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Regional Office for South-East Asia

Regional Technical Advisory Group (RTAG) for the Kala-azar Elimination Programme

Report of the Fifth Meeting
Paro, Bhutan, 17-19 September 2013

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Contents

Acronyms

ASHAs	accredited social health activists
DAT	direct agglutination test
DDT	dichlorodiphenyltrichloroethane
DNDi	drugs for neglected diseases initiative
EVM	environmental management
iOWH	one world health
IRS	indoor residual spraying
ISC	Indian subcontinent
ITNs	insecticide-treated nets
IVM	integrated vector management
KA	kala-azar
LAMB	liposomal amphotericin B
LAMP	loop-mediated isothermal amplification
LST	leishmanin skin testing
MoU	memorandum of understanding
MSF	Medicines sans Frontières
NTDs	neglected tropical diseases
PHC	primary health care
PKDL	post-kala-azar dermal leishmaniasis
QPCR	quantitative polymerase chain reaction
RDT	rapid diagnostic test

RTAG	Regional Technical Advisory Group
SEA	South-East Asia
SSG	sodium stibogluconate
TDR	Research and Training in Tropical Diseases
VL	visceral leishmaniasis
VL–HIV	visceral leishmaniasis–human immunodeficiency virus coinfection
WHO	World Health Organization

Executive summary

Kala-azar (KA) or visceral leishmaniasis (VL) is the second largest parasitic killer disease in the world after malaria and it is one of the most dangerous neglected tropical diseases (NTDs). The disease is prevalent in Bangladesh, India and Nepal in the WHO South-East Asia (SEA) Region. Recently, Bhutan started to report sporadic cases of KA. The disease affects the poorest communities in these countries and kills the patient if left untreated for a long time. Globally it is estimated that 200 000–400 000 new cases and 20 000–40 000 deaths occur every year. An estimated 147 million people in 119 districts in 4 countries, namely Bangladesh, Bhutan, India and Nepal, are at risk. India alone accounts for about 50% of the global burden. With little data on the burden of post-kala-azar dermal leishmaniasis (PKDL), surveillance needs to be established and/or strengthened for PKDL. The role of asymptomatic leishmania infection is not clear and further studies are needed. Diagnosis in past kala-azar cases, PKDL and asymptomatic infections, and test of cure are difficult as there are no tools currently available or the existing tools are not well standardized.

As recommended in the Fourth Meeting of the Regional Technical Advisory Group (RTAG), liposomal amphotericin B (LAMB) as single dose (10 mg/kg) (or multiple doses (15 mg/kg)) is the first choice regimen for the Indian subcontinent (ISC) in the attack phase. The combination regimens (LAMB/paromomycin, LAMB/miltefosine, and paromomycin/miltefosine) have been recommended as a second choice regimen, and to be used as a long-term strategy. Monotherapy with miltefosine was recommended to be phased out gradually. Miltefosine monotherapy has been observed to show decreasing cure rates with Nepal observing up to 20% relapses at 12 months after treatment. This was not related to the development of parasite drug resistance, lack of compliance or reinfection. Treatment of PKDL requires long courses of therapy and very few clinical trials have been conducted to compare the different regimens. The World Health Organization (WHO) has recently developed guidelines for the diagnosis and treatment of PKDL for the Indian Sub-Continent (ISC).

The strategy for vector control should incorporate the integrated vector management (IVM). Presently, three tools are considered to be useful for vector control in KA transmission: indoor residual spraying of insecticides, long-lasting insecticide impregnated bednets (LN) and environmental management (EVM).

KA can be eliminated from the SEA Region, as there is high political commitment between the governments. A memorandum of understanding (MoU) was signed in 2005 by the affected countries. Also there are other favourable factors for the elimination of the disease;man is the only host and the sandfly (*Phlebotomus argentipes*) is the only vector responsible for the transmission of the disease. We have an easy and reliable screening test, "rk39", an effective drug, such as oral miltefosine, and injectable AmBisome for the diagnosis and treatment of KA. Another drug such as injectable paromomycin is also available. The disease is limited in its geographical distribution to only 119 districts and, therefore, focused efforts can be mounted for its elimination.

