in Champasack and Sekong provinces have shown day 3 positivity rates of more than 10%. Thus, revision of the national malaria treatment guideline is planned after results of the DHA-PIP TES become available.

2.2.3 Viet Nam national malaria treatment guidelines

The malaria treatment guideline in Viet Nam was updated in 2016. First-line treatment for uncomplicated *P. falciparum* is DHA-PIP (40 mg DHA-PIP phosphate 320 mg) + PQ including mixed infections with *P. falciparum*. For uncomplicated *P. vivax, P. malariae* and *P. kwowlesi,* first-line treatment is CQ + PQ. For complicated malaria, all species, artesunate or quinine injection is recommended. For pregnant women, quinine + clindamycin is recommended for the first trimester for seven days and DHA-PIP in the second and third trimester for three days; and artesunate or quinine injection if the malaria is severe. Second-line treatment for *P. falciparum* is quinine + doxycycline or quinine + clindamycin for seven days.

First-line treatment for *P. vivax* is CQ phosphate, 25 mg base/kg for three days. Second-line treatment is DHA-PIP or other ACTs.

However, from the recent results of TES in 2016, there is resistance to DHA-PIP in Binh Phuoc, Dak Nong and Gia Lai. With this, the country is exploring change of first-line treatment in these provinces.

It was noted that *P. falciparum* and *P. vivax* are both decreasing but the proportion of *P. vivax* in relation to *P. falciparum* is increasing (79% *Pf* versus 20% *Pv* in 2006 and 56% *Pf* versus 42% *Pv* in 2016). This might mean that malaria control is effective but since PQ is not yet introduced (or compliance is very low), there are relapses. Also, it was noted that standby treatment with ACTs and treatment of clinical malaria with ACTs should be abandoned as soon as possible through scale-up of access to quality-assured laboratory diagnostics.

2.3 Technical session 3: Country presentations from Pacific countries

2.3.1 Papua New Guinea national malaria treatment guidelines

In its country presentation, Papua New Guinea highlighted that there have been stock-outs of ACTs, including PQ, since 2015. They associated these with the increased cases seen in those years.

Papua New Guinea still has to update its national malaria treatment guideline. The current guideline was revised in 2005–2009 and only implemented in 2011 with AL for *P. falciparum* as first-line treatment and DHA-PIP (3 days) as second-line treatment. First-line treatment for *P. vivax* is AL (3 days) + PQ (14 days) and second-line treatment is DHA-PIP (3 days) and PQ (14 days). For mixed infection of *P. falciparum /P. vivax*, treatment is the same as for *P. falciparum* and if *P. vivax/P. ovale* is confirmed, PQ is given. For severe *P. falciparum* or *P. vivax* malaria, artesunate intravenous (IV)/intramuscular (IM) or artemether IM followed by AL is given as first-line treatment; and quinine injection followed by oral doxycycline when patient is able to swallow as second-line treatment. However, the use of PQ for vivax infections is not routinely practised.

For pregnant women, uncomplicated malaria is treated with quinine plus SP in the first trimester and AL (first line) or quinine + SP (second line) during the second and third trimester. Severe malaria in pregnant women is treated with artesunate IV or IM (or artemether IM or quinine IM) followed by oral quinine and SP when the patient is able to swallow. For intermittent preventive treatment, three doses

of SP starting after 16 weeks and then after at least 4 weeks are given, though usage and compliance is poor.

The last TES was conducted in 2012–2014 for AL and DHA-PIP in Maprik and Alotau and ACPR showed 79–100% but no data on day 3 positivity. A TES for AL and CQ is currently planned and will be supported by WHO.

2.3.2 Philippines national malaria treatment guidelines

There is a decreasing trend in number of cases in the Philippines and most of the current cases are reported from Palawan province. Out of 86 provinces, only 8 provinces reported malaria cases in 2016. The majority of cases reported in Palawan and Maguindanao provinces is *P. falciparum,* while in other provinces with malaria *P. vivax* cases are mostly seen.

The national malaria treatment guideline in the Philippines was last revised in 2015 and this is included in the Malaria Manual of Procedure 2014-2020. First-line treatment for uncomplicated *P. falciparum, P. malariae* and *P. knowlesi* is AL (20–120 mg/ kg bw). A total dose range of 5-24 mg/kg bw/day of artemether and 29–144 mg/kg bw/day of lumefantrine is recommended given on a three-day schedule in six oral doses + PQ is also given at 0.25 mg/kg bw as a single oral dose on day 1 of treatment. Second-line treatment for uncomplicated *P. falciparum* is quinine sulfate 10 mg salt/kg bw every eight hours for seven days combined with either doxycycline (3 mg/kg bw) oral dose for seven days or tetracycline (250 mg/kg bw) four times a day for seven days or clindamycin (10 mg/kg bw) two times a day for seven days + PQ 0.25 mg/kg bw single dose on day 1 of treatment.

