

Management of Snake bites

Report of the Regional Meeting

Yangon, Myanmar, 30 November – 2 December 2009

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Contents

	<i>Page</i>
1. Background	1
2. Objectives	2
3. Inaugural session	2
4. Proceedings of the meeting.....	4
4.1 Global overview of snake-bites	4
4.2 Current status in SEA Region.....	6
4.3 Revised regional guidelines on management of snake-bites.....	10
4.4 Enhancing availability of antivenom serum.....	11
4.5 Improving access to antivenom in health facilities through the health system	12
5. Recommendations and conclusions	13

Annexes

1. Agenda	15
2. List of participants.....	16

1. Background

Snake-bites are well-known medical emergencies in many parts of the world, especially in rural areas. Agricultural workers and children are the most affected. The true worldwide incidence of snake-bite envenoming has proved difficult to estimate. The incidence of snake-bite mortality is particularly high in South-East Asia (SEA) Region. In India alone there may be as many as 50 000 snake-bite deaths each year. Many estimates of snake-bite mortality and permanent morbidity are based on hospital returns, which greatly underestimate the real impact of this health problem because most people affected by snake-bites do not seek hospital treatment but prefer traditional remedies.

Snake antivenom provides a life-saving measure. The current annual need for the treatment of snake-bite envenoming amounts to 10 million vials of antivenins. Unfortunately, the present worldwide production capacity is well below the need. Furthermore, the erosion of public health budgets has resulted in deterioration of infrastructure and equipment for antisera production in public institutions. This has resulted in a global reduction in antisera production and accessibility. This trend needs to be reversed through concerted action by national, regional and global health authorities and manufacturers and through effective public-private partnership.

In some of the countries in South-East Asia Region, the capacity to produce antivenom is either non-existent or inadequate. Because of the variations in the antigenic properties, it is important to use venom collected from a specific geographical area in the production of antivenom. Collaboration is needed between manufacturers and nationals for supply of venom.

WHO's Regional Office for South-East Asia (SEARO) developed guidelines on the management of snake-bites, which were also published as a special issue of the South-Asia Journal of Tropical Medicine and Public Health. WHO has supported countries in developing national guidelines, for example, in India (2007), and has also helped bring together experts for information sharing, as in Thailand and Myanmar. The regional guidelines are being revised and updated with the latest knowledge in the area.

The problem of snake-bites is overwhelmingly rural in nature. The prevention of mortality and morbidity depends upon the availability of antivenom in the health facilities in these settings. Mechanisms need to be developed to assure access to antivenom by all needy patients. The health system needs to respond to this challenge and logistics must be put in place to assure timely availability of antivenom at the point of use.

To discuss these issues, a regional meeting was organized at Yangon, Myanmar on 30 November–2 December 2009. The meeting was attended by 22 participants from Member States of the Region. Experts from Thailand and the United Kingdom facilitated the meeting. The meeting was chaired by Prof Visith Sitprijja, Director, Queen Saovabha Memorial Institute, Thai Red Cross Society, Bangkok, and co-chaired by Prof Khin Thida Thwin, Programme Manager (Snake-Bite Control) and Senior Consultant, Renal Medical Unit, Thinganikyun Sangpya Hospital, Myanmar. The list of participants and the programme of work are contained at Annex 1 and Annex 2.

2. Objectives

The following were the objectives of the meeting:

- (1) To review the situation of snake-bites as a public health problem in the South-East Asia Region and strategies being employed for prevention and control.
- (2) To share revised SEARO guidelines on management of snake-bites and discuss implementation at the country level, including utilization as a teaching tool in medical schools.
- (3) To review the availability of snake antivenom in the South-East Asia Region and identify mechanisms to enhance its production and availability at the point of use.

