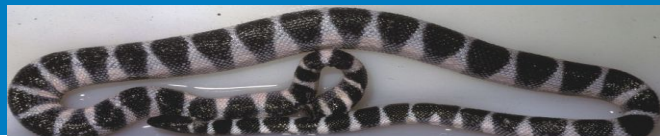
World Health Organization
Regional Office for South-East Asia

Guidelines for the management of snake-bites



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Guidelines for the management of snake-bites

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Contents

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Prof David Warrell, Emeritus Professor of Tropical Medicine, Oxford, UK wrote the first draft of the Guidelines. These were finalized through a meeting of experts held at Yangon, Myanmar in December 2009. The list of experts who contributed can be seen as Annex 7. Contributions of all the experts are sincerely acknowledged.

Foreword

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 incidence of snake-bite mortality is particularly high in South-East Asia.

Snake antivenom provides a specific lifesaving 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 these needs. This trend needs to be reversed through concerted actions by national, regional and world health authorities and manufacturers and through effective public–private partnership. The prevention of mortality and morbidity depend upon availability of antivenom in the health facilities in these settings and their rational use. Mechanisms need to be developed to ensure access to antivenom by all needy patients. The health system needs to respond to this challenge and logistics must be put in place to ensure timely availability of antivenom at the point of use.

WHO/SEARO had developed guidelines on the management of snake-bites which were also published as a special issue of the *Southeast Asian Journal of Tropical Medicine and Public Health* in 1999. WHO has supported countries in developing similar guidelines. To keep pace with the advances in science and on the basis of global experience, the regional guidelines have now been revised.

I hope that these guidelines will help Member States to improve their management of snake-bites, especially in the peripheral health services and shall be useful in saving human lives and mitigate misery due to snake-bites.

Samlee Plianbangchang

Dr Samlee Plianbangchang
Regional Director

Preface to the second edition

Geographical coverage

The geographical area specifically covered by this publication extends from India in the west to DPR Korea and Indonesia in the east, Nepal and Bhutan in the north, and to Sri Lanka and Indonesia in the south and south-east. Snakes inhabiting the Indonesian islands east of Wallace's line (West Papua and Maluku Islands) are part of the Australasian elapid fauna, differing from those west of this line.

Snake-bite is a neglected tropical disease

Early in 2009, snake-bite was finally included in the WHO's list of neglected tropical diseases http://www.who.int/neglected_diseases/en/ confirming the experience in many parts of this region that snake-bite is a common occupational hazard of farmers, plantation workers and others, resulting in tens of thousands of deaths each year and many cases of chronic physical handicap (WHO, 2007; Williams, 2010). Much is now known about the species of venomous snakes responsible for these bites, the nature of their venoms and the clinical effects of envenoming in human patients.

Antivenoms are essential drugs

The only specific antidotes to snake venoms are immunoglobulin antivenoms which are now recognised as essential drugs (19.2 Sera and immunoglobulins) http://www.who.int/selection_medicines/committees/expert/17/sixteenth_adult_list_en.pdf

Target readership

This publication aims to pass on a digest of available knowledge about all clinical aspects of snake-bite to medically trained personnel. The guidelines are intended for medical doctors, nurses, dispensers and community health workers who have the responsibility of treating victims of snake-bite. They aim to provide sufficient practical information to allow medically trained personnel to assess and treat patients with snake-bites at different levels of the health service.

Levels of evidence

Recommendations are based largely on observational studies ("O" see below), expert opinion ("E") and, in some cases, comparative trials ("T"), but in only one case on formal systematic reviews ("S").

Symbols for the evidence used as the basis of each recommendation (in order of level of evidence) are:

S formal systematic reviews, such as Cochrane Reviews of which there is only one in the field of snake-bite. These include more than one randomized controlled trial;

T comparative trials without formal systematic review;

O observational studies (e.g. surveillance or pharmacological data);

E expert opinion/consensus.

References and further reading

The restrictions on the size of this document prevented the inclusion of detailed references to all the original publications on which these recommendations were based. These can be found in the papers and reviews listed in "Further Reading".

Useful points raised by users of the first edition were the need to include the snake species in Indonesia east of Wallace's line (see above) and the importance of providing guidance on initial dosages of the antivenoms now listed in Annex 3 and Table 1.

WHO initiatives

This edition is updated to include the results of much additional clinical research published since 1999 including two WHO publications, "Rabies and envenomings : a neglected public health issue", report of a Consultative Meeting, WHO, Geneva, 10 January 2007 and "WHO Guidelines for the Production, Control and Regulation of Snake Antivenom Immunoglobulins" WHO Geneva 2010. These publications together with a venomous snakes and antivenoms website are available online at http://www.who.int/bloodproducts/snake_antivenoms/en/

Any recommendations must be continually reconsidered in the light of new evidence and experience. Comments from readers are welcomed so that future editions can be updated and improved.

1

Executive summary

i. It is clear that in many parts of the South East Asian region, snake-bite is an important medical emergency and cause of hospital admission. It results in the death or chronic disability of many active younger people, especially those involved in farming and plantation work. However, the true scale of mortality and acute and chronic morbidity from snake-bite remains uncertain because of inadequate reporting in almost every part of the region. To remedy this deficiency, it is strongly recommended that snake-bite should be made a specific notifiable disease in all countries in the South East Asian region.

ii. Snake-bite is an occupational disease of farmers, plantation workers, herdsmen, fishermen, snake restaurant workers and other food producers. It is therefore a medical problem that has important implications for the nutrition and economy of the countries where it occurs commonly. It is recommended that snake-bite should be formally recognised as an important occupational disease in the South East Asian region.

iii. Despite its importance, there have been fewer proper clinical studies of snake-bite than of almost any other tropical disease. Snake-bites probably cause more deaths in the region than do *Entamoeba histolytica* infections but only a small fraction of the research investment in amoebiasis has been devoted to the study of snake-bite. It is recommended that governments, academic institutions, pharmaceutical, agricultural and other industries and other funding bodies, should actively encourage and sponsor properly designed clinical studies of all aspects of snake-bite.

iv. Some ministries of health in the region have begun to organise training of doctors and other medical workers in the clinical management of snake-bite patients. However, medical personnel throughout the region would benefit from more formal instruction on all aspects of the subject. This should include the identification of medically-important species of

snakes, clinical diagnosis and the appropriate use of antivenoms and ancillary treatments. It is recommended that education and training on snake-bite should be included in the curriculum of medical schools and should be addressed specifically through the organisation of special training courses and other educational events.

v. Community education on snake-bite is outside the terms of reference of this publication.

However, it is clear that this is an essential component of any community public health programme. Community education about venomous snakes and snake-bite is strongly recommended as the method most likely to succeed in preventing bites.

vi. Most of the familiar methods for first-aid treatment of snake-bite, both western and "traditional/herbal", have been found to result in more harm (risk) than good (benefit). Their use should be discouraged and they should never be allowed to delay the movement of the patient to medical care at the hospital or dispensary. Recommended first-aid methods emphasise reassurance, immobilisation of the whole patient and particularly the bitten limb and movement of the patient to a place where they can receive medical care as soon as possible.

vii. Diagnosis of the species of snake responsible for the bite is important for optimal clinical management. This may be achieved by identifying the dead snake or by inference from the "clinical syndrome" of envenoming. A syndromic approach should be developed for diagnosing the species responsible for snake-bites in different parts of the region.

viii. Antivenom is the only effective antidote for snake venom. It is an essential element of treatment of systemic envenoming but may be insufficient on its own to save the patient's life. Antivenom may be expensive and in short supply.

a. It is recommended that antivenom should be used only in patients in whom the benefits of treatment are considered to exceed the risks of antivenom reactions. Indications for antivenom include signs of systemic and/or severe local envenoming.

b. Skin/conjunctival hypersensitivity testing does not reliably predict early or late antivenom reactions and is not recommended.

c. It is recommended that whenever possible antivenom should be given by slow intravenous injection or infusion.

d. Epinephrine (adrenaline) should always be drawn up in readiness in case of an early anaphylactic antivenom reaction.

e. No method of preventing antivenom reactions has been proved effective, including prophylactic epinephrine/adrenaline.

ix. When no antivenom is available, judicious conservative treatment can in many cases save the life of the patient.

x. In the case of neurotoxic envenoming with bulbar and respiratory paralysis, antivenom alone cannot be relied upon to prevent early death from asphyxiation. Artificial ventilation is essential in such cases.

xi. Conservative management and, in some cases, dialysis, is an effective supportive treatment for acute kidney injury in victims of Russell's viper, hump-nosed viper and sea snake-bites.

xii. Fasciotomy should not be carried out in snake-bite patients unless or until haemostatic abnormalities have been corrected, clinical features of an intracompartmental syndrome are present and a high intracompartmental pressure has been confirmed by direct measurement.

2

Prevention

2.1 How can snake-bites be avoided

Snake-bite is an environmental, occupational and climatic hazard in rural and urban areas of many countries of the South-East Asia Region of the WHO. Attention to the following recommendations for community education might reduce the risk of bites. Snakes have adapted to a wide range of habitats and prey species. All snakes are predatory carnivores, none is vegetarian although some eat eggs. Since snakes are preyed upon by other animals, they tend to be secretive and have evolved many survival strategies. By understanding something about the habits of snakes, simple precautions can be adopted to reduce the chance of encounters and consequently bites. One must know the local snakes, the sort of places where they prefer to live and hide, the time of year and time of day or night and the kind of weather when they are most likely to be actively out and about. Many species are mainly nocturnal (night hunters) e.g. kraits, but other species are mainly diurnal (day-time hunters). Be specially vigilant about snake-bites after rains, during flooding, at harvest time and at night. Snakes prefer not to confront large animals such as humans so give them the chance to slither away.

In the house: Snakes may enter the house in search of food or to find a hiding place for a while. Do not keep livestock, especially chickens, in the house, as snakes may come to hunt them. Store food in rat-proof containers. Regularly check houses for snakes and, if possible, avoid those types of house construction that will provide snakes with hiding places (e.g. thatched rooves with open eaves, mud and straw walls with large cracks and cavities and large unsealed spaces beneath floorboards). If possible, try to avoid sleeping on the ground. If you have to sleep on the ground use an insecticide-impregnated mosquito net that is well tucked in under the mattress or sleeping mat [Evidence level T]. This will protect against mosquitoes and other biting insects, centipedes, scorpions and snakes (Chappuis et al., 2007). No chemical has yet been discovered that is effectively repellent to snakes without being so toxic as to threaten the life of children and domestic animals.

In the farm yard, compound or garden: Try not to provide hiding places for snakes. Clear termite mounds, heaps of rubbish, building materials etc. from near the house. Do not have tree branches touching the house. Keep grass short or clear the ground around your house and clear low bushes in the vicinity so that snakes cannot hide close to the house. Keep your granary away from the house, it may attract rodents that snakes will hunt. Water sources, reservoirs and ponds may also attract prey animals such as frogs and toads. Listen to wild and domestic animals, especially birds, as they warn of a snake nearby. Use a light when you walk outside the house or visit the latrine at night.

In the countryside: Firewood collection at night is a real danger. Watch where you walk. Rather than walking bare-footed or wearing sandals, use proper shoes or boots and long trousers, especially when walking in the dark or in undergrowth. Step on to rocks or logs rather than straight over them – snakes may be sunning themselves on the sides. Do not put hands into holes or nests or any hidden places where snakes might rest. Use a light (torch, flashlight or lamp) when walking at night, especially after heavy rains. Be careful when handling dead or apparently dead snakes – even an accidental scratch from the fang of a snake's severed head may inject venom. Snake restaurants pose a threat of bites to staff and customers. Many snake-bites occur during ploughing, planting and harvesting and in the rainy season. Rain may wash snakes and debris into gutters at the edges of roads, and flush burrowing species out of their burrows. Hence, be careful when walking on roads after heavy rain, especially after dark.