First-line treatment for *P. vivax* and *P. ovale* is CQ given at an initial dose of 10 mg/kg bw on day 1 and day 2, then 5 mg/kg bw on day 3. PQ is also given at a dose of 0.25 mg/kg bw/day once daily for 14 days. Second-line treatment for *P.vivax* is AL (20–120 mg), six oral doses in three days + PQ 0.25 mg/kg bw once a day for 14 days to start on day 1.

First-line treatment for complicated or severe *P. falciparum* is artesunate IV at 2.4 mg/kg bw in three doses at 12-hour intervals, then shift to AL, six oral doses in three days + PQ.

Use of PQ is low for both management of falciparum and vivax infections, thus in 2018 the national Malaria Control Program will train health facilities on the new treatment guidelines to improve the use of PQ.

Latest TES were done for AL for uncomplicated *P. falciparum* in 2015 and CQ for uncomplicated *P. vivax* in 2016, both in Palawan province. ACPR following these studies was 98.7% and 98.6% respectively, indicating good response to treatment.

It was noted that in 2017, procurement of ACTs has increased because the Malaria Control Program plans to provide ACTs even in provinces with no malaria cases and in private hospitals to increase early access.

2.3.3 Solomon Islands national malaria treatment guidelines

Malaria cases decreased from 2007 to 2014 but increased in 2015 and 2016. The increase may be attributed to increased access to quality-assured diagnostics and improved reporting following strengthening of surveillance. Most of the cases reported in 2016 are from Malaita (29%) and Guadalcanal (23%) provinces.

The malaria treatment guideline in Solomon Islands was developed in 2008 and implemented in 2009. This guideline is still currently in use. First-line treatment for *P. falciparum* is AL and for *P. vivax* is AL + PQ (14 days). The country faces a challenge with rational use of ACTs, as evidenced by the fact that 224 680 AL treatment packs were procured in 2014, 315 120 treatment packs in 2015 and 151 200 in 2016. However, during these years, only around 90 000 cases were reported annually and stock-outs of ACT were also reported.

Second-line treatment for *P. falciparum* and *P. vivax* is artesunate injectable or quinine oral/injectable.

TES were done in 2012–2013 in Tetere using AL for uncomplicated *P. falciparum* (20 patients enrolled) and uncomplicated *P. vivax* (59 patients enrolled). TES results showed a 100% ACPR for AL in uncomplicated *P. falciparum* and 94.9% ACPR in uncomplicated *P. vivax*.

2.3.4 Vanuatu national malaria treatment guidelines

Vanuatu has two elimination provinces: Torba and Tafea. Malaria cases went down from 2003 to 2008 but slightly increased in 2009 and 2010 when RDTs were rolled out in 2009. ACTs were also introduced in 2009, thus cases started decreasing again in 2011. Community microscopy and RDTs were used to diagnose malaria. However, in 2014, microscopy was limited to hospitals to ensure quality. The proportion of *P. falciparum* cases went down, but that of *P. vivax* cases went up and this may be attributed to better diagnosis and possible relapses due to non-use of PQ. A malaria death was last reported in 2011.

The malaria treatment guideline in Vanuatu was first developed in 2005 with CQ + SP as first-line treatment. This was revised in 2009 and 2014 when AL became the first-line treatment for uncomplicated *P. falciparum* and *P. vivax*. For severe malaria, artesunate IM and IV is recommended.

For the second-line treatment for *P. falciparum*, DHA-PIP is recommended but not currently available in Vanuatu (i.e. not procured in 2014–2016). Second-line treatment for *P. vivax* is PQ (0.25 mg/kg for 14 days) and this was procured in 2015. Vanuatu is implementing low-dose PQ but not in full capacity as health workers do not feel comfortable giving PQ to patients.

A TES was done in 2011–2012 using AL for uncomplicated *P. falciparum* and *P. vivax*. However, there were zero patients detected and enrolled in the study site with *P. falciparum* and thus the study was not completed. For AL in *P. vivax*, there were 82 patients enrolled (80 patients completing 28 days follow-up) and showed a 98.8% ACPR. In 2013, TES for AL for both uncomplicated *P. falciparum* and *P. vivax* were started but not completed as there were issues of enrolment and follow-up of patients.