3. Inaugural session

In his message, WHO Regional Director for South-East Asia, Dr Samlee Plianbangchang, noted that the true worldwide incidence of snake-bite envenoming has proved difficult to estimate. Though reliable data and

epidemiological information on snake-bites are not available, It has been estimated that there are 4.5 million snake-bites annually, resulting in around 2 million envenomings, more than 80 000 deaths and perhaps three times that number of permanent disabilities. The incidence of snake-bite mortality is particularly high in South-East Asia. The actual global impact of this neglected health problem is much higher. In fact it has been rightly observed that snake-bite is the most neglected of all major public health problems.

When evaluated in terms of disability-adjusted life years (DALYs), the impact of snake-bites is very high because most victims are children or young agricultural workers, many of whom suffer from physical or psychological disabilities. The impact of snake-bite on the economy is also highly significant, as many of the affected people are agricultural workers whose families, community and country are highly dependent on the food they produce.

The WHO regional guidelines have now been revised with the latest knowledge; this workshop's purpose is to finalize these guidelines. In addition, the participants would also discuss the approaches that the health system needs to adopt to put in place the logistics to ensure timely availability of antivenom at the point of use.

Dr Samlee Plianbangchang assured participants that WHO would continue to provide the required technical support in strengthening health systems to provide improved services for mitigating mortality and morbidity due to snake-bites.

Dr Khin Pyone Kyi, Director General, Department of Medical Research, Lower Myanmar, inaugurated the meeting. She welcomed the participants and thanked WHO for holding this meeting in Myanmar. She highlighted the importance being accorded by the Government of Myanmar to snake-bites and recent activities in the country. Several research projects were being implemented in Myanmar, especially to increase the availability of safe anti snake venom.

Dr Kyi highlighted the importance of regional cooperation in this important area. She also requested WHO to continue to provide technical support to countries to reduce the impact of snake-bites.

4. Proceedings of the meeting

The meeting included the presentation of country reports to review the current status of snake-bite management, including epidemiology of snakes, in the respective countries; presentations and discussions on underlying fundamental issues in production and distribution of safe and potent antivenom serum; and review of the updated WHO/SEARO guidelines on the management of snake-bites.

4.1 Global overview of snake-bites

Prof David Warrell provided an overview of the global status of snake-bites. Venomous snakes are present all over the world with few exceptions. They inhabit seas, freshwater, deserts, high altitudes and even near volcanos.

Incidence of snake-bites varies geographically and depends upon frequency and nature of contact between snakes and humans. The factors affecting this interaction are: population densities (humans and snakes); diurnal and seasonal variations in activity (rains, flooding, disasters); human behaviour and occupations (e.g. agricultural activities harvesting, neglect of protective clothing) and snakes' "irritability" (readiness to strike) when alarmed/provoked, which varies between species. Climate change is also believed to have the potential to increase human and snake interaction.

Globally, most affected by snake-bites are rural communities in tropical countries, children (30-50%), young agricultural workers and indigenous peoples.

Snake-bite-attributable mortality

Apart from a handful of community surveys, no reliable epidemiological data have been published. Attempted global reviews suffer from incompleteness, faulty or undisclosed methods of acquisition and unscientific extrapolations. Several studies have been published, of which following three are important:

<i>Authors</i>	<i>Year</i>	<i>Estimated deaths/year</i>
<i>Swaroop and Grab</i> ¹	1954	30 000 – 40 000
<i>Chippaux</i> ²	1998	12 345
<i>Kasturiratne et al.</i> ³	2008	19 886 – 93 945

Swaroop and Grab (1954) recognised that their global total of 30 000 – 40 000 snake-bite deaths/year underestimated true mortality because they relied on hospital and dispensary admissions, and they excluded Central Europe and North Asia. The study by Chippaux (1998) made extrapolations from point incidences obtained in particular locations within countries to estimate global annual totals of 5 400 000 bites, over 2 500 000 envenomings and around 125 000 deaths. Kasturiratne et al. (2008) ignored the essential heterogeneity of snake-bite incidence within and between countries by generalizing and extrapolating incidences between adjacent territories, resulting in some questionable results (e.g. in Caribbean and West Pacific islands). Their estimated ranges vary from 421 000 – 1 841 000 envenomings and 2000 – 94 000 deaths globally each year.