On the road: Drivers or cyclists should never intentionally run over snakes on the road. The snake may not be instantly killed and may lie injured and pose a risk to pedestrians. The snake may also be injured and trapped under the vehicle, from where it will crawl out once the vehicle has stopped or has been parked in the house compound or garage.

In rivers, estuaries and the sea: To prevent sea snake-bites, fishermen should avoid touching sea snakes caught in nets and on lines. The head and tail are not easily distinguishable. There is a risk of bites to bathers and those washing clothes in the muddy water of estuaries, river mouths and some coastlines.

General: Avoid snakes as far as possible, including those displayed by snake charmers who are frequently bitten. Never handle, threaten or attack a snake and never intentionally trap or corner a snake in an enclosed space. Keep young children away from areas known to be snake-infested. In occupations that carry a risk of snake-bite, such as rice farming and fish farming, employers might be held responsible for providing protective clothing (boots). In Myanmar, farmers can take out special low-cost insurance to cover them specifically against snake-bite.

2.2 Implementing preventive strategies for community education

The above recommendations for preventing snake-bite can be disseminated for national or local use as guidelines, training modules, leaflets, video clips and posters that can be displayed on the walls of hospital and clinic waiting areas for the attention of patients and their families. At the village level, drama and puppet shows have been used successfully to portray snake-bite scenarios. Media such as radio and TV can be used for health promotion and advantage can be taken of FM radio phone-ins to publicise the problem. Increasingly, young people and advertisers use mobile phones and social networking (YouTube, Twitter) to communicate information. Religious organizations and charities such as Rotary Club and Lions Club might be persuaded to promote snake-bite awareness. It is especially valuable to win the support of high profile media figures such as film stars, pop stars, sporting heroes and politicians.

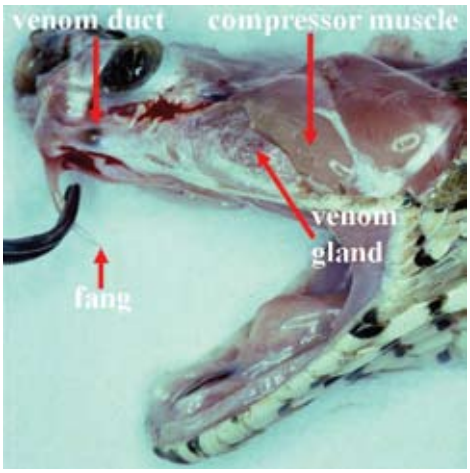
3

Venomous snakes of South-East Asia

3.1 The venom apparatus

The ability to inject venom into prey animals by means of cannulated, modified teeth evolved over 140 million years ago in bird-like dinosaurs and later in snakes (Gong et al., 2010). The venom glands of Elapidae and Viperidae are situated behind the eye, surrounded by compressor muscles (Gans and Gans 1978; Junghanss and Bodio 1995) (Fig. 1).

Figure 1: Venom apparatus of an eastern Russell's viper *(Daboia siamensis)* (Copyright DA Warrell)



The venom duct opens within the sheath at the base of the fang and venom is conducted to its tip through a groove or canal, as through a hypodermic needle. In Elapidae, the (proteroglyph) fangs are mounted on a relatively fixed maxilla at the front of the mouth (Fig. 2a). In Viperidae, the (solenoglyph) fangs are mounted on a rotatable maxilla so that they can be folded flat against the roof of the mouth (Fig. 2b). In Colubridae (used here in the broad sense, including some newly separated families), venom secreted by Duvernoy's (supralabial) glands tracks down grooves

in the anterior surfaces of (opisthoglyph) fangs at the posterior end of the maxilla (Fig. 2c). Fangs allow the snake to introduce venom deep into the tissues of its natural prey. If a human is bitten, venom is usually injected subcutaneously or intramuscularly. Spitting cobras can squeeze the venom out of the tips of their fangs producing a fine spray directed towards the eyes of an aggressor. The average dry weight of venom injected at a strike is approximately 60 mg in *N. naja*, 13 mg in *E. carinatus* and 63 mg in *D. russelii*.

Figure 2a: Short, permanently erect, front fangs of a typical elapid (Sri Lankan cobra - *Naja naja*) (Copyright DA Warrell)

Figure 2b: Long, hinged, front fangs of a typical viper (Thailand Russell's viper *Daboia siamensis*). A reserve fang is seen immediately behind the active fang. (Copyright DA Warrell)

Figure 2c: Rear fangs of a dangerously venomous Colubrid snake, the red-necked keelback (*Rhabdophis subminiatus*) (Copyright DA Warrell)

3.2 Classification of venomous snakes: Medically important species in South-East Asia Region countries (WHO 2010)

There are three families of venomous snakes in South-East Asia, Elapidae, Viperidae and Colubridae.

Elapidae: have relatively short fixed front (proteroglyph) fangs (Fig. 2a). This family includes cobras, king cobra, kraits, coral snakes, Australasian snakes and sea snakes. Elapidae are relatively long, thin, uniformly-coloured snakes with large smooth symmetrical scales (plates) on the top (dorsum) of the head. There is no loreal scale between the pre-ocular and nasal scales. Some, notably cobras, raise the front part of their body off the ground and spread and flatten the neck to form a hood (Fig. 3-8). Several species of cobra can spit their venom for one metre or more towards the eyes of perceived enemies. Venomous sea snakes have flattened paddle-like tails and their ventral scales are greatly reduced in size or lost (Fig. 20-24).

Some of the Elapidae inhabiting SEARO countries (References to reports of bites by these species are given in parenthesis):

Cobras (genus *Naja*):

Figure 3: Common spectacled cobra *(Naja naja)*: (a) and (b) Sri Lanka, (c) India (Copyright DA Warrell), (d) Nepal (Copyright Mark O'Shea)

Common spectacled Indian cobra *N. naja* (Fig. 3) (Theakston *et al.*, 1990)

Figure 4: North Indian or Oxus cobra *(Naja oxiana)* (Copyright DA Warrell)

North Indian or Oxus cobra *N. oxiana* (Fig. 4) (Warrell, 1995).

Figure 5: Monocellate cobras *(Naja kaouthia)* (Copyright DA Warrell) (a) specimen from India (b) specimen from Thailand (c) specimen from Thailand showing single "eye" marking on back of hood (Copyright DA Warrell)

Monocellate cobra *N. kaouthia* (Fig. 5a-c) (Reid 1964; Warrell 1986; Viravan *et al.*, 1992)

Figure 5d: Andaman cobra *Naja sagittifera* juvenile specimen (Copyright Ashok Captain)

Andaman cobra *Naja sagittifera* (Fig. 5d)

Figure 6: Indo-Chinese spitting cobra *(Naja siamensis)* specimens from Thailand (Copyright DA Warrell)
(a) Brown-coloured specimen (b) Black and white specimen with ill-defined spectacle marking on hood

Spitting cobras: *N. siamensis* (Fig. 6) (Warrell 1986; Warrell 1989; Wüster et al., 1997), *N. sumatrana* (Fig. 7), *N. sputatrix, N. mandalayensis* etc

Figure 7: Sumatran spitting cobra *(Naja sumatrana)* (Copyright DA Warrell)
(a) black phase (b) golden phase

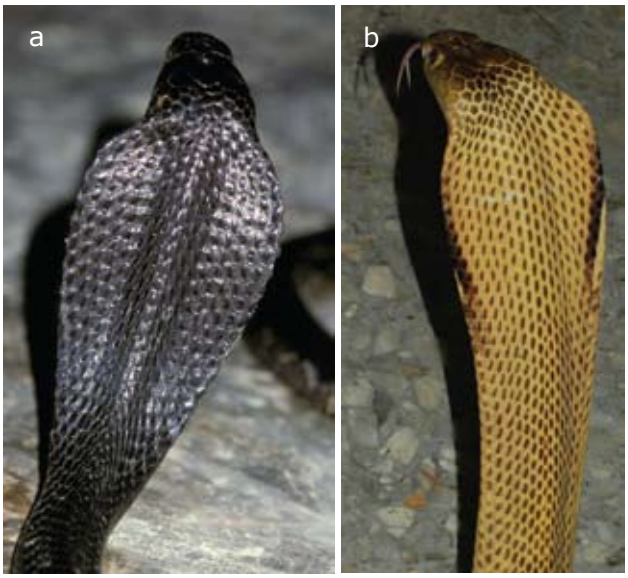
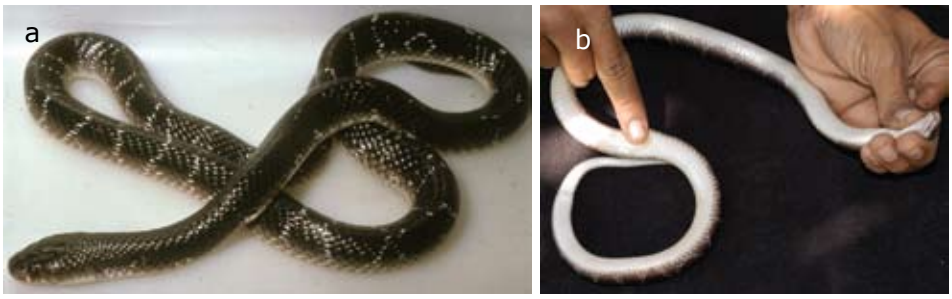


Figure 8: King cobra or hamadryad *(Ophiophagus hannah)*
(Copyright DA Warrell)
(a) The famous king cobra dance in Yangon, Myanmar
(b) Specimen from Thailand more than 3.5 metres in total length
(c) (d) (e) Dorsal and lateral views of head of Thai (c,d) and Indian (e) specimens showing the two large occipital scales (arrows) which distinguish this species from cobras (Naja)

King cobra: *Ophiophagus hannah* (Fig.. 8) (Tin-Myint et al., 1991)

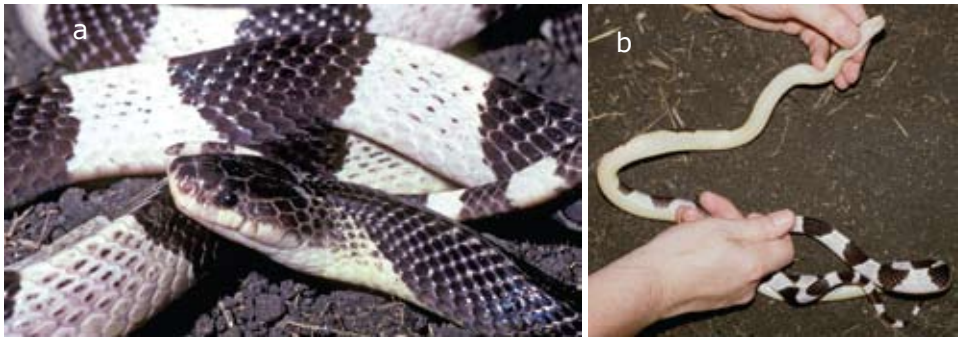
Kraits (genus *Bungarus*):

Figure 9: Common krait *(Bungarus caeruleus)* (Copyright DA Warrell)
(a) Sri Lankan specimen showing narrow white dorsal bands
(b) Indian specimen showing pure white ventrals



Common krait *B. caeruleus* (Fig. 9) (Theakston et al., 1990; Ariaratnam et al., 2009)

Figure 10: Malayan krait *(Bungarus candidus)* Thai specimen (Copyright DA Warrell)
(a) Showing dorsal black saddle-shaped markings
(b) Showing pure white ventrals



Malayan krait *B. candidus* (Fig. 10) (Warrell et al., 1983)

Figure 11: Chinese krait *(Bungarus multicinctus)* (Copyright DA Warrell)

Chinese krait *B. multicinctus* (Fig. 11) (Tun-Pe et al., 1997; Ha-Tran-Hung et al., 2009)

Figure 12: Greater black krait *(Bungarus niger)* Nepal
(Copyright F. Tillack)

Greater black krait B. niger (Fig. 12) (Faiz et al., 2010)

Figure 13: Banded krait *(Bungarus fasciatus)* Thai specimens
(Copyright DA Warrell)
(a) Showing black and yellow bands
(b) Showing circumferential black bands and blunt-tipped tail (scale in cms).