The Fifth RTAG jointly organized by WHO/Regional Office for South-East Asia and WHO Country Office, Bhutan, was held in Paro, Bhutan, from 17 to 19 September 2013. The purpose of the meeting was to review the progress and achievements of the KA elimination programme, to assess the implementation of national plans of action, to discuss developments in technology for incorporation into the elimination programme and to make recommendations to the Regional Director (RD). The meeting was attended by members of RTAG, experts, WHO staff from headquarters, the Regional Office, as well as from the WHO Country Office, Bhutan.

1. Opening session

Dr Nani Nair, WHO Representative to Bhutan, welcomed the participants and read out the Regional Director's message. The Regional Director, Regional Office for South-East Asia, in his message remarked that: "KA or VL is predominantly a disease of the poorest of the poor which, if untreated, can kill the patients. Globally it is estimated that 200 000–400 000 new cases and 20 000–40 000 deaths occur every year, of which more than 90% of VL cases occur in six countries, Bangladesh, Brazil, Ethiopia, India, Nepal and Sudan. An estimated 147 million people in 119 districts in 4 countries, namely Bangladesh, Bhutan, India and Nepal, are at risk. India alone accounts for about 50% of the global burden. The disease also affects socioeconomic development in affected areas". He further stated that KA can be eliminated in the SEA Region due to favourable factors such as man being the only host and the sandfly (*P. argentipes)* is the only vector responsible for the transmission of the disease. He reiterated that there is an easy and reliable screening test, "rk39", an effective drug, such as oral miltefosine, and injectable AmBisome for the treatment of KA. Another drug such as injectable paromomycin is also available. The disease is limited in its geographical distribution to only 119 districts and, therefore, focused efforts can be mounted for its elimination. He is delighted to state that there is a strong political will, commitment of resources, development of capacity and stronger surveillance in the Region.

The Regional Director reiterated the commitment of WHO to support the four Member States in our Region in their quest for the elimination of KA. The elimination of KA has been intensified and it is proposed to further accelerate efforts in the affected districts in Bangladesh, Bhutan, India and Nepal. A roadmap has been prepared. The manufacturer ensured donation of AmBisome for 5 years to WHO for Bangladesh and part of the first instalment was received by the country. The price of AmBisome was also reduced through WHO negotiations. KA cases and deaths have been reduced from 33 600 to 23 000 and from 106 to 30, respectively, in 2012 as compared to 2010 due to effective diagnosis and prompt treatment.

Dr A P Dash, Regional Adviser, highlighted the objectives and importance of the meeting.

2. Objectives

The objectives of this meeting were as follows:

- to review the progress and achievements of the Kala-azar Elimination Programme and implementation of the recommendations of the Fourth RTAG meeting on KA;
- to assess the progress in implementation of the National Plans of Action of Bangladesh, Bhutan, India and Nepal for elimination of KA, and to recommend appropriate strategies for additional improvements;
- to discuss other technical issues on the new developments of technology and tools and recommend them for inclusion in the strategies;
- to make appropriate recommendation(s) for consideration by WHO/Regional Office for South-East Asia.

Professor CP Thakur, India, and Professor Be-Nazir Ahmed, Bangladesh, were nominated as Chair and Co-Chair, respectively, and Professor Sumon Rijal, Nepal, was nominated as the Rapporteur.

3. On visceral leishmaniasis situation: global perspective and in the four countries of the Indian subcontinent

The ISC, Brazil and East Africa are highly endemic regions for VL or KA. The annual incidence of global KA cases reported is 58 200 of which 42 619 (>70%) is contributed from the ISC. The revised global and ISC annual incidence estimate of KA is 201 500–378 500 and 160 000–320 000, respectively. Outbreaks continue to occur, causing high mortality, with a recent outbreak in South Sudan.

There are currently no accurate data on the burden of PKDL and surveillance needs to be established and/or strengthened in the PKDL endemic countries. Visceral leishmaniasis-human immunodeficiency virus

(VL–HIV) coinfection is a serious concern and is reported from 36 countries, and there is a need to establish HIV–leishmania surveillance activity in VL endemic areas. In all the areas where there is an overlapping of the two diseases, WHO recommends strong collaboration and integration between the control programmes of VL and HIV.