The global estimated data on snake-bite morbidity and mortality that has widespread agreement is shown in Table 1 and Fig 1:

Table 1: Global estimates of snake-bites

	Bites	Envenomings	Deaths
Americas	500 000	200 000 (40%)	4000 (2%)
Africa	1 million	400 000 (40%)	20 000 (5%)
Asia	3 million	1.2 million (40%)	60 000 (5%) (India 50 000)
Oceania	5000	2500 (50%)	250 (10%)
Total	>4.5 million	~ 2 million	>80 000

¹ Swaroop S, Grab B. Snake bite mortality in the world. *Bull World Health Organ* 1954; **10**: 35–76.

² Chippaux J-P. Snake-bites: appraisal of the global situation. *Bull World Health Organ* 1998; **75**: 515–24.

³ Kasturiratne A, Wickremasinghe AR, de Silva N, et al. The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Med* 2008; **5**: e218.

The estimated 2 million snake-bite envenomings per year have serious therapeutic implications. Assuming that each case needs a treatment course of 1-20 (average 5) vials of antivenom, the annual global requirement is around 10 million vials. In addition, for the rational use of antivenin, appropriate guidelines and training for health-care workers are required.

4.2 Current status in SEA Region

Status of snake-bites and their management in the South-East Asia Region

A large number of species of snakes are prevalent in SEA Region. New species are also being detected. Both Elapidae and Viperidae species are prevalent. These have been summarized in Tables 2 and 3. Snakes shown as belonging to category 1 are considered of great medical importance because of the associated mortality and morbidity in given setting while those in category 2 have lesser medical importance in areas of their prevalence.

Table 2: Snakes prevalent in the SEA Region (Elapidae)

Country	BAN	BHU	KRD	IND	INO	MAV	MMR	NEP	SRL	THA	TLS
<i>Bungarus bungaroides</i>								2			
<i>Bungarus caeruleus</i>	1	–	NA	1				1	1		
<i>Bungarus candidus</i>					1		2			1	
<i>Bungarus ceylonicus</i>									2		
<i>Bungarus fasciatus</i>	2	2	NA	2	2			2		2	
<i>Bungarus flaviceps</i>					2					2	
<i>Bungarus lividus</i>	2	–	NA								
<i>Bungarus magnimaculatus</i>							1				
<i>Bungarus multicinctus</i>							1				
<i>Bungarus niger</i>	1	1	NA	2				1			
<i>Bungarus sindanus</i>				2							
<i>Bungarus walli</i>	1	–	NA	2							
<i>Naja kaouthia</i>	1	–	NA	1			1			1	
<i>Naja mandalayensis</i>							1				
<i>Naja naja</i>	2	1	NA	1				1	1		

Country	BAN	BHU	KRD	IND	INO	MAV	MMR	NEP	SRL	THA	TLS
<i>Naja oxiana</i>				2							
<i>Naja sagittifera</i>				2							
<i>Naja siamensis</i>										1	
<i>Naja sputatrix</i>					1						2
<i>Naja sumatrana</i>					1					2	
<i>Ophiophagus Hannah</i>	2	2	NA	2	2		2	2		2	

*Category 1: Greater medical importance in given setting; Category 2: Of lesser medical importance
 NA: Information not available

Table 3: Snakes prevalent in SEA Region: Viperidae

Country	BAN	BHU	DPRK	IND	INO	MAV	MMR	NEP	SRL	THA	TLS
<i>Ovophis monicola</i>							2				
<i>Calloselasma rhodostoma</i>					1					1	
<i>Calloselasma rhodostoma</i>							2				
<i>Cryptelytrops albolabris</i>				2	1		1			1	
<i>Cryptelytrops erythrus</i>	1	2	NA	-			1				
<i>Cryptelytrops insularis</i>					2						1
<i>Cryptelytrops macrops</i>										2	
<i>Cryptelytrops purpureomaculatus</i>	2	-	NA	2	2						
<i>Cryptelytrops septentrionalis</i>	2	-	NA	-							
<i>Cryptelytrops septentrionalis</i>								2			
<i>Daboia russelii</i>	2	2	NA	1				1	1		
<i>Daboia siamensis</i>					1		1			1	
<i>Echis carinatus</i>	-	-	NA	1					2		
<i>Himalayophis tibetanus</i>								2			
<i>Hypnale hypnale</i>	-	-	NA	1							