2.4 Technical session 4: Country presentations from 2020 eliminating countries

2.4.1 China national malaria treatment guidelines

Malaria cases in China are continuously decreasing with only 3143 cases in 2016 (99.9% imported) and 1610 in January–June 2017 (100% imported cases). The three (out of 3143) indigenous cases were all *P. vivax*. Imported cases were determined after case investigation of the Chinese Center for Disease Control and Prevention (China CDC).

From 2000 to 2009, the national malaria treatment guideline recommended first-line treatment CQ + PQ for *P. vivax*; monotherapy of artesunate, DHA, artemether + PQ or ACT for *P. falciparum*; and artemether or artesunate injection for severe *P. falciparum*. In 2010, the treatment guideline was revised with CQ + PQ still for *P. vivax*, ACT for *P. falciparum*, and artemether and artesunate injection for severe *P. falciparum*. In the 2016 revision of the treatment guideline, first-line treatment for *P. vivax* and *P. falciparum* were still the same but for severe malaria, artesunate, artemether or pyronaridine injection was recommended.

Specifically, the following are the first-line treatment for *P. falciparum* in the last 3 years: DHA + PIP 8 tablets (2 tablets each for 0, 8, 24 and 32 hours); artesunate + amodiaquine 6 tablets (2 tablets each for day 1, 2 and 3); and artemisinin + PPQ 4 tablets (2 tablets each for day 1 and 2). Second-line treatment for (and severe) *P. falciparum* are: artesunate injection (artesunate 2.4 mg/kg, 0, 12 and 24 hours IV injection) and once a day until the patient is able to take oral medication, artemether injection (initially artemether 3.2 mg/kg IM injection ,then 1.6 mg/kg daily until the patient is able to take oral medication), and pyronaridine injection (pyronaridine 3.2 mg/kg (160 mg for an adult) IM injection or IV drip for three days).

First-line treatment for *P. vivax* is CQ (1.2 g for three days) + PQ (180 mg for eight days). For anti-relapse treatment PQ 180 mg is recommended. Second-line treatment for *P. vivax* is ACT (DHA-PIP 8 tablets for three 3 days) + PQ (180 mg for eight days). Anti-relapse treatment is PQ 180 mg.

TES were conducted in 2012–2013, 2015 and 2016 for DHA-PIP and all showed 99–100% ACPR.

To address malaria in the border areas of China and Myanmar, there are three levels of service provision. The first level is in the villages near the border where laboratory diagnosis and treatment are given free of charge to villagers from both China and Myanmar. The second level is in the border area where microscopy clinics have been established. And the third level is the different nongovernmental organizations providing diagnosis and treatment in the border areas.

2.4.2 Malaysia national malaria treatment guidelines

Malaria cases in Malaysia have been decreasing since 2009. Interestingly, human malaria cases are decreasing, but the number of zoonotic malaria cases (i.e. *P. knowlesi*) is increasing. Malaria treatment guidelines were published in 1994, 2000, 2008 and most recently in 2013. ACT was first introduced in 2008.

The current treatment guideline recommends AL (three days with total six doses) + PQ (0.75 mg/kg (max 45 mg) at day 1 of treatment) for uncomplicated *P. falciparum* malaria. Second-line treatment is ASMQ fixed-dose combination tablet or oral quinine (10 mg/kg) every eight hours with oral doxycycline (100 mg twice a day for seven days).

For severe *P. falciparum* malaria, first-line treatment is artesunate IV, then a complete course or oral ACT (AL or ASMQ) + PQ 0.75 mg/kg (max 45 mg) at day 1 of treatment. Second-line treatment is quinine IV and oral doxycycline. For pregnant women, oral quinine and oral clindamycin are recommended in the first trimester and ACT (AL) during the second and third trimester.

For uncomplicated *P. vivax/P. ovale*, ACT (AL) and PQ (30 mg once daily for 14 days). For severe *P. vivax/P. ovale* malaria, artesunate IV is recommended. For pregnant women, oral quinine and oral clindamycin are recommended in the first trimester and ACT (AL) during the second and third trimester + PQ (30 mg once daily for 14 days given post-delivery).

For uncomplicated *P. malariae/P. knowlesi*, AL is given as first-line treatment and ASMQ or oral CQ as second-line treatment. For severe *P. malariae/P. knowlesi*, artesunate IV is recommended while for pregnant women, oral quinine and oral clindamycin are given in the first trimester and AL in the second and third trimester.

TES in Malaysia is integrated into the mainstream surveillance system since 2014. Therapeutic efficacy of AL for uncomplicated *P. falciparum* and *P. knowlesi* was studied yearly in 2014–2017. All cases of confirmed *P. falciparum/P. knowlesi* malaria were enrolled taking into consideration inclusion criteria. ACPR in all TES is 100% and day 3 positivity is less than 10%.