There is a trend of decreasing VL cases recorded in all the three countries, India, Bangladesh and Nepal, with the latter two showing a substantial decrease in the last few years. All the 12 endemic districts in Nepal and a substantial proportion of the subdistricts and upazilas in Bangladesh and India, respectively, have shown to have reached the elimination target of KA cases (less than 1:10 000) based on the data recorded in the programme. However, this may not include all cases within the country. In Bihar, it has been observed that 15–20% of the cases are being treated in the private health facilities for which data are not being captured in the government database. Therefore, there is a need to develop epidemiological protocol with specific criteria to verify status of elimination. In Nepal, over the past few years, cases are being reported from non-endemic districts, mostly in the hilly region. Entomological and epidemiological surveillance has not been conducted in these regions so far.

In addition to the passive surveillance, active disease surveillance including camp approach and house-to-house search in outbreak areas is being conducted in the three countries. Also combined PKDL and leprosy camp search has been organized to detect PKDL cases. In India, the accredited social health activists (ASHAs) are also being utilized for detection of cases and case holding. Recent studies have shown that this strategy has increased the proportion of the cases being referred by the ASHAs.

Regarding the drug policy, Bangladesh has replaced miltefosine monotherapy by single-dose LAMB which is being introduced. It is to be provided from 37 centres, which will then be increased to 100 centres within the country. Nepal has also changed its drug policy of gradually phasing out miltefosine monotherapy, which would be replaced by LAMB monotherapy and combination regimens. In India, the drug policy has been revised for upscaling of the combination regimens within the programme.

Feasibility studies of the combinations and single-dose monotherapy are ongoing and the results are awaited.

Ratio of asymptomatic *Leishmania donovani* infection to VL cases has been observed to be 4:1 in Bangladesh and 10:1 in India and Nepal. Though it has been postulated that they could be important reservoirs as seen in asymptomatic infected dogs in *Leishmania infantum*, the exact role in the transmission of anthroponotic *L. donovani* is not yet clear.

The main tool for the vector control is IRS with insecticides in the three endemic countries. India is using dichlorodiphenyltrichloroethane (DDT) while the other two countries are using synthetic pyrethroids. Also insecticide-treated nets (ITNs) are being distributed to households with KA and PKDL cases. The coverage of IRS in the targeted households in Bangladesh and Nepal has achieved 100%.

Indigenous VL cases have been reported from several foci in Bhutan, including some foci at 2000 meters high since 2010. The causative agent is *L. donovani*. Currently, cases have been sporadic, coming from seven districts. There is no specific country strategy which needs to be developed. Cases are being treated with pentavalent antimonials, the only available drug in the country. There is also a need to conduct active case finding around the index cases and vector surveillance.

4. On diagnosis of kala-azar

Accurate diagnosis for VL is crucial as the currently available drugs are toxic and/or costly. Also increase access to care is a major challenge in VL case management. The only available rapid diagnostic test (RDT) suitable for field application, "rk39 dipstick", is being used as a diagnostic test for the VL elimination initiative. However, it has limitations as it is not useful to diagnose relapse and assess cure. The high prevalence of antibodies in the endemic population can affect the specificity of the serological tests if the RDT is not applied on clinically defined VL suspect case.

VL diagnosis is provided free in all the three countries and attempts have been made to decentralize to improve access. In Bangladesh,

diagnosis is made available in 100 health facilities, while it is available up to the primary health care (PHC) level in the endemic districts in Nepal.

The network of VL reference laboratories from Brazil, East Africa and ISC had validated five brands of the marketed RDT for accuracy, reproducibility, ease of use and heat stability. Report of this validation has been published by TDR/WHO and this should be helpful for the selection of the RDT for the programme. There is currently no quality assurance system for the diagnostic tests within the programme and efforts should be made to establish this. The RDTs are recommended to be applied on serum, which is not feasible in field conditions. Recently completed studies have shown that the performance in blood versus the serum was comparable.

Urinary latex agglutination test detecting leishmania antigen, which had demonstrated poor sensitivity, is currently being further developed to improve its performance. Nucleic acid-based tests, e.g. QPCR and loop-mediated isothermal amplification (LAMP) assay, have shown good performance. LAMP in addition to being very economical, also avoids the post-PCR steps which allow its implementation in peripheral level hospitals. However, these molecular tests currently lack standardization. Thus, they need to be further evaluated, standardized and simplified before their use in the field.