Banded krait *B. fasciatus* (Fig. 13) (Tun-Pe et al., 1997)

Figure 14: Red-headed krait *(Bungarus flaviceps)* Thai specimen
(Copyright DA Warrell)

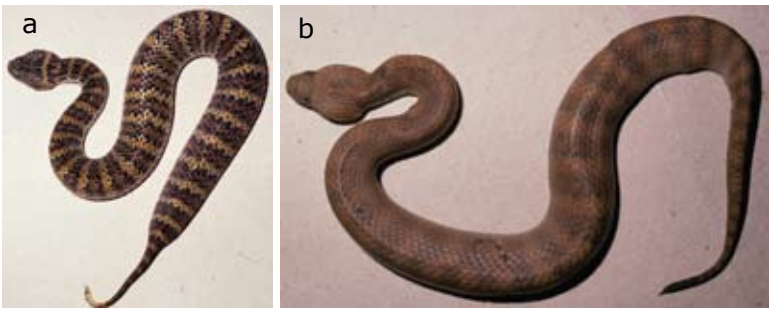
Red-headed krait *B. flaviceps* (Fig. 14), Wall's krait *B. walli*

Figure 15: Spotted coral snake *(Calliophis maculiceps)* Thai specimen (Copyright DA Warrell)

Spotted coral snake *Calliophis maculiceps* (Fig. 15) (Warrell, 1995).

Australasian elapids:

Figure 16a and b: Death adder *(Acanthophis laevis)* (Copyright DA Warrell) (a) Specimen from West Papua, Indonesia (b) Specimen from Seram, Indonesia



Death adders (Genus *Acanthophis*): *A. laevis* (Fig. 16a) and *A. rugosus* (Lalloo et al., 1996)

New Guinea small-eyed snake *Micropechis ikaheka* (Fig. 16b) (Warrell et al., 1996)

Figure 16c: New Guinea small-eyed snake *(Micropechis ikaheka)*. Specimen from Arso, West Papua, Indonesia 1.69m in total length responsible for a case of envenoming (see Warrell et al., 1996).

Figure 17: Papuan taipan *(Oxuyuranus scutellatus canni)* SaiBai Island, Torres Strait Islands (Copyright DA Warrell)

Papuan Taipan *Oxyuranus scutellatus canni* (Fig. 17) (Lalloo et al., 1995)

Figure 18: Papuan black snake *(Pseudechis papuanus)* SaiBai Island, Torres Strait Islands (Copyright DA Warrell)

Papuan black snake *Pseudechis papuanus* (Fig. 18) (Lalloo et al., 1994)

Figure 19: Eastern brown snake *(Pseudechis textilis)* (Copyright DA Warrell)

Brown snakes (Genus *Pseudonaja*) (Fig. 19) (White, 1995)

Figure 20: Beaked sea snake *(Enhydrina schistosa)* Bunapas Mission, Ramu River, Papua New Guinea (scale in cms) (Copyright DA Warrell)

Figure 21a: Blue spotted sea snake *(Hydrophis cyanocinctus)* (Copyright DA Warrell)

Figure 21b: Banded sea snake *(Hydrophis fasciatus atriceps) (Copyright DA Warrell)*

Figure 21c: Flattened paddle-like tail of sea snakes: *Hydrophis cyanocinctus* (above); *Lapemis curtus* (below) (Copyright DA Warrell)

Figure 22: Hardwick's sea snake *(Lapemis curtus)* showing tiny fangs (arrow) (Copyright DA Warrell)

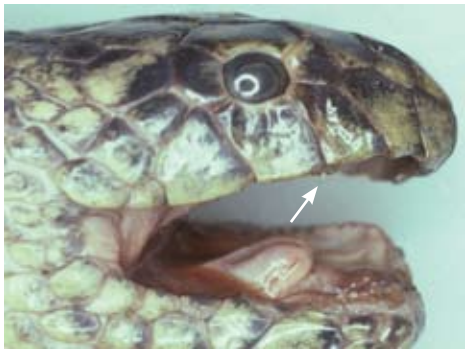


Figure 23: Yellow-bellied sea snake *(Pelamis platurus)* (FitzSimons Snake Park)

Figure 24: Sea krait *(Laticauda colubrina)* (Copyright DA Warrell) Madang, Papua New Guinea
(a) Showing blue and banded pattern and amphibious behaviour
(b) Showing fangs

Sea snakes (Reid 1975, 1979; Reid and Lim 1975; Warrell 1994): important species include *Enhydrina schistosa* (Fig. 20), *Hydrophis sp.* (Fig. 21), *Lapemis curtus* (Fig. 22), *Pelamis platurus* (Fig. 23) and *Laticauda colubrina* (Fig. 24).

Viperidae have relatively long fangs (solenoglyph) which are normally folded flat against the upper jaw but, when the snake strikes, they are erected (Fig. 2b). There are two subfamilies, typical vipers (Viperinae) and pit vipers (Crotalinae). The Crotalinae have a special sense organ, the loreal pit organ, to detect their warm-blooded prey. This is situated between the nostril and the eye (Fig. 25).

Viperidae are relatively short, thick-bodied snakes with many small rough scales on the top (dorsum) of the head and characteristic patterns of coloured markings on the dorsal surface of the body (Fig. 26).

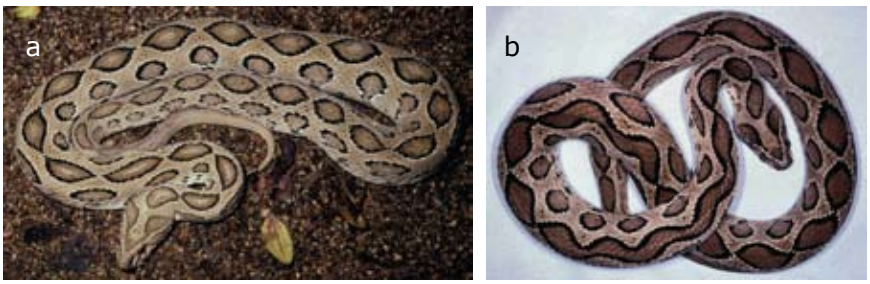
Figure 25: Head of a typical pit viper – dark green pit viper *(Cryptelytrops macrops)* showing the pit organ situated between the nostril and the eye (arrow) (Copyright DA Warrell)

Dark green pit viper *Cryptelytrops macrops* (Fig. 25) (Hutton et al., 1990; Warrell 1990b)

Some of the Viperidae inhabiting South-East Asia Region countries

Typical vipers (sub-family Viperinae):

Figure 26: Western Russell's viper *(Daboia russelii)*
(Copyright DA Warrell)
(a) Specimen from southern India
(b) Specimen from Sri Lanka



Russell's vipers, Western, *Daboia russelii* (Fig. 26) (Phillips et al., 1988; Warrell 1989; Gawarammana *et al.*, 2009); and Eastern, *D. siamensis* (Fig. 27) (Myint-Lwin *et* al., 1985; Tun-Pe *et al.*, 1987; Than-Than et al., 1987; Than-Than et al., 1988; Warrell 1989; Than-Than *et al.*, 1989; Thein-Than et al., 1991; Tin-Nu-Swe et al., 1993; Belt et al., 1997)

Figure 27: Eastern Russell's vipers *(Daboia siamensis)* (Copyright DA Warrell) (a) Specimen from Myanmar; (b) Specimen from Thailand (c) Specimen from East Java, Indonesia; (d) Specimen from Flores, Indonesia

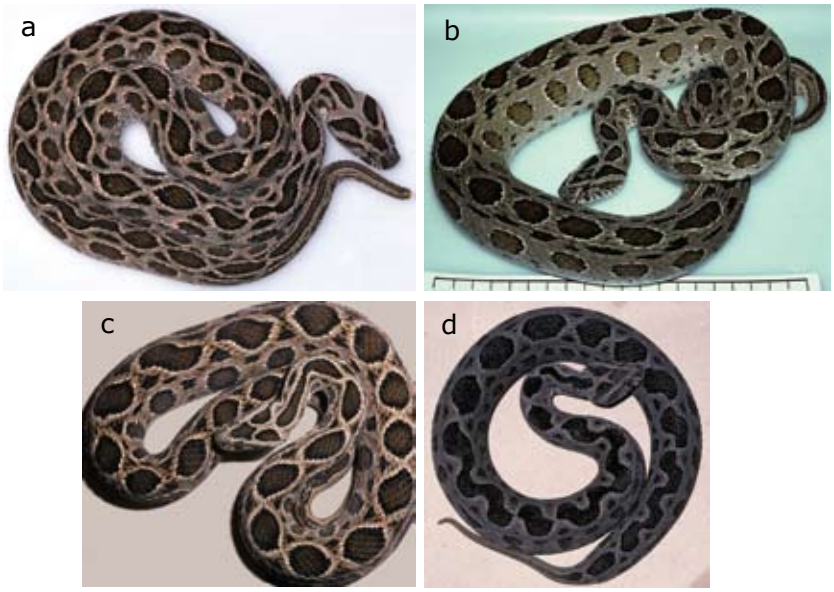
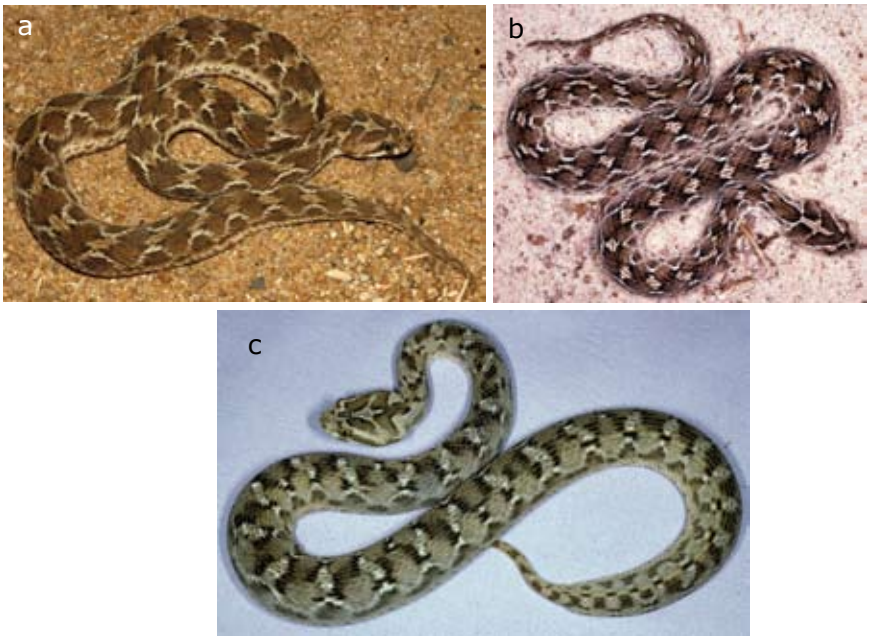


Figure 28: Saw-scaled vipers *(Echis carinatus)* (Copyright DA Warrell) (a) *Echis carinatus carinatus* Specimen from southern India (b) *Echis carinatus carinatus* Specimen from Sri Lanka (c) *Echis carinatus sochureki*



Saw-scaled or carpet vipers *Echis carinatus* (Fig. 28) (Bhat 1974; Warrell and Arnett 1976; Kochar et al., 2007)

Figure 28b: Levantine or blunt-nosed viper (*Macrovipera lebetina*) (Copyright DA Warrell)