2.4.3 Republic of Korea national malaria treatment guidelines

The Republic of Korea was in the pre-elimination phase from 2007 to 2011 and has been in the elimination phase since 2012. An average of approximately 600 malaria cases (domestic and imported) were diagnosed from 2011 to 2016 and all domestic cases are *P. vivax* malaria. Patients are mostly local citizens, active soldiers and discharged soldiers (within two years after military service at the demilitarized zone).

Cases of domestic malaria patients are *P. vivax* and first-line treatment since 1998 is CQ 25 mg base/kg for three days + PQ (15 mg base (14 days) or 0.25 mg/kg/day (3.5 mg base/kg)). For second-line treatment, mefloquine + PQ are given. There is no reported G6PD deficiency among patients in the country. For pregnant women, CQ is also recommended but with no PQ. All malaria

cases with *P. falciparum* were imported cases and doctors follow the WHO malaria treatment guidelines.

For imported cases, Korea Centers for Disease Control and Prevention produces an annual publication on the national malaria control guideline, which includes status of drug resistance in malaria risk countries. Drugs used for imported malaria cases are: atovaquone-proguanil, mefloquine, quinine sulfate, artesunate injectable, quinidine gluconate injectable and quinine hydrochloride injectable.

Malaria chemoprophylaxis for *P. vivax* is given to soldiers stationed in malaria risk areas since 1996 which contains CQ (15 weeks from July to October) + PQ (14 days in October).

2.5 Technical session 5: Addressing regional priorities and challenges

2.5.1 Addressing challenges to universal access through strengthening surveillance and community case management – *Dr R. Abeyasinghe*

One of the three pillars of the WHO *Global Technical Strategy for Malaria 2016–2030* highlights the need for universal access to malaria prevention, diagnosis and treatment to dramatically reduce morbidity and mortality. Challenges to universal access include: poor understanding of disease distribution in time and space; inaccurate quantification of requirements; maldistribution of commodities and services; limited physical access due to terrain and topography; cultural beliefs and practices; and availability of poor-quality alternatives.

To ensure universal access to diagnostic testing of all suspected malaria cases: all patients who are suspected to have malaria should have the diagnosis confirmed by parasite detection methods such as quality-assured microscopy or RDT; both public and private sector health services should confirm diagnosis before administering antimalarial treatment; and every confirmed case should be tracked and reported in the surveillance system in order to inform programme planning. Thus universal access to diagnostic testing will reduce the overuse of ACTs – the first-line treatment for uncomplicated malaria – and contribute to reducing the drug pressure on the parasite population.

Scaling up community-based diagnostic testing treatment involves training and deployment of community health workers and volunteers who can substantially complement and extend the reach of public health services, particularly in rural and remote areas, where health infrastructures tend to be the weakest and malaria transmission the highest. The strategic use of community health workers and volunteers in malaria prevention and care not only bridges health system gaps, but ensures a continuum of care for the most disadvantaged populations.

Community case management (CCM) is recommended by WHO to improve access to prompt effective treatment of malaria episodes by trained community members living as close as possible to the patients. The use of ACTs in this context is feasible, acceptable and effective. Pre-referral treatment for severe malaria with rectal artesunate and use of RDTs are also recommended in this context. CCM of malaria is best integrated into community management of childhood illness.

Community health workers are an integral part of the health system and they provide a link between the community and the formal health system (they liaise with health workers in the formal health system). They are important in providing care to vulnerable groups in remote areas with little access to health facilities and assist in providing access to preventive services (mosquito net distribution) and/or patient care in countries. Strengthening private sector case detection and management can also increase access in some situations and countries

Another pillar of the *Global Technical Strategy for Malaria 2016–2030* is to transform malaria surveillance into a core intervention. Strengthening malaria surveillance is fundamental to programme planning and implementation and is a crucial factor for accelerating progress. In the three eliminating countries (China, Malaysia and the Republic of Korea), surveillance systems have been strengthened and they could thus report domestic and imported cases, among others.

Early steps to strengthen surveillance systems include: testing all individuals with suspected malaria and recording the number of persons tested, details of all confirmed cases; enhancing the quality and timeliness of case reporting through training and supervision; including community case detection, confirmation and reporting of malaria cases; including cases detected by all parts of the health system; and developing reference laboratory capacity for verification of parasitological diagnosis of malaria.