The markers currently used to document incident leishmania infections (DAT, LST and rk39 elisa) have not been firmly established and, thus, there is a need to develop tools for epidemiological surveillance.

There is also a need for diagnostic tests for test of cure and surveillance tools for drug resistance at reference centres, and the newer technologies should be exploited for this.

5. On treatment

LAMB as a single dose (10 mg/kg) (or multiple doses (15 mg/kg)) is the first choice regimen for the ISC recommended by the WHO Expert Committee on Leishmaniasis, given its high efficacy, safety, ease of use and assured compliance. Results of a phase 3 trial evaluating three regimens for combination therapy show excellent efficacy and safety of all the three

regimens. The combination regimens (LAMB/paromomycin; LAMB/miltefosine and paromomycin/miltefosine) have been recommended as a second choice regimen, and monotherapy with miltefosine or paromomycin is a fourth choice (after amphotericin B) in the recommendation of the expert committee.

Miltefosine has been or is in the process of being phased out in the programme of the three countries. Recent studies have observed a 20% relapse with miltefosine in Nepal and this was not related to the development of parasite drug resistance, lack of compliance or reinfection. Children (<12 years) were found to be at a higher risk of relapse, and pharmacokinetic modelling studies have shown that children are less exposed as compared to adults with the currently recommended dose of 2.5 mg/kg/day.

Similarly, the efficacy of miltefosine was also observed to have been reduced in India to around 90% in hospitalized patients when compared to the phase III studies done more than a decade ago. The other drawback of miltefosine is its contraindication in pregnancy and in women of childbearing age unless they use contraception. A feasibility study of a single dose of LAMB (10 mg/kg) conducted in a rural hospital (upazila health centre) in Bangladesh showed high acceptance (98.4%), high cure rate (ITT 96.6%) and safety. Also feasibility studies by MSF in India and Bangladesh using 20 mg/kg and 15 mg/kg in divided doses, respectively, observed very high cure rates (96%), was safe and feasible to be administered at PHC level. The majority of the relapses occurred between 6 and 12 months. Feasibility studies of single-dose LAMB and combination therapy at PHC and district-level hospitals are currently ongoing in Bihar, and initial results show high cure rates and very few adverse events.

Bangladesh and Nepal have also initiated a VL-focused pharmacovigilance within the programme and this is also being planned in India.

With reports of relapses after treatment occurring beyond 6 months, it is important to document outcomes for at least 12 months after treatment when the new regimens are introduced. Also the difference in the relapse rates, e.g. with miltefosine seen in the different countries emphasizes the need to monitor the outcome within each country. Late outcome monitoring within the programme is currently not yet established and operation research should be conducted to find out the best approaches.

6. On post-kala azar dermal leishmaniasis

PKDL is an important reservoir for VL and its treatment is an important public health measure to control KA. The incidence of PKDL has been observed to be declining in Bihar but still quite high in Bangladesh. It has been observed that the incidence of PKDL is higher after treatment with sodium stibogluconate (SSG) as compared to amphotericin B. Management of PKDL cases is a challenge for the programme as they do not normally present to the health services. Confirmation of diagnosis is difficult as the macular lesions are almost always negative in microscopy. Recent observations have shown a high positivity of rk39 RDT applied to slit aspirate. Also molecular methods, e.g. QPCR and LAMP, have shown high sensitivity in PKDL in few studies.

Treatment of PKDL requires long courses of therapy and very few clinical trials have been conducted to compare the different regimens. Cohorts of PKDL have been treated with miltefosine for 12 weeks in Bihar and Nepal with good tolerance and efficacy. Alternative regimens include amphotericin deoxycholate (4 courses of 20 injections over 5–6 months) and LAMB. WHO has recently developed guidelines for the diagnosis and treatment of PKDL for the ISC.

The efficacy of current regimens on PKDL needs to be documented and these experiences would be helpful for standardizing the regimens. PKDL detection within the programme should be done by active case finding as PKDL patients usually present very late.

Research is required to develop shorter and safer treatment regimens for PKDL, to develop better diagnostic tools for PKDL including the role of molecular tools and to find out the duration of infectiousness in a PKDL patient.