Levantine or blunt-nosed viper *Macrovipera lebetina* (Fig. 28b) (Sharma et al., 2008)

Pit vipers (sub-family Crotalinae):

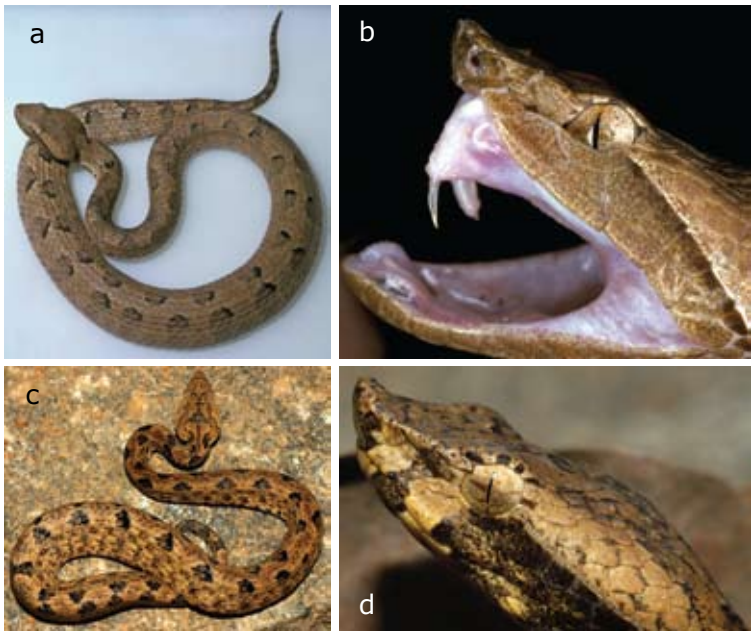
Figure 29: Malayan pit viper *(Calloselasma rhodostoma)* Thai specimen (Copyright DA Warrell)
(a) Showing characteristic posture and triangular dorsal markings (scale in cms) (b) Showing supralabial markings

Malayan pit viper *Calloselasma rhodostoma* (Fig. 29) (Reid et al., 1963a; Reid *et al.*, 1963b; Reid 1968; Warrell et al., 1986)

Figure 30a: Mount Kinabalu pit viper *(Garthia chaseni)* (Copyright Prof RS Thorpe)

Mount Kinabalu pit viper *Garthia chaseni* (Fig. 30a) (Haile 1963; Warrell 1995)

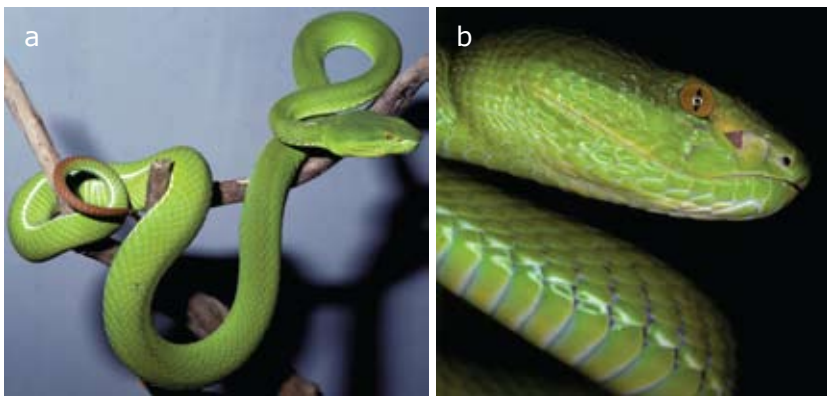
Figure 30b-e: Hump-nosed viper *(Hypnale hypnale)*
(Copyright DA Warrell)
(a) Specimen from Sri Lanka
(b) Specimen from Sri Lanka showing long fangs
(c) Specimen from south western India
(d) Specimen from south western India showing upturned snout



Hump-nosed viper *Hypnale hypnale* (Fig. 30a-d) (Joseph et al., 2007; Ariaratnam et al.,2008)

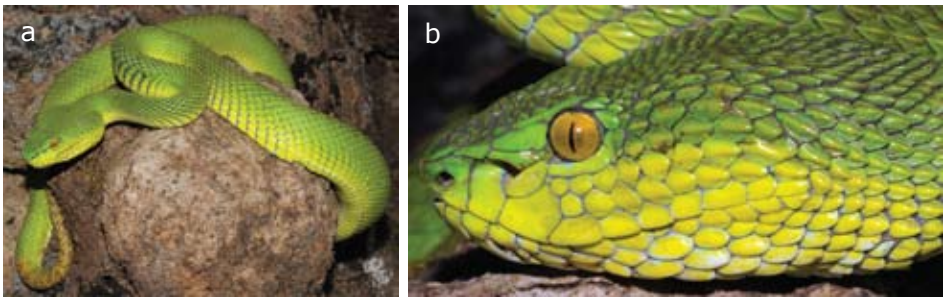
Green pit vipers, bamboo vipers, palm vipers and habus (formerly all genus *Trimeresurus)*

Figure 31: White-lipped green pit viper *(Cryptelytrops albolabris)* Thai specimen (Copyright DA Warrell)
(a) Showing colouring and distinctive brown-topped tail
(b) Showing details of the head: note smooth temporal scales



White-lipped green pit viper *Cryptelytrops albolabris* (Fig. 31) (Hutton et al., 1990; Rojnuckarin et al., 2006)

Figure 32: Spot-tailed green pit viper *(Cryptelytrops erythrurus)*
Specimen from near Yangon, Myanmar (Copyright DA Warrell)
(a) Showing colouring and brown spotted tail
(b) Showing details of head; note keeled temporal scales.



Spot-tailed green pit viper *Cryptelytrops erythrurus* (Fig. 32) (Warrell 1995); Kanchanaburi pit viper *Cryptelytrops kanburiensis* (Warrell et al., 1992)

Figure 33a,b: Mangrove pit viper *(Cryptelytrops purpureomaculatus)*
(Copyright DA Warrell)
(a) Specimen from Kanchanaburi, Thailand
(b) Specimen from upper Myanmar

Mangrove pit viper *Cryptelytrops purpureomaculatus* (Fig. 33a-b) (Warrell 1995)

Figure 33c: Beautiful pit viper *(Cryptelytrops venustus)* specimen from Thung Song, Thailand (Copyright DA Warrell)

Beautiful pit viper *Cryptelytrops venustus* (Fig. 33c)

Figure 34a: Mamushi or Fu-she *(Gloydius brevicaudus)* from China (Copyright DA Warrell)

Mamushis (Genus *Gloydius*): *G. brevicaudus* (Fig. 34a) (Warrell 1995)

Figure 34b: Hagen's pit viper *(Parias hageni)* Trang, Thailand (Copyright DA Warrell)

Hagen's pit viper *Parias hageni* (Fig. 34c)

Figure 35a: Pope's pit viper *(Popeia popeiorum)* Thailand (Copyright DA Warrell)

Pope's pit viper *Popeia popeiorum* (Fig. 35a)

Figure 35b: Chinese habu *(Protobothrops mucrosquamatus)* Specimen from China (Copyright DA Warrell)

Chinese habu *Protobothrops mucrosquamatus* (Fig. 35b) (Warrell 1995)

Figure 36: Indian bamboo viper *(Trimeresurus gramineus)* (Copyright DA Warrell)

Indian bamboo viper *Trimeresurus gramineus* (Fig. 36)

Figure 37: Palm viper *(Trimeresurus puniceus)* Specimen from Cilacap, West Java, Indonesia (Copyright DA Warrell)

Palm viper *Trimeresurus puniceus* (Fig. 37)

Figure 38a: Sri Lankan pit viper *(Trimeresurus trigonocephalus)* (Copyright DA Warrell)

Sri Lankan viper *Trimeresurus trigonocephalus* (Fig. 38a) (Warrell 1995)

Figure 38b: Wagler's (temple) pit viper *(Tropidolaemus wagleri)* specimens in the snake temple, Penang, Malaysia (Copyright DA Warrell)

Wagler's (temple) pit viper *Tropidolaemus wagleri* (Fig. 38b) (Reid 1968)

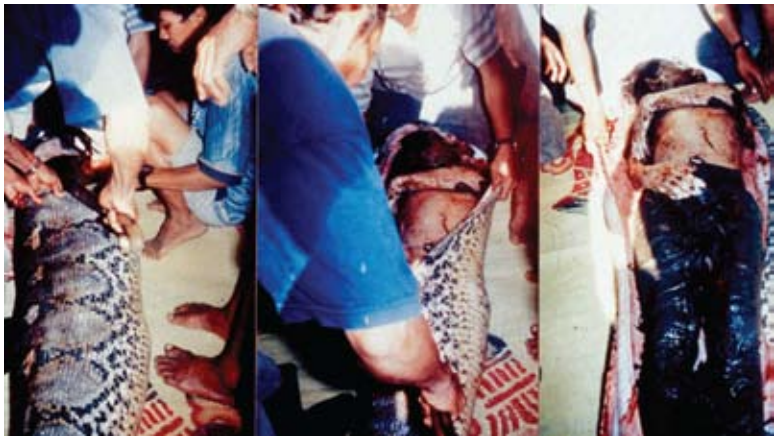
Figure 38c: Banded temple viper *(Tropidolaemus semiannulatus)* Borneo

Banded temple viper *Tropidolaemus subannulatus* (Fig. 38c)

Figure 39a: Chinese bamboo viper *(Viridovipera stejnegeri)* Specimen from China (Copyright DA Warrell)

Chinese bamboo viper *Viridovipera stejnegeri* (Fig. 39) (Warrell 1995)

Figure 39b: Reticulated python *(Python reticularis)* containing the body of a farmer it had swallowed at Palu, Sulawesi, Indonesia (Copyright Excel Sawuwu)



Other medically important venomous snakes

Two species of medically important Colubridae have been identified in the SEA Region, the red-necked keelback *Rhabdophis subminiatus* (Fig. 2c) and Yamakagashi *R. tigrinus* (Warrell 1995).

Large pythons (Boidae), notably the reticulated python *Python reticularis* in Indonesia, have been reported to attack and even ingest humans, usually inebriated farmers (Fig. 39b).

3.3 How to identify venomous snakes

Unfortunately, there is no simple rule for identifying a dangerous venomous snake. Some harmless snakes have evolved to look almost identical to venomous ones. Examples are various species of *Lycodon, Dryocalamus* and *Cercaspis* that mimic the appearance of the kraits *B. candidus, B. caeruleus* and *B. ceylonicus;* and *Boiga multomaculata* that mimics *Daboia siamensis*. However, some of the most notorious venomous snakes can be recognized by their size, shape, colour, pattern of markings, behaviour and the sound they make when they feel threatened. For example, the defensive behaviour of the cobras is well known (Fig. 3-8): they rear up, spread a hood, hiss and make repeated strikes towards the aggressor. Colouring can vary a lot. However, some patterns, like the large white, dark-rimmed annular (ring) spots of the Russell's vipers (Fig. 26, 27) or the alternating black and yellow circumferential bands of the banded krait (Fig. 13) are distinctive. The blowing hiss of the Russell's viper and the grating rasp of the saw-scaled viper are warning and identifying sounds.

4

Snake venoms*

4.1 Venom composition

More than 90% of snake venom (dry weight) is protein. Each venom contains more than a hundred different proteins: enzymes (constituting 80-90% of viperid and 25-70% of elapid venoms), non-enzymatic polypeptide toxins, and non-toxic proteins such as nerve growth factor.

Venom enzymes

These include digestive hydrolases, hyaluronidase, and activators or inactivators of physiological processes, such as kininogenase. Most venoms contain L-amino acid oxidase, phosphomono- and diesterases, 5'-nucleotidase, DNAase, NAD-nucleosidase, phospholipase A_2 and peptidases.

Zinc metalloproteinase haemorrhagins: Damage vascular endothelium, causing bleeding.