Country	BAN	BHU	DPRK	IND	INO	MAV	MMR	NEP	SRL	THA	TLS
<i>Hypnale nepa</i>									2		
<i>Hypnale walli</i>									2		
<i>Macrovipera lebetina</i>				2							
<i>Protobothrops jerdonii</i>								2			
<i>Protobothrops kaulbacki</i>							2				
<i>Protobothrops mucrosquamatus</i>							2				
<i>Trimeresurus gramineus</i>				2							
<i>Trimeresurus malabaricus</i>				2							
<i>Trimeresurus trigonocephalus</i>									2		
<i>Viridovipera stejneri</i>								2			

*Category 1: Greater medical importance in given setting; Category 2: Of lesser medical importance
 NA: Information not available

Table 4 shows summary of available data on number of snake-bites and deaths due to snake-bites in the South-East Asia Region. The data have been summarized from the country reports presented in the meeting.

Table 4: Overview of status of snake-bites in SEA Region

Country	Estimated number of bites	Estimated number of deaths	National guidelines	Training	AVS Prodn/Import	Reporting system
BAN	700 000	6000	Yes (2008 Rev.)	Yes	Import	Nil
BHU	NA	NA	Yes	No	Import	Nil
DPRK	NA	NA	NA	NA	NA	NA
IND	77 000	1100 (20 000)	Yes (2007)	No	Yes Polyvalent	Yes
INO	NA	NA	NA	NA	Yes	NA
MAV	Nil	Nil	No	No	No	No

Country	Estimated number of bites	Estimated number of deaths	National guidelines	Training	AVS Prodn/Import	Reporting system
MMR	10 000	769	No		Yes Monovalent and Import	Yes
NEP	1000	200	Yes	No	Import	No
SRL	35 000	100-150		No	Import	Yes
THA	10 000	<0.5%	Yes	Yes	Yes Monovalent	Yes
TLS	NA				No	

NA: Information not available

Snake-bites have been responsible for substantial mortality in the Indian subcontinent for the last several centuries. Published data in 1870 (“Destruction of life in India by poisonous snakes”) showed that around 11 000 deaths were caused by snake-bites every year (Joseph Fayrer. *Nature* 1882; 27:205-8). Another study published in 1924 described 19 867 deaths from snake-bite (Indian Sanitary Report. *British Medical Journal* 1927: 538–39).

A nationwide survey, the largest of its type in Bangladesh, funded by the government and the World Bank, revealed there are around 700 000 snake-bite incidents every year in Bangladesh, of which approximately 6000 are fatal.

The need for reliable epidemiological data on a sustainable basis to facilitate advocacy was noted; it will also assist in the development of evidence based policy and programmes at country levels.

Sea water snake

Envenoming by sea snakes (Hydrophiinae) and sea kraits (Laticaudinae) usually involves a painless bite that may not be noticed by the victim. Fangs and other teeth may be left in the wound. There is minimal or no local swelling and involvement of local lymph nodes is unusual. Generalized rhabdomyolysis is usually the dominant effect of envenoming by these snakes. Early symptoms include headache, a thick feeling of the tongue, thirst, sweating and vomiting. Generalized aching, stiffness and tenderness

of the muscles becomes noticeable between 30 minutes and three and a half hours after the bite. Trismus is common. Passive stretching of the muscles is painful. Later, there is progressive flaccid paralysis starting with ptosis as in other neurotoxic envenomings.