2.5.2 Addressing the challenge of vivax malaria – determining G6PD status including use of POC diagnostics and use of primaquine – *Dr P. Olumese*

P. vivax burden and the contribution of malaria relapses to transmission were discussed. The therapeutic objective of treating uncomplicated *P. vivax* (and *P. ovale*) malaria was highlighted, which includes curing both blood-stage and liver-stage infections to prevent recrudescence and relapse, respectively. Antimalarial medicines (i.e. ACTs) are used to cure blood-stage infection and PQ is used to cure liver-stage infection, thus preventing relapses. PQ is currently the only available anti-relapse medicine. However, its full potential is not realized because it produces dose-dependent acute haemolytic anaemia (AHA) in individuals with G6PD deficiency. The challenge is that G6PD testing is often not available at POC, and PQ is either given without prior G6PD testing, exposing some patients to the risk of drug-induced AHA, or not administered, exposing patients to the risk of repeated relapses with consequent morbidity and contribution to transmission.

WHO recommends that in all transmission settings, treatment of *P. vivax* or *P. ovale* malaria should include PQ unless contraindicated[2] to prevent relapses. The G6PD status of patients should be used to guide administration of PQ for preventing relapse. In G6PD-normal individuals, a 14-day course (0.25–0.5 mg/kg bw daily) of PQ should be used. In people with G6PD deficiency, consider using PQ base at 0.75 mg/kg bw once a week for eight weeks, with close medical supervision for potential PQ-induced haemolysis. When G6PD status is unknown and G6PD testing is not available, the decision to prescribe PQ must be based on assessment of the risks and benefits of adding PQ. In women who are pregnant or breastfeeding, consider weekly chemoprophylaxis with CQ until delivery and breastfeeding is complete, then treat with 14 days of PQ to prevent future relapses.

The expected benefits of following the above guideline are decreased morbidity due to *P. vivax/P. ovale* relapses and reduced risk to develop AHA in G6PD-deficient patients. When there are fewer cases of *P. vivax/P. ovale* relapse and AHA, this will unburden the health system through a decreased need for malaria and AHA management (including blood transfusion services) and will also contribute to reducing transmission of these parasites.

Current limitations of available POC G6PD testing was also discussed as well as WHO's preferred product characteristics for POC G6PD test kits.

2.5.3 Management of resistance to ACTs including artemisinin and partner drugs – accelerated elimination of falciparum – *Dr D. Bustos* and *Dr R. Abeyasinghe*

Parasite resistance to artemisinins, the key compound in ACTs, is now confirmed in five countries of the GMS – Cambodia, the Lao People's Democratic Republic, Myanmar, Thailand and Viet Nam. The spread and/or de novo emergence of artemisinin and partner drug resistance beyond the GMS poses a global threat. Artemisinin (partial) resistance is delayed resistance which shows day 3 positivity and is confirmed with presence of K13 mutation. ACT failure is when there is treatment failure following treatment with an ACT due to partner drug failure, regardless of the presence of artemisinin resistance. ACT resistance means resistance to both compounds – that is, artemisinin resistance and partner drug resistance.

[2] Primaquine (PQ) is contraindicated in pregnant women, infants aged less than 6 months, and breastfeeding women of infants aged less than 6 months.

Multidrug resistance requires resistance to more than two operational antimalarial compounds of different chemical classes.

WHO recommends countries to routinely conduct TES to measure the clinical and parasitological efficacy of ACTs and detect changes in treatment outcomes. TES remains the "gold standard" for evidence to guide drug policy. As countries progress to very low numbers of malaria cases, monitoring drug efficacy should be integrated into the national malaria case surveillance system. In the GMS, drug resistance surveillance (DRS) is now being piloted in Thailand and Viet Nam. Malaysia has commenced integrated drug efficacy surveillance in 2012 (five species), and the Philippines plans to do so in 2018.

When artemisinins start to fail (partial) resistance, parasite clearance is slowed, and ACT failure rates and gametocytemia increases. There is greater selective pressure on the partner drug, to which resistance is also increasing. As partner drug resistance increases, failures occur earlier by day 14 or day 21. There is also continued use of ineffective drugs that fuels the spread of resistance. To manage cases in this situation, it is necessary to always have an effective ACT or any other antimalarial as applicable in the area and have buffer stock of other ACTs available in known artemisinin-resistant areas. It is important to ensure that PQ (as gametocytocidal) is given with supervised treatment. For uncomplicated malaria in artemisinin-resistant areas, any one of these ACTs should work; if it fails, move to second-line ACT: DHA-PIP, AL, artesunate + amodiaquine, ASMQ, artesunate + pyronaridine. Quinine + doxycycline should also be available. For severe malaria in artemisinin-resistant areas, parenteral artesunate (or artemether IM) and parenteral quinine should be given in full doses for a minimum of 24 hours. Note that in patients with impaired consciousness or previous mefloquine intake, ASMQ should be avoided. A decision map on when to change drug policy was also presented and discussed.