Procoagulant enzymes: Venoms of Viperidae and some Elapidae and Colubridae contain serine proteases and other procoagulant enzymes that are thrombin-like or activate factor X, prothrombin and other clotting factors. These enzymes stimulate blood clotting with formation of fibrin in the blood stream. Paradoxically, this process results in incoagulable blood because most of the fibrin clot is broken down immediately by the body's own plasmin fibrinolytic system and, sometimes within 30 minutes of the bite, the levels of clotting factors are so depleted ("consumption coagulopathy") that the blood will not clot. Some venoms contain multiple anti-haemostatic factors. For example, Russell's viper venom contains toxins that activate factors V, X, IX and XIII, fibrinolysis, protein C, platelet aggregation, anticoagulation and haemorrhage.

*(Bucherl et al., 1968,1971; Gans and Gans 1978; Lee 1979; Harvey 1991; Ménez 2003; Warrell 2010)

Phospholipase A_2 (lecithinase): The most widespread and extensively studied of all venom enzymes. It damages mitochondria, red blood cells, leucocytes, platelets, peripheral nerve endings, skeletal muscle, vascular endothelium, and other membranes, produces presynaptic neurotoxic activity, opiate-like sedative effects, leads to the autopharmacological release of histamine and anti-coagulation.

Acetylcholinesterase: Although found in most elapid venoms, it does not contribute to their neurotoxicity.

Hyaluronidase: Promotes the spread of venom through tissues.

Proteolytic enzymes (metalloproteinases, endopeptidases or hydrolases) and polypetide cytotoxins ("cardiotoxins"): Increase vascular permeability causing oedema, blistering, bruising and necrosis at the site of the bite.

Venom polypeptide toxins ("neurotoxins")

Postsynaptic (α) neurotoxins such as α-bungarotoxin and cobrotoxin, consist of 60-62 or 66-74 amino acids. They bind to acetylcholine receptors at the motor endplate. Presynaptic (β) neurotoxins such as β-bungarotoxin, crotoxin, and taipoxin, contain 120-140 amino acids and a phospholipase A subunit. These release acetylcholine at the nerve endings at neuromuscular junctions and then damage the endings, preventing further release of transmitter.

4.2 Quantity of venom injected at a bite, "dry bites"

This is very variable, depending on the species and size of the snake, the mechanical efficiency of the bite, whether one or two fangs penetrated the skin and whether there were repeated strikes. Either because of mechanical inefficiency or the snake's control of venom discharge, a proportion of bites by venomous snakes does not result in the injection of sufficient venom to cause clinical effects. About 50% of bites by Malayan pit vipers and Russell's vipers, 30% of bites by cobras and 5%-10% of bites by saw-scaled vipers do not result in any symptoms or signs of envenoming. Snakes do not exhaust their store of venom, even after several strikes, and they are no less venomous after eating their prey (Tun-Pe et al., 1991).

Although large snakes tend to inject more venom than smaller specimens of the same species, the venom of smaller, younger vipers may be richer in some dangerous components, such as those affecting haemostasis.

Recommendation: Bites by small snakes should not be ignored or dismissed. They should be taken just as seriously as bites by large snakes of the same species.

5

Epidemiology of snake-bite in South-East Asia Region

5.1 Introduction

It is generally recognised that the epidemiology of snake-bite in the South-East Asia (SEA) region has not been adequately studied and that the published data, based almost exclusively on hospital returns to the Ministries of Health, are likely to be unreliable and therefore misleading. One reason is that many snake-bite victims are treated not in hospitals but by traditional healers (Warrell, 1992). In the past half century, only three attempts have been made to assess global snake-bite mortality. In 1954, Swaroop and Grab of the Statistical Studies Section, WHO, estimated that among half a million snake-bites and between 30 000 and 40 000 snake-bite deaths each year in the world as a whole, there were between 25 000 and 35 000 deaths in Asia. Their analysis was based on registration of deaths occuring in different countries, but they recognised the following deficiencies in this method:

(1) "Available statistical data are known to be unreliable and, at best, can serve to provide only an approximate and highly conservative estimate of the relative magnitude of the snake-bite problem."

(2) "The chance of snake-bite deaths being missed are perhaps even greater than for deaths occurring from several other causes."

(3) "The recorded figures of snake-bite deaths may therefore be regarded as under-estimates of the total fatality from this cause, the degree of under-recording varying from place to place."

In 1998, Chippaux published an appraisal of the global situation, again based mainly on hospital records or health authority statistics, quoting 114 publications. He speculated that the total number of snake-bites each year might exceed five million with a snake-bite mortality of 125 000 each year in the world as a whole, including four million snake-bites, two million snake-bite envenomings, and 100 000 snake-bite deaths each year in Asia.

In 2008 Kasturiratne *et al.* estimated 237 379–1184 550 envenomings with 15 385–57 636 deaths in the Asia-Pacific Region (South Asia 14 112-33 666 – rate 0.912-2.175/100 000/year; East Asia 462-4,829 – rate 0.033-0.347/100 000/year). Their most conservative estimate of the highest number of deaths due to snake-bite was 14 000 in South Asia. Various studies suggest that bites with envenoming constitute 12%-50% of the total number of bites in Asia and 18%-30% in India and Pakistan.

A fundamental problem throughout much of the Asia-Pacific Region is that snake-bite treatment has remained in the domain of traditional, herbal or ayurvedic practitioners, so that the majority of snake-bite victims are not seen or recorded in western-style hospitals or dispensaries. For example, in Wat Promlok, Nakorn Srithamarat, Thailand, one "moor glang baan" (traditional therapist) treated 72-393 snake-bite victims each year between 1985 and 2002.

In the Terai of Nepal, a community-based study established the high fatality rate of 161/100 000/year, attributable mainly to krait bites (Sharma et al., 2004). Few other community studies have been attempted (Hati et al. 1992). In some countries, such as Sri Lanka, there has, over the last two decades, been a dramatic shift in patients' preference for treatment from ayurvedic to Western medicine.

Despite these deficiencies in study methods and data, some useful conclusions can be inferred.

Recommendation: To remedy the deficiency in reliable snake-bite data, it is strongly recommended that snake-bites should be made a specific notifiable disease in all countries in the WHO South-East Asia Region and that death certification should use the specific International Classification of Diseases code T63.0.

5.2 Determinants of snake-bite incidence and severity of envenoming

The incidence of snake-bites depends critically on the frequency of contact between snakes and humans. Except at times of flooding, snakes are elusive and reclusive and so contact with humans is likely only when humans move into the snakes' favoured habitat (rice fields in the case of Russell's vipers and cobras; rubber and coffee plantations in the case of Malayan pit vipers) or when nocturnally active snakes are trodden upon by people walking along paths in the dark. Seasonal peaks of snake-bite incidence are usually associated with increases in agricultural activity or seasonal rains, perhaps coinciding with unusual movement and activity by snakes. Different species of snakes vary in their willingness to strike when disturbed. Typically

"irritable" species include Russell's vipers (*Daboia russelii* and *D. siamensis*) and saw-scaled vipers (*Echis*).

Bites may be inflicted in the home by peri-domestic species such as cobras (*Naja*) which may live in roof spaces or under the floor and by kraits (*Bungarus*) which enter human dwellings at night in search of their prey and may bite people who move in their sleep. The risk of envenoming after bites by venomous snakes varies with the species but is on an average only about 50%. Bites in which the fangs pierce the skin but no envenoming results are known as "dry bites". The explanation for dry bites is either mechanical inefficiency of the venom apparatus striking at an unnatural angle (or through clothing) or perhaps voluntary retention of venom by the snake.

Epidemics of snake-bite may result from heavy flooding, as has been reported from India, Bangladesh and Myanmar, and when the snakes' habitat is invaded by a large workforce involved in road building or logging and as a result of irrigation schemes (e.g. the Mahaweli Irrigation Scheme in Sri Lanka) that alter the climate and ecology of a large area, making it newly attractive both for snakes and farmers. There was no immediate increase in snake-bites in Myanmar after Cyclone Nargis but an increase was recorded in the aftermath 9-12 months later.

5.3 Epidemiological characteristics of snake-bite victims

Males are more often bitten than females, except where the work force is predominantly female (e.g. tea and coffee picking). The peak age for bites is children (WHO UNICEF, 2008) and young adults. There is some evidence that peak case fatality is in young children and the elderly. In pregnant women, snake-bite carries definite but unquantified risks to mother and fetus, mainly from bleeding and abortion. Most snake-bites are inflicted on the feet and ankles of agricultural workers.

5.4 Circumstances of snake-bites

Most snake-bites happen when the snake is trodden on, either in the dark or in undergrowth, by someone who is bare-footed or wearing only sandals. The snake may be picked up, unintentionally in a handful of foliage or intentionally by someone who is trying to show off. Some bites occur when the snake (usually a krait) comes in to the home at night in search of its prey (other snakes, lizards, frogs, mice) and someone sleeping on the floor rolls over onto the snake in their sleep. Not all snake-bites happen in rural areas. For example, in some large cities, such as Jammu in India, people who sleep in small huts (*jhuggies*) are frequently bitten by kraits during the night and wake with paralysis (Saini et al., 1986).

5.5 Snake-bite as an occupational disease

In SEA Region countries, the risk of snake-bite is strongly associated with occupations: farming (rice), plantation work (rubber, coffee), herding, hunting, fishing and fish farming, catching and handling snakes for food (in snake restaurants), displaying and performing with snakes (snake charmers), manufacturing leather (especially sea snakes), and in the preparation of traditional (Chinese) medicines.

Box: **Snake-bite: An occupational disease in South-East Asia**

Farmers (rice)
Plantation workers (rubber, coffee)
Herdsmen
Hunters
Snake-handlers (snake charmers and in snake restaurants and traditional Chinese pharmacies)
Fishermen and fish farmers
Sea-snake catchers (for sea snake skins, leather)

5.6 Death from snake-bite

Contributing factors

Few attempts have been made to examine the factors responsible for death in cases of bites by identified species of snakes. In a study of 46 cases of identified snake-bite in Thailand, the three species causing most deaths were Malayan krait (*Bungarus candidus*), Malayan pit viper (*Calloselasma rhodostoma*) and cobras (*Naja* species) (Looareesuwan et al., 1988). Factors identified as contributing to a fatal outcome included problems with antivenom use (inadequate dose or use of a monospecific antivenom of inappropriate specificity), delayed hospital treatment resulting from prolonged visits to traditional healers and problems with transportation, death on the way to hospital, inadequate artificial ventilation or failure to attempt such treatment, failure to treat hypovolaemia in shocked patients, airway obstruction, complicating infections, and failure to observe patients closely after they were admitted to hospital.

Time between snake-bite and death

Although very rapid death after snake-bite has rarely been reported (e.g. reputedly "a few minutes" after a bite by the king cobra *Ophiophagus hannah*), it is clear from studies of large series of snake-bite deaths that many hours usually elapse between bite and death in the case of elapid envenoming, and several days in the case of viper envenoming (Reid 1968; Warrell 1995).

5.7 Snake-bite in different countries of SEA Region

For each Member country of SEA Region , some information on the estimated incidence of snake-bite is given based on reports published and unpublished. The most important snake species from a medical point of view are given in the boxes, according to the following definitions (WHO, 2010):

CATEGORY 1: Highest medical importance: Highly venomous snakes which are common or widespread and cause numerous snake-bites, resulting in high levels of morbidity, disability or mortality.

CATEGORY 2: Secondary medical importance: Highly venomous snakes capable of causing morbidity, disability or death, but (a) for which exact epidemiological or clinical data are lacking or (b) are less frequently implicated because of their behaviour, habitat preferences or occurrence in areas remote to large human populations.