The patient remains conscious until the respiratory muscles are sufficiently affected to cause respiratory failure. Myoglobinaemia and myoglobinuria develop three to eight hours after the bite. These are suspected when the serum/plasma appears brownish and the urine dark reddish brown (“cola-coloured”). Bedside “stix” tests will appear positive for haemoglobin/blood in urine containing myoglobin. Myoglobin and potassium released from damaged skeletal muscles may cause renal failure, while hyperkalaemia developing within 6–12 hours of the bite may precipitate cardiac arrest.

4.3 Revised regional guidelines on management of snake-bites

The revised WHO/SEARO guidelines on snake-bite management encompass prevention, epidemiology, clinical features, laboratory investigations, clinical management as well as care of patients with sequelae. These issues were taken up extensively by all the participants. The primary objective was to review the guidelines and make evidence-based suggestions to enhance the merit of the document. Several technical suggestions made by the participants were discussed and incorporated in the guidelines. It was agreed that an executive summary and a glossary would enhance the value and usefulness of the guidelines.

Implementation of Regional Guidelines

Availability of guidelines is a critical step in ensuring rational use of antivenom serum. However, the participants recognized that effective utilization of these guidelines requires an enabling environment. Important components of this environment are:

- Adaptation of regional guidelines as national standard treatment guidelines by the Member countries
- Periodic revision of guidelines in the light of scientific evidence
- Training and continuous medical education of health-care workers in diagnosis and management of cases of snake-bite

- Continuous availability of antivenom serum and infrastructure for its proper storage and shipment
- Functional referral mechanism
- Emphasizing the community awareness on prevention of snake-bites and modifying treatment-seeking behaviour

The health administrators must strive to undertake the above-mentioned activities to make best use of the available resources for mitigating misery and mortality due to snake-bites.

4.4 Enhancing availability of antivenom serum

Six manufacturing units in SEA Region are currently engaged in the production of equine antivenom serum. Three of these are in India and one each in Indonesia, Myanmar and Thailand. The installed production capacity is:

Country	No. of production units	Annual production of vials of 10 ml each	Type of product
India	3	1.5 million	Polyvalent
Indonesia	1	40 000	Polyvalent
Myanmar	1	52 000	Mainly monovalent
Thailand	1	100 000	Mainly monovalent

All production units were producing lyophilized antivenom with a shelf life of around 5 years. Limited quantity of antivenom was produced in liquid form with a shelf life of two years.

The Thai Red Cross Society has a production plant with approved Good Manufacturing Practice. Seven types of monovalent antivenom and two types of polyvalent antivenom (haematopolyvalent and neuropolyvalent) were currently being produced. The Thai Unit has been exporting antivenom mainly to Malaysia and Myanmar and also in small quantities to Bhutan, United States and Vietnam. Because of very low content of protein

(8 mg%) in antivenom produced by the Thai Red Cross Society, the adverse reactions due to this product are much less compared to reports in the contemporary literature using products from other manufacturers.

Indian antivenom manufacturers produce polyvalent antivenom only, and have been exporting to Pakistan, Nepal, Sri Lanka and several African countries.

While all production units were working optimally to produce antivenom, there was some scope for enhancement of production capacity. In Thailand, a 100% increase was possible, whereas in India, an increase of about 25% was feasible. The Myanmar Pharmaceutical Factory is working at peak capacity and any substantial increase in annual production was perceived to be difficult. To overcome the shortage of antivenom, Myanmar has undertaken a pilot project to produce chicken-derived antivenom, but the commercial production is yet to take place. A shift from equine to sheep-based production has also been attempted.

It was observed that until more countries (especially Bangladesh and Nepal) become self-reliant through indigenous production of antivenom, they, as well as other countries such as Bhutan, Myanmar, and Sri Lanka, may need to develop bilateral arrangements with production units in India, Indonesia and Thailand to meet their requirements through procurement of product or by providing the country-specific venom to commission production of antivenom for their use. WHO was requested to provide technical support and play a facilitating role.