7. On vector control

The strategy for vector control should incorporate IVM. The principles, objectives and the process of IVM were presented. IVM is a rational decision-making process for the optimal use of resources for vector control. The approach seeks to improve the efficacy, cost-effectiveness, ecological

soundness and sustainability of disease-vector control. The main objective is to reduce longevity of the adult vectors, eliminate the breeding sites, decrease contact of vector with humans, and reduce the density of the vector. The five key elements of IVM include capacity building and training, advocacy, collaboration, evidence-based decision-making and integrated approach.

Presently, three tools are considered to be useful for vector control in KA transmission: IRS, LN and EVM.

IRS has a lethal effect during direct contact and excito-repellency effect. Studies have found IRS when conducted properly to have a greater impact compared to LN and EVM. However, the monitoring for quality spray is a challenge within the programme.

With regard to LN, studies have not been conclusive. LN may not be effective against vectors, biting/resting outdoors. For LN to be effective, transmission should be intradomicillary and the vector should be nocturnal feeder. Transmission of *P. argentipes* has been known to occur in peri-domestic areas of houses in the proximity of cattle sheds. Most of the efficacy studies are based on the reduction of vector density and not on the comparison of the human biting index before and after the use of LN which is recommended. Ongoing research is also being conducted on wall lining sheets impregnated with insecticides.

Environmental control has been done by plastering with 30% lime on inner walls of the mud houses up to 1.25 m and cement skirting of 9 inch along the floor and wall inside human dwellings and cattle sheds. In operational research, it was observed that the cost per house was the lowest for LN, slightly higher for IRS and almost double for EVM.

IRS is the main strategy for vector control in all the three countries. Bangladesh has started IRS only since 2010, and the impact on the decrease in the case numbers has been substantial. Bangladesh is using deltamethrin; Nepal used alpha-cypermethrin 10 WP up to mid-2013, which has been replaced by lambda-cyhalothrin; and India has been using DDT 50%. Monitoring of IRS in India and Nepal has found several lacunae, including delay in the timing of the spraying, reduced coverage and patchy spraying. Also the results of the WHO/TDR studies on IRS show that the

quality of IRS operations in India and Nepal needs to be improved. The programme managers need to be sensitized with the results of these studies. A monitoring and evaluation toolkit has been developed by WHO/TDR for IRS and this should be adapted in the programme. Resistance of the sandfly to DDT used in India, in some areas, e.g. Muzaffarpur, has been observed. Concurrent use of synthetic pyrethroids for both IRS and LN can predispose to the development of resistance.

In addition to IRS, the programmes in Bangladesh and Nepal have been distributing LN to KA and PKDL households.

The group felt that capacity strengthening is essential for implementation of the IVM. There is an acute shortage of entomologists, which needs to be addressed through intersectoral collaborations.

In summary, IRS is currently the best available option for sandfly control and should be reinforced in each country. The vector control measures should be part of the public health strategies in the countries and this should include a national insecticidal policy.

8. Supportive strategies: policy support and advocacy, partnership, resource mobilization, institutional support and cross-border collaboration

There are numerous challenges for the elimination of KA in the Region. The population at risk are among the poorest in the community and often malnourished. Access to care is difficult. The gap between the reported and the actual case numbers is unknown, posing difficulties in the programme planning. The emergence of HIV-VL coinfections poses a challenge for achieving cure. Population explosion with urbanization has its effect on vector dynamics. Migration of populations and cross-border movement are other issues. Climate change with movement of the vectors to new areas has its potential to spread disease to nonendemic areas.

Over the last few years, we have also seen an impact on the decrease in the case numbers in all the three countries with many of the foci

reaching the targets of the elimination. This needs to be sustained, which includes strengthening of the control efforts, development of new tools and operational research. Resource mobilization is a challenge and highlighting the current achievements would be important.

VL reference laboratory network involving research laboratories in Bangladesh, Brazil, East Africa (Sudan), India and Nepal has validated commercially available RDT to aid in the selection of the product for the programmes and such networks should be encouraged, sustained and supported. There should be collaboration with and support to universities and specialized institutes for the establishment of reference laboratories for ensuring QC/QA for diagnostics, for monitoring drug-resistant parasites and for surveillance of KA transmission in communities.