Bangladesh: In 1988-1989, a study discovered records of 764 bites and 168 deaths (22% case fatality), of which 34% were cobra (*Naja naja, N. kaouthia*) bites, carrying a 40% case fatality. A total of 8 000 bites per year across Bangladesh was estimated (Sarkar et al., 1999). A postal survey suggested 4.3 bites/100 000/year, rising to 7 per 100 000 in areas like Chittagong Division, with an overall case fatality of 20% (Huq et al., 1995). Forty-five per cent of victims are said to be farmers and 23% housewives. Most patients are treated by traditional healers (*ozhas*) and 20% of fatal cases receive no conventional medical treatment (Ali Reza Khan. Indo-Asian News Service, Dhaka October 12, 2001). In one five-year study of 336 cases of snake-bite at Mymensingh Medical College Hospital, 70% of cases were aged 11-30 years and 75% were males (Bhuiyan, WHO, New Delhi, 1981, unpublished).

During the severe flooding of July-August 2007, there were 76 cases of snake-bite with 13 deaths. Kraits are responsible for many bites and fatalities and the importance of the greater black krait (*Bungarus niger*) has recently emerged, a species previously unreported from Bangladesh. Other medically important kraits include *B. caeruleus* and *B. walli (*formerly *B. sindanus walli)*. Green pit vipers *Cryptelytrops* (*Trimeresurus*) *erythrurus* cause many bites and some morbidity but few if any fatalities. Russell's viper (*Daboia russelii*) formerly regarded as an important species in now appears to be restricted to a few western areas and no bites have been reported in recent yearts. A recent survey funded by the government and World Bank, revealed that there were around 700 000 snakebites/year in Bangladesh with 6000 fatalities *(http://www.bdnews24.com/details.php?id=139775&cid=2).*

Only 3% of bite victims attend a hospital or seek help from a trained doctor, 6% seek assistance from village doctors and most of the rest use

traditional healers. About 75% of snake-bite victims receive some kind of treatment within two hours of being bitten. Peak snake-bite incidence is during May-October. It was highest in Barisal (2 667/100 000/year) and lowest in Sylhet (321/100 000/year). In Dhaka, incidence was 440/100 000/year.

Category 1:	**Elapidae:** *Bungarus caeruleus, Bungarus niger, Bungarus walli; Naja kaouthia;* **Viperidae:** *Cryptelytrops erythrurus*
Category 2:	**Elapidae:**, *Bungarus fasciatus*, *Bungarus lividus*; *Naja naja*; *Ophiophagus hannah*; **Viperidae:** *Cryptelytrops purpureomaculatus*, *Cryptelytrops septentrionalis*; *Daboia russelii* (in the west)

Bhutan: In 2000, 2 085 bites and stings were reported. Four elapid species have been reported from lowland regions of Bhutan (less than 500 metres above mean sea level): cobra (*Naja naja*), king cobra (*Ophiophagus hannah*) and two species of krait (*Bungarus niger* and *B. fasciatus*). Other venomous species such as *N. kaouthia*, *Sinomicrurus macclellandi, Daboia russelii* ("Bhutan Hills" according to MA Smith 1943), and several pit vipers may well occur there as well. There is no published information on snake-bites in Bhutan but there are said to be many bites causing local pain and swelling and there were a minimum of two fatalities in one year. Antivenom is imported from India (200 vials each year).

Category 1:	**Elapidae:** *Bungarus niger; Naja naja*
Category 2:	**Elapidae:** *Bungarus fasciatus*; *Ophiophagus hannah*; **Viperidae:** *Cryptelytrops erythrurus*; *Daboia russelii*

Democratic People's Republic of Korea: Two species of adders *(Vipera berus and V. sachalinensis),* several species of mamushi *(genus Gloydius)* and the yamakagashi *(Rhabdophis tigrinus)* occur in DPR Korea but there is no information on snake-bites.

Published data are restricted to the Republic of Korea (e.g. Soh et al., 1978; Sawai, 1993).

Category 1:	*Gloydius brevicaudus*
Category 2:	*Gloydius intermedius, Gloydius ussuriensis, Vipera berus*

India: the numbers of snake-bite fatalities in India has long been controversial. Estimates as low as 61 507 bites and 1,124 deaths in 2006

and 76,948 bites and 1,359 deaths in 2007 [Government of India data: pp 107–108 of *http://cbhidghs.nic.in/writereaddata/mainlinkFile/Health%20Status%20Indicators.pdf*) and as high as 50 000 deaths each year have been published. The Registrar-General of India's "Million Death Study", 2001-2003, is expected to provide reliable evidence of substantial mortality (exceeding 50 000 per year) as it is based on **R**epresentative, **R**e-sampled, **R**outine **H**ousehold **I**nterview of **M**ortality with **M**edical **E**valuation ("RHIME"), covering all age groups across the entire country with geographical, seasonal and occupational data. Previous studies included a field survey in randomly selected villages in Barddhaman (Burdwan) district, West Bengal that suggested that among the total population of nearly five million people, nearly 8 000 were bitten and 800 killed by snakes each year, an average incidence of 16.4 deaths/100 000/year (Hati et al., 1992). In Maharashtra State, between 1974-78, there were an average of 1 224 deaths/year (2.43 deaths/100 000/year). "The big four" medically important species had been considered to be *Naja naja, Bungarus caeruleus*, *Daboia russelii* and *Echis carinatus* but other species have now been proved important in particular areas, such as *Naja oxiana* (north-west), N. kaouthia (north-east), *Hypnale hypnale* (south-west coast and Western Ghats (Joseph et al., 2007)), *Echis carinatus sochureki* (Rajasthan) (Kochar et al., 2007) and *Trimeresurus malabaricus* (Hassan district, Mysore, Karnataka).

Category 1:	**Elapidae:** *Bungarus caeruleus; Naja kaouthia* (north-east), *Naja naja* (throughout) **Viperidae:** *Daboia russelii, Echis carinatus; Hypnale hypnale* (south-west)
Category 2:	**Elapidae:** *Bungarus fasciatus, Bungarus niger, Bungarus sindanus, Bungarus walli; Naja oxiana* (north-west), *Naja sagittifera* (Andaman Islands); *Ophiophagus hannah* (south, north-east, Andaman Islands); **Viperidae:** *Cryptelytrops albolabris, Cryptelytrops purpureomaculatus* (east), *Trimeresurus malabaricus* (south-west), *Trimeresurus gramineus* (south India, Andaman & Nicobar Islands), *Macrovipera lebetina* (north-west).

Indonesia: Although fewer than 20 snake-bite deaths are registered each year in this vast archipelago, several thousand deaths are suspected to occur. Species responsible for most bites include *Cryptelytrops (Trimeresurus) albolabris*, *Bungarus candidus*, spitting cobras (*Naja sumatrana and N. sputatrix*), *Calloselasma rhodostoma* (Java), *Daboia siamensis* (Java, Komodo, Flores and Lomblen) and death adders (*Acanthophis* spp.)(West Papua). The national antivenom producer BioFarma manufactures a trivalent antivenom against *Naja sputatrix, Bungarus fasciatus* and *Calloselasma rhodostoma*. No

cases of *B. fasciatus* bites are known but deaths from *B. candidus* (Java), *D. siamensis* (Java, Flores, Komodo) and Acanthophis (West Papua) have been reported.

Indonesia (Sumatra, Java, Borneo, Sulawesi and Lesser Sunda Islands but West of Wallace's line i.e. excluding West Papua and Maluku Islands):

Category 1:	**Elapidae:** *Bungarus candidus* (Sumatra and Java), *Naja sputatrix* (Java and Lesser Sunda Islands), *Naja sumatrana* (Sumatra and Borneo) **Viperidae:** *Calloselasma rhodostoma* (Java), *Cryptelytrops albolabris; Daboia siamensis* (formerly *D. s. limitis* and *D. s. sublimitis*)
Category 2:	**Elapidae:** *Bungarus fasciatus, Bungarus flaviceps* (Sumatra and Borneo); *Calliophis bivirgatus; Ophiophagus hannah* (Sumatra, Borneo and Java); **Viperidae:** *Cryptelytrops insularis, Cryptelytrops purpureomaculatus* (Sumatra)

Indonesia (East of Wallace's Line, i.e. West Papua and Maluku)**:**

Category 1:	**Elapidae:** *Acanthophis laevis*
Category 2:	**Elapidae:** *Acanthophis rugosus, Micropechis ikaheka, Oxyuranus scutellatus, Pseudechis papuanus, Pseudechis rossignolii, Pseudonaja textilis*

Maldives: Only one species of sea snake (*Pelamis platurus*) and two species of harmless land snakes (*Lycodon aulicus* or *L. capucinus* and *Typhlops brahminus*) occur. There have been no reports of bites. A living specimen of *Naja kaouthia* was found in the wild. It had presumably been imported in cargo from South Asia.

Myanmar: In the 1930s the annual snake-bite mortality reported in Burma exceeded 2000 (15.4/100 000/year). Thirty years later it was still estimated to exceed 1000 (3.3/100 000/year). Russell's viper (*Daboia siamensis*) bite was once the fifth and is now the twelth leading cause of death in this country. In 1991, there were 14000 bites with 1 000 deaths and in 1997, 8000 bites with 500 deaths. From 2005 until 2008, 8994-11172 bites were reported annually with 748-794 deaths. The average case fatality is 7.9%. Underreporting is estimated to be about 12%. In some townships in Irrawaddy division, case fatality still ranges from 10%-40% and may be increasing. 90% of bites are caused by Russell's vipers (*Daboia siamensis*). Other important species are cobras (*Naja kaouthia* and *N. mandalayensis*), kraits (*Bungarus* spp.) and green pit vipers [*Cryptelytrops* (*Trimeresurus*) *erythrurus*]. Annual antivenom production by Myanmar Pharmaceutical Factory

is 46 000 vials of Russell's viper and 6 000 vials of cobra antivenom. This is inadequate for national needs and so currently 3 869 vials of Thai Red Cross Russell's viper antivenom are imported each year.

Category 1:	**Elapidae:** *Bungarus magnimaculatus, Bungarus multicinctus, Naja kaouthia, Naja mandalayensis;* **Viperidae:** *Cryptelytrops albolabris, Cryptelytrops erythrurus; Daboia siamensis*
Category 2:	**Elapidae:** *Bungarus candidus, Ophiophagus hannah,* **Viperidae:** *Calloselasma rhodostoma (southern Peninsula), Ovophis monticola, Protobothrops kaulbacki, Protobothrops mucrosquamatus*

Nepal: The highest recorded incidence was 162 death/100 000/year, determined in the Eastern Terai (Sharma et al., 2004). In this study, only 20% of the deaths occurred in hospitals. Increased risk of fatality was associated with being bitten inside the house while resting between midnight and 0060 hours, suggesting bites by the common krait (*Bungarus caeruleus*) (see below). Other risk factors were an initial visit to a traditional healer and delayed transport to the hospital. Medically important species include *Naja naja, Bungarus caeruleus, B. walli* and *Daboia russelii*. In the country as a whole, 1 000 bites and 200 deaths have been estimated but one survey suggested 20 000 bites and 1 000 deaths/year (Bhetwal et al., 1998).