The need for an accelerated elimination strategy in the GMS due to resistance was again emphasized. Falciparum malaria in the GMS is becoming increasingly resistant to antimalarial medicines in different areas of the GMS. If this continues to happen, it could become untreatable with the current antimalarials within a few years. However, now that malaria burden is low in the GMS, eliminating *P. falciparum* from the subregion should be prioritized.

The goals of the Strategy for Malaria Elimination in the Greater Mekong Subregion 2016–2030 are to eliminate malaria by 2030 in the GMS, including eliminating *P. falciparum* malaria by 2025, and to maintain malaria-free status and prevent reintroduction, where transmission has been interrupted. The Strategy also outlines regional and country priorities to achieve the goals and objectives as well as key interventions to accelerate achievement of goals.

2.5.4 Management of knowlesi malaria – *Dr N. Anstey*

The rise of *P. knowlesi* malaria in east Malaysia and predicted distribution of human *P. knowlesi* infection in a few neighbouring countries of the WHO Western Pacific Region were described. Current diagnosis of *P. knowlesi* is by microscopy. However, microscopy has limitations as there are no clear morphological characteristics to identify knowlesi parasites and hence there is considerable misdiagnosis where *P. knowlesi* is misdiagnosed as *P. falciparum*, *P. vivax* or *P. malariae.* as evidenced in several research studies in Malaysia. Thus, molecular testing using nucleic acid amplification methods such as PCR is recommended to confirm *P. knowlesi* diagnosis.

The demographic distribution of *P. knowlesi* cases was shown referencing several studies conducted in Malaysia. Studies in Malaysia also suggest that severe malaria following *P. knowlesi* infection occurs at lower parasitaemia than *P. falciparum* or *P. vivax,* though most patients have uncomplicated malaria. Very few numbers of severe *P. knowlesi* were observed but mostly in adults. Importantly there were no reported severe *P. knowlesi* cases or deaths in children.

Age (over 45 years) and parasitaemia (> 15,000/µL) are the two independent predictors of severe knowlesi malaria. Treatment of uncomplicated *P. knowlesi* is ACT (AL as first-line and ASMQ or oral

CQ as second-line treatment). For severe *P. knowlesi*, artesunate IV is recommended, while for pregnant women oral quinine and oral clindamycin are given in the first trimester and AL in the second and third trimester.

2.6 Technical session 6: WHO guidelines on management of severe malaria

2.6.1 Update on guidelines for the management of severe malaria – *Dr P. Olumese*

Severe malaria is defined by clinical and laboratory evidence of vital organ dysfunction. It is most commonly caused by falciparum; however, vivax and knowlesi also cause severe disease. At-risk populations are those in high-transmission areas, particularly young children (< 5 years old) and non-immune visitors (of any age) from non-endemic areas.

The main objective of management of severe malaria is to prevent patient from dying. Secondary objectives are to prevent disabilities and prevention of recrudescent infection. Thus, severe malaria is a medical emergency requiring rapid diagnosis, and starting effective treatment at the highest possible level of care is critically important for successful outcomes. A high index of suspicion and travel history are also important.

All cases of suspected severe malaria should have a parasitological test to confirm the diagnosis. In the absence or delay of parasitological tests, patients with suspected severe malaria and other high-risk groups should be treated on clinical grounds. Diagnosis includes confirming the presence of parasites and extent of organ dysfunction. Results of initial diagnostic evaluation can guide the management of the patient as well as serve as prognostic indicators of the disease.

The management of severe malaria comprises four main areas: (1) clinical assessment of patient: (2) specific antimalarial treatment; (3) additional treatments (managements of other complications); and (4) supportive care. Antimalarial treatment includes: artesunate IV or IM for at least 24 hours and until able to tolerate oral medication (all age groups, pregnant women in all trimesters and lactating women). After at least 24 hours of parenteral therapy and ability to tolerate oral therapy, complete treatment with 3 days of ACT should follow. Artesunate is given at 2.4 mg/kg/dose but to ensure an equivalent drug exposure, children weighing less than 20 kg should receive a higher dose of artesunate (3 mg/kg/dose). If artesunate is not available, use artemether in preference to quinine. Where complete treatment of severe malaria is not possible but injections are available, a single dose of artesunate IM is given as pre-referral medication followed by referral to an appropriate facility for further care. Where artesunate IM is not available, use artemether IM, or, if that is not available, use quinine IM. Where intramuscular injections are unavailable, treat children less than 6 years of age with a single rectal dose (10 mg/kg) of artesunate and refer immediately to an appropriate facility for further care. Other complications such as severe anaemia, hypoglycaemia, respiratory oedema and renal failure should also be managed.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