Global focus has been reinvigorated for neglected tropical diseases including leishmaniasis. The London Declaration in 2012 and World Health Assembly Resolution in 2013 provide opportunities to reinforce and accelerate the activities and to develop new partnerships. Donation of AmBisome by Gilead through WHO has been made available to Bangladesh, which will also be made available to Nepal. Partnerships with agencies like DNDi, iOWH, WHO/TDR and BMGF have aided the development of better regimens for treatment. There is also a need for capacity building of the primary care facilities. Support to local manufacturers from the Region would bring down the cost of therapy.

Also coordination within the three countries to generate evidence and develop common policies would aid in the cross-border issues. Multisectoral cooperation and capacity building across all relevant sectors, including health, education, agriculture, environment, water, forestry, and urban and rural development, are required.

Increasing number of partners in the Region implies greater need for improved coordination and harmonization of the activities. There is a need to establish a coordination mechanism to regularly monitor progress and map partner contributions. An intercountry technical coordination committee consisting of program directors from the four countries and focal person from the regional office of the developmental partners should be created. The terms of reference could include review/update of regional strategy and action plan; advocating countries and development partners

for adoption of policies, mobilization of resources and implementation of the action plan; and monitoring implementation, epidemiology and vector status.

9. On monitoring and evaluation

The progress and the gaps within the programme in the three endemic countries were presented. All the countries have adequate stock of drugs, RDTs and insecticides. WHO/TDR implementation research has developed a "monitoring and evaluation toolkit for indoor residual spraying" and "indicators for monitoring and evaluation of the kala-azar elimination" was adopted at a workshop convened in June 2009 in Dhaka.

The three key indicators for the elimination initiative are:

- *detection rate*: number of new cases of KA detected per year in the district/upazila/subdistrict over the total population in the same area;
- *treatment completion rate*: percentage of cases of KA who completed a full course of first-line drugs;
- *coverage rate of vector control*: percentage of households (and cattle sheds) protected / all households at risk

There is an overall declining trend in the incident cases in all the major endemic countries in the Region in the last 2 years. However, the issue which is of concern and not clear is whether the cases are diagnosed and treated early. Delayed diagnosis has a negative impact both in sustaining transmission and in the prognosis of the disease in patients. Also the treatment completion rate and defaulter rates need to be documented systematically. This has become particularly important with reports of increased relapses with miltefosine in some studies.

Regarding the vectors control, with IRS being the main tool, the quality of IRS operations is a major issue and the WHO/TDR monitoring toolkit needs to be adapted.

Underreporting of cases is still observed in some countries which have an effect in the planning and execution of the control efforts. The surveillance of the cases needs to also capture cases treated in the private sector and monitoring of HIV/VL coinfections should be established in the programme.

In general, it was felt that monitoring and evaluation of the VL elimination initiative should be strengthened.

10. Recommendations

- Epidemiological data of the past few years show that there is a decrease in the reported number of KA cases in Bangladesh, India and Nepal with a significant proportion of the blocks (subdistricts), upazilas and districts, respectively, showing less than 1 case in 10 000 population. In order to ascertain the true picture, there is a need to develop epidemiological protocol with specific criteria to verify the status of elimination. WHO needs to establish a task force or working group.
- Surveillance systems along with active case finding need to be strengthened, including nonendemic areas reporting KA cases, for early detection of cases including PKDL.
- Bhutan continues to have occurrence of sporadic cases. The country needs to develop a strategy for KA elimination. WHO and development partners should support the activities for KA control. Sri Lanka and Thailand are also reporting KA cases. It is required to assess the epidemiological situation and develop country-specific strategy.
- There are limited or no easy-to-apply tools currently available for the diagnosis of VL in cases with past history of KA, asymptomatic leishmania infections, PKDL and a test of cure. Nucleic acid-based tests, e.g. Q PCR and LAMP, show good performance but lack standardization. Standardization of the nucleic acid-based tests and validation of these tools in phase III diagnostic studies should be done. Also there is a need to develop and validate biomarkers to accurately detect asymptomatic leishmania infections and

determine the role of asymptomatic carriers in the transmission of infection.