Category 1:	**Elapidae:** *Bungarus caeruleus, Bungarus niger; Naja naja, Naja kaouthia* **Viperidae:** *Daboia russelii*
Category 2:	**Elapidae:** *Bungarus bungaroides, Bungarus fasciatus, Bungarus lividus, Bungarus walli, Ophiophagus hannah, Hemibungarus macclellandii* **Viperidae:** *Cryptelytrops septentrionalis, Cryptelytrops albolabris, Cryptelytrops erythrurus, Trimeresurus gramineus, Gloydius himalayanus, Ovophis monticola, Himalayophis tibetanus, Protobothrops jerdonii, Viridovipera stejnegeri, Viridovipera yunnanensis*

Sri Lanka: According to the Epidemiology Unit, Ministry of Health, reported snake-bite numbers increased from 12 175 per year in 1991 to peak at 37 244 in 2002 and 36 861 in 2005. Fatalities peaked at 194 in 2000 and there were 134 in 2005. There are currently 30 000 – 35 000 bites and 100-150 deaths each year. In hospitals, case fatality decreased from 3.5% in 1985 to 0.2% in 2006. However, these data are based on hospital returns which are likely to miss at least 5% of deaths. Comparison of

hospital data with death certifications in Monaragala district during a 5-year period (1999-2003) revealed a 63% underestimate by hospital records of the true number of snake-bite deaths (Fox et al., 2006), partly explained by the fact that 36% of snake-bite victims did not seek or achieve hospital treatment. In Kandy district, snake-bite fatality based on death certification was 2/100 000/year during the period 1967-87, amounting to about 0.5% of all deaths. Bites are caused by *Daboia russelii* (30%), hump-nosed viper (*Hypnale hypnale*) (22%), *Naja naja* (17%) and kraits (mainly *Bungarus caeruleus* but a few *B. ceylonicus*) (15%).

Category 1:	**Elapidae:** *Bungarus caeruleus; Naja naja* **Viperidae:** *Daboia russelii, Hypnale hypnale*
Category 2:	**Elapidae:** *Bungarus ceylonicus* **Viperidae:** *Echis carinatus, Hypnale nepa, Hypnale walli, Trimeresurus trigonocephalus*

Thailand: Improved surveillance explained the reporting of increasing numbers of snake-bite cases from an average of 2 316/year in the 1950s to 9 071 (14.5/100 000) in 2002 and 8 299 (13.25/100 000) in 2006. Mortality has declined from an average of 178/year in the 1950s to fewer than 10/year recently. Over the last 5 years, both incidence and case fatality have declined to 8 000 – 10 000 bites/year (12-18/100 000/year) with an admirably low case fatality of 0.5%. *Calloselasma rhodostoma* causes 40% of attributable bites, *Cryptelytrops (Trimeresurus) albolabris* and *C. macrops* 37%, *Naja kaouthia* and *N. siamensis* 16% and *Daboia siamensis* 2%. However, *Bungarus candidus* also causes fatalities.

Category 1:	**Elapidae:** *Bungarus candidus, Naja kaouthia, Naja siamensis;* **Viperidae:** *Calloselasma rhodostoma, Cryptelytrops albolabris, Daboia siamensis*
Category 2:	**Elapidae:** *Bungarus fasciatus, Bungarus flaviceps, Naja sumatrana, Ophiophagus hannah* **Viperidae:** *Cryptelytrops macrops, Cryptelytrops purpureomaculatus*

Timor-Leste: No data on snake-bite incidence are available.

Category 1:	**Viperidae:** *Cryptelytrops insularis*
Category 2:	**Elapidae:** *Naja sputatrix (unconfirmed)*

There are perhaps one million envenomings and more than 75 000 deaths/year in the SEA Region. Important species include *Naja naja, N. kaouthia, N. oxiana, Bungarus caeruleus, B. multicinctus, Daboia russelii, D. siamensis, Echis carinatus, Calloselasma rhodostoma, Hypnale hypnale, Cryptelytrops (Trimeresurus) albolabris* and *Trimeresurus gramineus.*

5.8 Consequences of snake-bite

Victims of snake-bite may suffer any or all of the following:

(1) Local envenoming confined to the part of the body that has been bitten. These effects may be debilitating, sometimes permanently.

(2) Systemic envenoming involving organs and tissues away from the part of the body that has been bitten. These effects may be life-threatening and debilitating, sometimes permanently.

(3) Effects of anxiety prompted by the frightening experience of being bitten and by exaggerated beliefs about the potency and speed of action of snake venoms. These symptoms can be misleading for medical personnel.

(4) Effects of first-aid and other pre-hospital treatments that may cause misleading clinical features. These may be debilitating and rarely even life-threatening.

(3) and (4) may develop in patients who are envenomed and in those who are not envenomed (bite by a non-venomous snake or by a venomous snake that failed to inject venom) or who were not in fact bitten by a snake at all but by a rodent or lizard or even impaled by a thorn.

6

Symptoms and signs of snake-bite

6.1 When venom has not been injected

Some people who are bitten by snakes or suspect or imagine that they have been bitten, may develop quite striking symptoms and signs even when no venom has been injected. This results from an understandable fear of the consequences of a real venomous bite. Anxious people may over-breathe so that they develop pins and needles of the extremities, stiffness or tetany of their hands and feet and dizziness. Others may develop vasovagal shock after the bite or suspected bite-faintness and collapse with profound slowing of the heart. Others may become highly agitated and irrational and may develop a wide range of misleading symptoms. Blood pressure and pulse rate may increase and there may be sweating and trembling. Another source of symptoms and signs not caused by snake venom is first aid and traditional treatments (Harris et al., 2010). Constricting bands or tourniquets may cause pain, swelling and congestion that suggest local envenoming. Ingested herbal remedies may cause vomiting. Instillation of irritant plant juices into the eyes may cause conjunctivitis. Forcible insufflation of oils into the respiratory tract may lead to aspiration pneumonia, bronchospasm, ruptured ear drums and pneumothorax. Incisions, cauterization, immersion in scalding liquid and heating over a fire can result in devastating injuries.

6.2 When venom has been injected

Early symptoms and signs

Following the immediate pain of mechanical penetration of the skin by the snake's fangs, there may be increasing local pain (burning, bursting, throbbing) at the site of the bite, local swelling that gradually extends proximally up the bitten limb and tender, painful enlargement of the regional lymph nodes draining the site of the bite (in the groin-femoral or inguinal, following bites in the lower limb; at the elbow – epitrochlear-or in the axilla following bites in the upper limb). However, bites by kraits, sea snakes and Philippine cobras may be virtually painless and may cause negligible local swelling. Someone

who is sleeping may not even wake up when bitten by a krait and there may be no detectable fang marks or signs of local envenoming.

Clinical patterns of envenoming by snakes in South-East Asia Region

Symptoms and signs vary according to the species of snake responsible for the bite and the amount of venom injected. Sometimes the identity of the biting snake can be confirmed by examining the dead snake. It may be strongly suspected from the patient's description or the circumstances of the bite or from knowledge of the clinical effects of the venom of that species. This information will enable the doctor to choose an appropriate antivenom, anticipate the likely complications and, therefore, take appropriate action. If the biting species is unknown, the patient should be observed closely to allow recognition of the emerging pattern of symptoms, signs and results of laboratory tests ("the clinical syndrome"), together with other evidence, that may suggest which species was responsible (see Annex 1).

Local symptoms and signs in the bitten part:

- fang marks (Fig. 40a)
- local pain
- local bleeding (Fig. 40b)
- bruising (Fig. 40c)
- lymphangitis (raised red lines tracking up the bitten limb)
- lymph node enlargement
- inflammation (swelling, redness, heat)
- blistering (Fig. 40c, 40d, 41)
- local infection, abscess formation
- necrosis (Fig. 42)

Generalized (systemic) symptoms and signs

General

Nausea, vomiting, malaise, abdominal pain, weakness, drowsiness, prostration.

Cardiovascular (Viperidae)

Visual disturbances, dizziness, faintness, collapse, shock, hypotension, cardiac arrhythmias, pulmonary oedema, conjunctival oedema (chemosis) (Fig. 43)

Figure 40: Local signs of envenoming (Copyright DA Warrell)
(a) Fang marks 2.5 cm apart inflicted by a large Russell's viper in Sri Lanka
(b) Persistent local bleeding from fang marks 40 minutes after a bite by a Malayan pit viper
(c) Swelling, blistering and bruising following a bite by a Malayan pit viper
(d) Blistering with early necrosis at the site of a monocellate cobra bite.

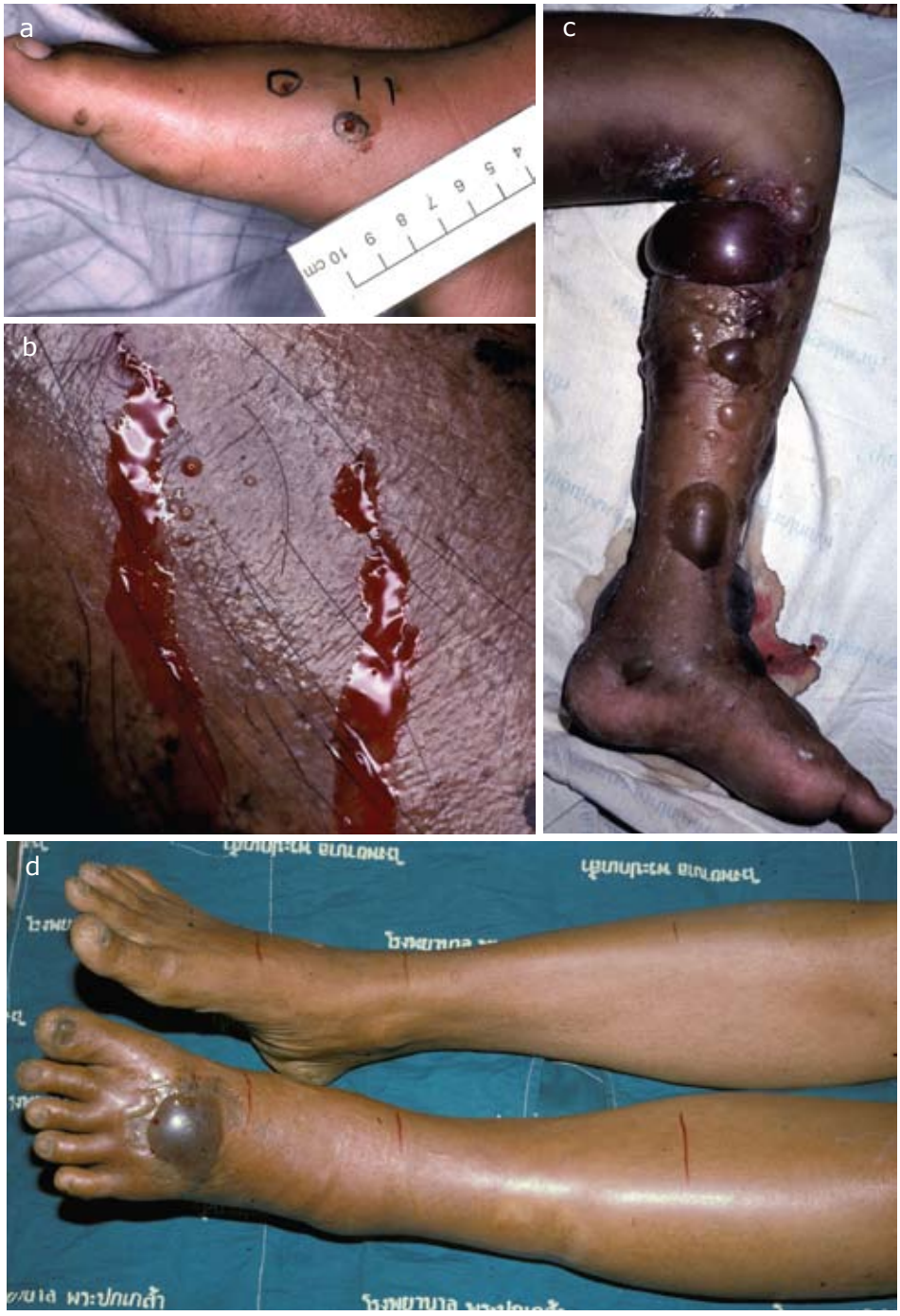


Figure 41: Blistering and early tissue necrosis following a bite by an Indo-Chinese spitting cobra *(Naja siamensis)* in south Viet Nam (Copyright DA Warrell)