- Universal access to quality-assured malaria diagnosis and treatment is important to achieve malaria elimination
- It was emphasized that parasitological confirmation of malaria in all settings by quality-assured diagnosis should be done before use of antimalarial treatment. Treatment solely on the basis of clinical suspicion should be considered only when access to parasitological diagnosis is not available within two hours of the patient arriving to seek treatment.
- Early and accurate parasitological diagnosis is important to ensure care of parasite-positive patients and achieve better compliance with antimalarial regimens. This is also to facilitate better management of non-malarial febrile illnesses.
- Prompt and effective treatment is important to prevent progression from uncomplicated malaria to severe forms, and to limit further transmission of malaria.

- Regular conduct of TES on antimalarials is the cornerstone for revising national treatment guidelines and ensuring effective treatment of malaria patients.
- Malaria-endemic countries in the Western Pacific Region have revised their national malaria treatment guidelines in the last three years, except Papua New Guinea and Solomon Islands who revised their treatment guidelines in 2009.
- All malaria-endemic countries in the Region are following WHO's recommendation on the use of ACT.
- Papua New Guinea, Solomon Islands, Vanuatu and Viet Nam have not yet introduced in their national treatment guidelines the use of single low-dose PQ (0.25 mg/kg) with ACT to patients with *P. falciparum* malaria as a gametocytocidal to reduce transmission. Effective implementation of this policy is delayed in Cambodia, the Lao People's Democratic Republic and the Philippines.
- Stock-outs of first- and second-line treatments for malaria were experienced in some countries and reported to have contributed to an increase in the number of cases reported by Papua New Guinea in 2016. Such stock-outs need to be prevented as they contribute to increased transmission and deaths.
- As the malaria burden goes down, it becomes difficult to source ACTs. Thus, countries with support from partners such as WHO should maintain a stockpile of ACTs which can be easily accessed when needed.
- Community case management of malaria delivered in areas with limited access to health facilities (more than two hours' travel time away), delivered through trained community workers will contribute to achieving universal access to malaria diagnostic and treatment services.
- The private sector, through a public–private mix, may also have a role in increasing access to malaria diagnostics and treatment. For example, they may assist in project development sites by providing access to quality-assured commodities, and assisting in surveillance and reporting.
- All three countries that are in the elimination phase (China, Malaysia and the Republic of Korea) have started using PQ early and have strengthened their surveillance system.

3.2 Recommendations for Member States

Member States are encouraged to do the following:

1. Start full national implementation of the use of low-dose PQ for *P. falciparum* malaria as early as possible to further reduce transmission, which is especially urgent in countries reporting resistance to artemisinin and its partner drugs.
2. Conduct training and information dissemination campaigns to inform clinicians on the new treatment guidelines, which include the use of a single dose of PQ for *P. falciparum* malaria to reduce transmission.
3. Strengthen malaria surveillance systems and use data for accurate quantification and logistics management to prevent stock-outs of ACTs.
4. Review their plans according to the guideline documents developed by WHO on the quality assurance of malaria microscopy and RDTs, and establish/strengthen systems and procedures for quality assurance of malaria diagnosis.
5. Ensure early implementation of PQ regimens to treat *P. vivax* malaria in view of the increasing proportion of *P. vivax* infections, including measures to ensure compliance with such regimens.
6. Improve access to quality-assured diagnostics and treatment, particularly in most vulnerable communities, and explore community case management and private sector participation.
7. Conduct regular TES following the WHO protocols, including the use of study results to review and update national treatment guidelines.

3.3 Recommendations for WHO

WHO is requested to do the following:

1. Provide technical assistance to countries in reviewing and updating their national malaria treatment guidelines, including working at individual country levels to correct gaps seen in existing national treatment guidelines.
2. Support the full implementation of updated national treatment guidelines through the provision of technical assistance and monitoring of such implementation, including support for preventing stock-outs of first- and second-line treatments.
3. Continue working with countries on improving access to quality-assured malaria diagnostics and treatment, particularly by strengthening surveillance systems and analysing data generated to identify both in time and space where transmission requires intervention.
4. Facilitate the implementation of WHO-recommended PQ regimens for *P. falciparum* and *P. vivax* malaria, and, wherever relevant, support the piloting of point-of-care tests to detect glucose-6-phosphate dehydrogenase deficiency for management of *P. vivax* malaria.