- As per the Fourth RTAG recommendation, Bangladesh has introduced single-dose LAMB. India and Nepal need to introduce single-dose LAMB based on the results of the feasibility study. Bangladesh and Nepal have included combination regimens in their treatment policy and India is also in the process. The countries need to consider combination regimens based on the results of the feasibility studies. Emphasis should be laid on strengthening and capacity building of the health facilities and staff pharmacovigilance data which should be continuously collected for all the drugs used within the programme.
- WHO and other agencies should make efforts to ensure the continued production and supply of the limited anti-VL drugs. Access of anti-VL drugs should be made available to low endemic countries with low disease burden (e.g. Bhutan and Thailand).
- PKDL is an important reservoir for VL transmission and little information is known of the risk factors for its development. Diagnosis and treatment should be based on the WHO recommendation. Research should be expedited to develop and validate tools for diagnosis and conduct clinical trials to develop safer and shorter regimens including combination therapy.
- Effective implementation of IVM should be the mainstay of vector control. Vector surveillance, monitoring insecticide resistance and quality of IRS operations need to be strengthened and institutionalized. The monitoring and evaluation toolkit developed by WHO/TDR should be adapted in the country programmes.
- With the involvement of many partners, including academia, industry, donors, etc., in the various activities of the elimination programme, a mechanism for coordination and mapping of the activities/roles needs to be established. WHO/SEARO should take the lead. Also coordination mechanisms among the countries need to be strengthened for cross-border issues and migration.
- WHO and countries need to review the progress towards the elimination goal and define the post-elimination strategy.

Annex 1

Agenda

(1) Opening

(2) Situation of Kala-azar

(3) Country situation

(4) Update on technical issues

(5) Supportive strategies

(6) Research in support of elimination

(7) Conclusion and recommendations

Annex 2
List of participants

Bangladesh

Professor Be-Nazir Ahmed
Director (Disease Control)
Line Director, Communicable Disease Control
National Focal Point, IHR and HPED
Directorate General of Health Services (DGHS)
Ministry of Health and Family Welfare (MHFW)
Dhaka

Dr Dinesh Mondal
Scientist
Parasitology Unit, Laboratory Sciences Division
International Centre for Diarrhoeal Disease Research (ICDDR,B)
Dhaka

Bhutan

Mr Rinzin Namgay
Vector-Borne Disease Control Programme
Department of Public Health
Ministry of Health

India

Dr Poonam Salotra
Deputy Director
National Institute of Pathology
Indian Council for Medical Research
New Delhi

Professor C. P. Thakur
Chairman
Balaji Uthan Sansthan Kala-azar Research Centre
Patna, Bihar

Professor R. C. Mahajan
SN Bose INSA Research Professor
Emeritus Professor, Department of Parasitology
Postgraduate Institute of Medical Education and Research (PGIMER)
Chandigarh

Dr Pradeep Das
Director
Rajendra Memorial Research Institute of Medical Sciences (RMRIMS)
Patna, Bihar

Nepal

Professor Suman Rijal
Professor
Department of Internal Medicine
B.P. Koirala Institute of Health Sciences (BPKIHS)
Dharan

Thailand

Ms Kobkan Kanjanopas
Bureau of Vector-Borne Disease
Department of Disease Control
Ministry of Public Health

Observers

Dr Krishna Prasad Sharma
Pathologist
Eastern Regional Referral Hospital
Mongar, Bhutan

Dr Lhacha Wangdi
Medical Officer
Trashigang Hospital
Trashigang, Bhutan

Mr Tobgyel
Programme Officer
VDCP
Gelephu, Bhutan

Mr Nima Wangdi Gyeltshen
Entomologist
VDCP
Gelephu, Bhutan

Special Invitees

Dr Karma Lazeen
Ministry of Health
Thimphu, Bhutan

Dr Nines Lima
Tropical Medicine Advisor MSF-OCBA
Barcelona, Spain

WHO Secretariat

Dr Nani Nair
WR Bhutan
Thimphu, Bhutan

Dr Daniel Argaw Dagne
Leishmaniasis Control
(HTM/NTD/IDM)
World Health Organization
Geneva, Switzerland

Dr A.P. Dash
Regional Adviser (VBN)
WHO/Regional Office for South-East Asia

Dr Rita Kusriastuti
Medical Officer (VBN)
WHO/Regional Office for South-East Asia