4.5 Improving access to antivenom in health facilities through the health system

Dr Khin Thida Thwin discussed various issues that have a bearing upon making available a safe product to the end-user and saving the life of the patient. These included training of the staff as well as making available the infrastructure that enables delivery of efficient services. Several issues that need to be considered and advocated by her were:

- Policy and programme
- Access to services and products
- Quality of services and products

- Rational use of services and products
- Safety of products and services
- Intersectoral collaboration
- Strengthening existing mechanisms
- Research, operational or basic

5. Recommendations and conclusions

The participants endorsed the updated WHO/SEARO guidelines on management of snake-bites. The following recommendations were also made:

For Member States in the South-East Asia Region

Member States should:

- (1) Develop comprehensive national guidelines on rational management of Snake-bites and ensure access to antivenom serum on an equitable basis;
- (2) Strengthen health system requirements, including those of physical infrastructure and skilled human resources to provide efficient case management services to victims of snake-bites;
- (3) Augment production of antivenom within the country utilizing the indigenous venom, and/or commission its production in any production facility outside the country;
- (4) Institute a surveillance mechanism to generate reliable epidemiological data on snakes, disease burden and adverse reactions to antivenom serum;
- (5) Promote community awareness to overcome religious, social and cultural myths associated with snake-bites and their management;
- (6) Seek intercountry cooperation to harmonize cross-border activities and regulations;
- (7) Undertake operational research for better understanding of the disease epidemiology and development of effective and economical tools for minimizing mortality and morbidity due to snake-bites.

For the World Health Organization

WHO should:

- (1) Publish and disseminate revised guidelines on snake-bite management;
- (2) Undertake advocacy with national authorities to develop and implement national guidelines on snake-bite management;
- (3) Support capacity building in various aspects of management, technical skills and regulatory mechanisms of snake-bite management;
- (4) Facilitate intercountry cooperation especially in areas of antivenom production, capacity building, cross-border activities and venom banking;
- (5) Collect and share global data on all aspects of snake-bites;
- (6) Support operational research on snake-bites management and epidemiology; and
- (7) Organize regional meetings on a regular basis for exchange of experiences within the Region.

The meeting concluded with a vote of thanks to WHO and the Government of Myanmar for hosting this timely meeting.

Annex 1

Agenda

- (1) Inauguration and Introduction
- (2) Review of epidemiology of snakes and status of snake bites management in the Region
- (3) Recent advances in management of snake bites
- (4) Revised WHO/SEARO Guidelines on management of snake bites in South-East Asia and its implementation in the countries
- (5) Production capacity for antivenom in the Region and current requirements
- (6) Enhancing availability of antivenom in countries with inadequate or no production capacity
- (7) Strengthening of health systems to improve access to antivenom
- (8) Development of key follow-up action points
- (9) Conclusions and Recommendations
- (10) Closing session

Annex 2

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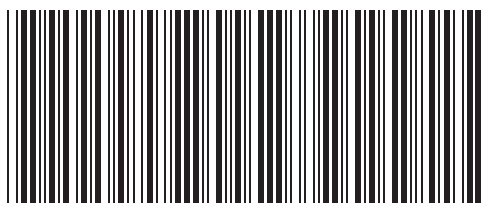
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Snake-bites are well-known medical emergencies in many parts of the world, especially in rural areas. Agricultural workers and children are the most affected. Snake antivenom provides a life-saving measure. The prevention of mortality and morbidity depends upon the availability of antivenom in the health facilities in these settings. Mechanisms need to be developed to assure access to antivenom by all needy patients. The health system needs to respond to this challenge and logistics must be put in place to assure timely availability of antivenom at the point of use. WHO's Regional Office for South-East Asia (SEARO) developed guidelines on the management of snake-bites, which are being revised and updated with the latest knowledge in the area. These issues were discussed in a regional meeting that was organized at Yangon, Myanmar on 30 November-2 December 2009. This report summarizes the deliberations made in this meeting.



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