ANNEX 1

AGENDA

Day 1: Wednesday, 30 August 2017		
08:30 – 09:00	Registration	
Opening Session		
09:00 – 09:30	Welcome address	Dr Shin Young-soo Regional Director, WPRO (To be determined) Ministry of Health, Vietnam
	Meeting objectives	Dr Rabindra Abeyasinghe Coordinator, WPRO/MVP
	Self-introduction of participants and observers	
	Nomination of the Chair and Rapporteur	
	Administrative announcements	Ms Glenda Gonzales, Technical Officer, WPRO/MVP
09:30 – 10:00	*Group photograph followed by coffee/tea break*	
Session 1:	***Global and regional updates***	
10:00 – 10:30	Regional action framework for malaria control and elimination in the Western Pacific, 2016-2020 and the need for implementation of updated national treatment guidelines	Dr Rabindra Abeyasinghe
10:30 – 11:00	Revised WHO treatment guidelines for malaria – what's new from an Asia Pacific perspective	Dr Peter Olumese, Medical Officer, Prevention, Diagnostics and Treatment, Global Malaria Program
11:00 – 11:30	*Discussion*	
11:30 – 12:00	An update on antimalarial drug resistance status in the Western Pacific Region *Discussion*	Dr Dorina Bustos, Malaria Technical Officer, Thailand
12:00 – 12:30	Ensuring universal access to quality assured diagnosis and effective malaria treatment in the Western Pacific Region *Discussion*	Ms Glenda Gonzales /Dr Rabindra Abeyasinghe
12:30 – 13:30	*Lunch break*	
Session 2:	***Country Presentations from Greater Mekong Subregion***	
13:30 – 14:00	National Malaria Treatment Guidelines in Cambodia	Cambodia
	Discussion (15 min)	
14:00 – 14:30	National Malaria Treatment Guidelines in the Lao People's Democratic Republic	Lao People's Democratic Republic
	Discussion	
14:00 – 14:30	National Malaria Treatment Guidelines in Viet Nam	Viet Nam
	Discussion	

14:30 – 15:00	*Coffee / tea break*	
Session 3:	***Country Presentations from Pacific Countries***	
15:00 – 15:30	National Malaria Treatment Guidelines in Papua New Guinea	Papua New Guinea
	Discussion	
15:30 – 16:00	National Malaria Treatment Guidelines in Philippines	Philippines
	Discussion	
16:00 – 16:30	National Malaria Treatment Guidelines in Solomon Islands	Solomon Islands
	Discussion	
16:30 – 17:00	National Malaria Treatment Guidelines in Vanuatu	Vanuatu
	Discussion	
17:00 – 19:00	*Reception dinner*	

Day 2: Thursday, 31 August 2017		
Session 4:	***Country Presentations from E2020 eliminating countries***	
08:30 – 09:00	National Malaria Treatment Guidelines in China	China
	Discussion	
09:00 –09:30	National Malaria Treatment Guidelines Malaysia	Malaysia
	Discussion	
09:30 – 10:30	National Malaria Treatment Guidelines in Republic of Korea	Republic of Korea
	Discussion	
10:30 – 11:00	*Coffee/tea break*	
Session 5:	***Addressing regional priorities and challenges***	
11:00 – 11:45	Ensuring universal access to quality assured malaria diagnostics and treatment – addressing regional challenges through strengthening surveillance and community based case management	Dr Rabindra Abeyasinghe
	Discussion	
11:45 – 12:30	Addressing the challenge of vivax malaria – determining G6PD status including use of POC diagnostics and use of primaquine	Dr Peter Olumese
	Discussion	
12:30 – 13:30	*Lunch break*	
13:30 – 14:30	Management of resistance to ACTs including artemisinin and partner drugs – accelerated elimination of falciparum	Dr Dorina Bustos/ Dr Rabindra Abeyasinghe
	Discussion	
14:30 – 15:00	Management of knowlesi malaria	Dr Nicholas Mark Anstey
	Discussion	
15:00 – 15:30	*Coffee/tea break*	

Session 6:	***WHO guidelines on management of severe malaria***	
15:30 – 16:15	Update on guidelines for the management of severe malaria	Dr Peter Olumese
	Discussion	
Session 7:	***Next Steps & closing***	
16:15 – 16:45	Discussion on next steps and identification of country priorities	Dr Rabindra Abeyasinghe
16:45 – 17:00	Closing	Dr Rabindra Abeyasinghe

ANNEX 2

LIST OF PARTICIPANTS

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