Dr Nima Wangchuk
National Professional Officer
WHO Representative Office
Thimphu, Bhutan

Ms Om Rinji
Administrative Assistant
WHO Representative Office
Thimphu, Bhutan

Mr Brijesh Kumar
Administrative Staff
WHO/Regional Office for South-East Asia

Annex 3

Message from Dr Samlee Plianbangchang, Regional Director WHO South-East Asia Region

[Read by Dr Nani Nair, WHO Representative to Bhutan]

Distinguished experts, participants, ladies and gentlemen,

It is with great pleasure that I welcome you all and convey greetings from the Regional Director, Dr Samlee Plianbangchang. The Regional Director would have very much liked to attend this meeting but is unable to do so because of urgent commitments. In the circumstances, I have the honour to deliver his message. I quote.

Kala-azar or visceral leishmaniasis (VL), is predominantly a disease of the poorest of the poor which, if not treated, can kill. Globally it is estimated that, 200 000 to 400 000 new cases and 20 000 – 40 000 deaths occur every year, of which >90% of VL cases occur in six countries: Bangladesh, India, Nepal, Sudan, Ethiopia and Brazil. An estimated 147 million people in 119 districts in four countries namely Bangladesh, Bhutan, India and Nepal are at risk. India alone accounts for about 50% of the global burden. The disease also affects socioeconomic development in affected areas.

Kala-azar can be eliminated in the South-East Asia Region due to favorable factors like: man is the only host and the sandfly, *Phlebotomus argentipes,* is the only vector responsible for transmission of the disease. We have an easy and reliable screening test, 'rk39', for diagnosis of kala-azar and an effective drug, like: oral miltefosine, and injectable AmBisome. Another drug such as injectable Paromomycin is also available. The disease is limited in its geographical distribution to only 119 districts and, therefore, focused efforts can be mounted for its elimination. I am happy to state that there is a strong political will, commitment of resources, development of capacity and stronger surveillance in the Region.

Distinguished participants,

The five strategic elements for elimination of kala-azar are (i) early diagnosis and complete treatment; (ii) integrated vector management; (iii) effective disease surveillance; (iv) social mobilization and building partnerships; and (v) operational research.

I would like to reiterate WHO's commitment to support the four Member States in our Region in their quest for elimination of kala-azar. We will continue to build partnerships and mobilize the additional resources required in the elimination efforts.

The elimination of kala-azar has been intensified and it is proposed to further accelerate efforts in the affected districts in Bangladesh, Bhutan, India and Nepal. A roadmap has been prepared. The manufacturer ensured donation of AmBisome for five years to WHO for Bangladesh and part of the first installment was received by the county. The price of AmBisome was also reduced through WHO negotiations. Kala-azar cases and deaths have been reduced to 23 000 from 33 600 and to 30 from 106 respectively in 2012 as compared to 2010 due to effective diagnosis and prompt treatment.

I am very happy that this RTAG meeting is being attended by eminent experts in the field including colleague from WHO/HQ. This meeting provides a forum for reviewing the progress towards elimination, exchanging information, and making recommendations on the way forward, based on the lessons learnt. I also hope that the meeting would help to further strengthen partnerships. I look forward to inputs from research that will help to further refine the operational plans. "Unquote"

I will, of course, apprise the Regional Director of the outcome of this meeting. In conclusion, I wish you fruitful deliberations and a pleasant stay in Bhutan.

Kala-azar or visceral leishmaniasis is one of the important neglected tropical diseases that have significant public health importance in Bangladesh, Bhutan, India and Nepal. About 147 million people in 119 districts are at risk of kala-azar in these four endemic countries. Elimination of kala-azar in countries of the WHO South-East Asia Region is feasible.

The Fifth Meeting of the Regional Technical Advisory Group (RTAG) jointly organized by WHO/SEARO and WRO Bhutan was held in Paro, Bhutan, from 17 to 19 September 2013 to review the progress and achievements of the kala-azar elimination programme, to assess the implementation of national plans of action, to discuss developments in technology for incorporation into the elimination programme and to make recommendations to the Regional Director.

World Health Organization
Regional Office for South-East Asia
World Health House
Indraprastha Estate
Mahatma Gandhi Marg
New Delhi-110002, India
www.searo.who.int

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