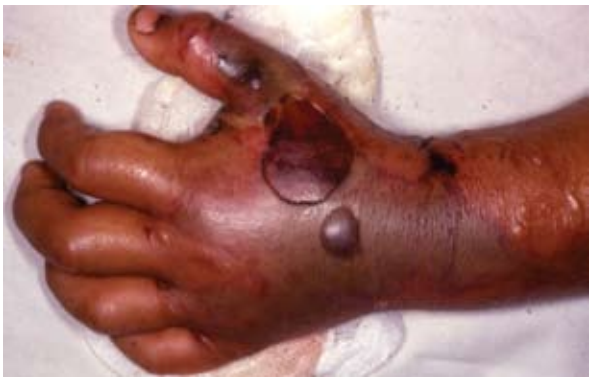


Figure 42: Tissue necrosis requiring surgical debridement (Copyright DA Warrell)
(a) Following a bite by an Indian cobra
(b) Following a bite by a Malayan pit viper

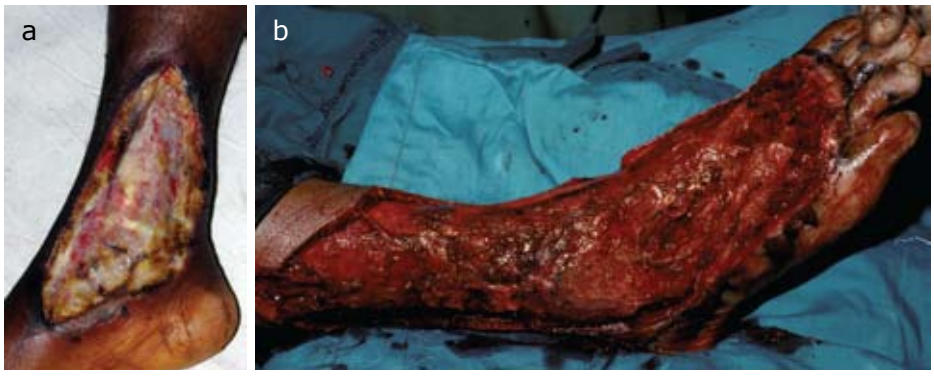
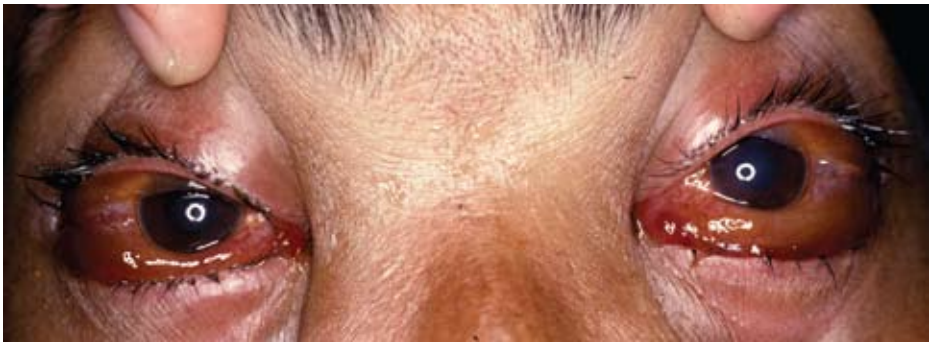


Figure 43: Bilateral conjunctival oedema (chemosis) after a bite by a Myanmar Russell's viper (Copyright DA Warrell)



Bleeding and clotting disorders (Viperidae)

- Traumatic bleeding from recent wounds (including prolonged bleeding from the fang marks (Fig. 40b, venipunctures etc) and from old partly-healed wounds
- Spontaneous systemic bleeding - from gums (Fig. 44), epistaxis, bleeding into the tears, intracranial haemorrhage (meningism from subarachnoid haemorrhage, lateralizing signs and/or coma from cerebral haemorrhage – Fig. 45), haemoptysis (Fig. 46), haematemesis), rectal bleeding or melaena, haematuria, vaginal bleeding, ante-partum haemorrhage in pregnant women, bleeding into the mucosae (e.g. conjunctivae – Fig. 47), skin (petechiae, purpura, discoid haemorrhages – Fig. 48 and ecchymoses) and retina.

Figure 44: Bleeding from gingival sulci in a patient bitten by a Malayan pit viper (Copyright DA Warrell)

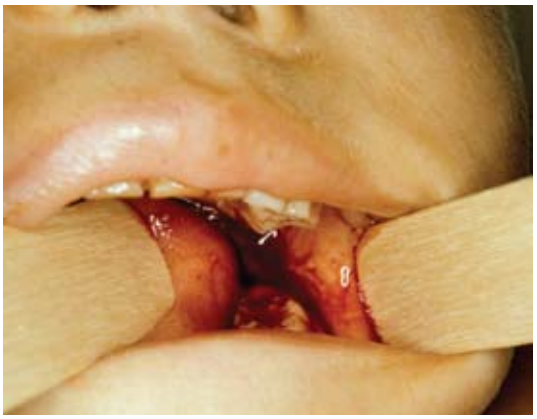


Figure 45: Fatal cerebral haemorrhage in a victim of Russell's viper bite in Myanmar (Copyright Dr U Hla Mon)

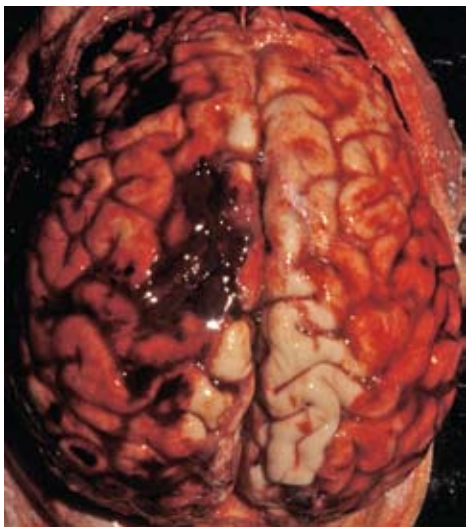


Figure 46: Haemoptysis from a tuberculous lung cavity in a patient bitten by a Malayan pit viper (Copyright DA Warrell)

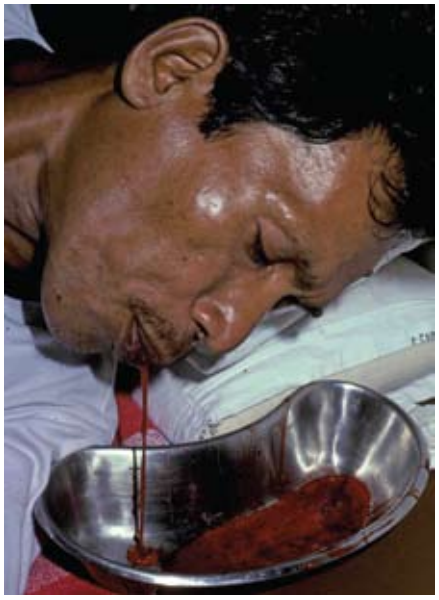
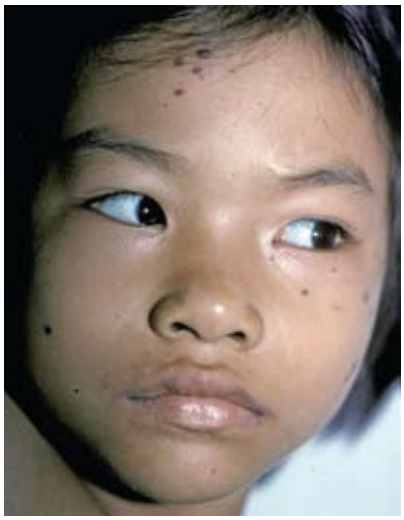


Figure 47: Subconjunctival haemorrhages in a patient bitten by a Myanmar Russell's viper (Copyright DA Warrell)

Figure 48: Cutaneous discoid haemorrhages in a patient bitten by a Malayan pit viper in Viet Nam (Copyright DA Warrell)



Cerebral arterial thrombosis (western Russell's v*iper Daboia russelii)*

Thrombotic strokes, confirmed by angiography or imaging, are reported rarely after envenoming by *D. russelii* in Sri Lanka (Gawarammana et al., 2009).

Neurological (Elapidae, Russell's viper)

Drowsiness, paraesthesiae, abnormalities of taste and smell, "heavy" eyelids, ptosis (Fig. 49a, 49b), external ophthalmoplegia (Fig. 50), paralysis of facial muscles and other muscles innervated by the cranial nerves, nasal voice or aphonia, regurgitation through the nose, difficulty in swallowing secretions, respiratory and generalised flaccid paralysis.

Figure 49: Bilateral ptosis (Copyright DA Warrell)
(a) in a patient bitten by a common krait in Sri Lanka
(b) in a patient bitten by a Russell's viper in Sri Lanka

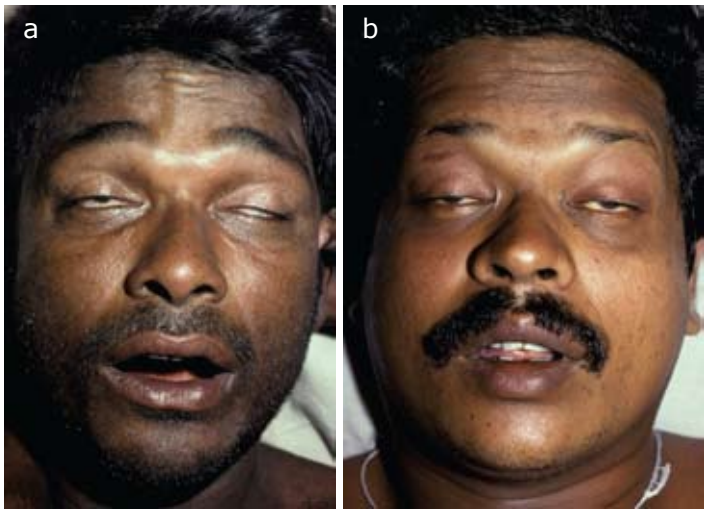
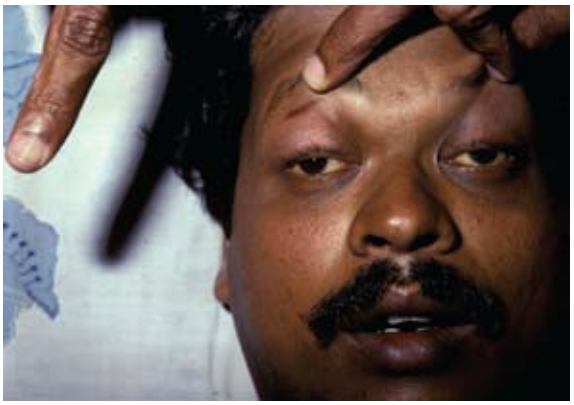


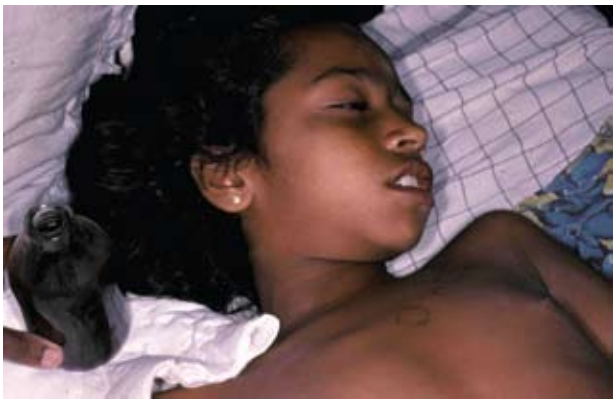
Figure 50: External ophthalmoplegia in a patient bitten by a Russell's viper in Sri Lanka. The patient is attempting to look to his right. The eyes must be held open because of the bilateral ptosis (Copyright DA Warrell)



Skeletal muscle breakdown (sea snakes, some krait species – *Bungarus niger* and *B. candidus*, western Russell's viper *Daboia russelii*)

Generalized pain, stiffness and tenderness of muscles, trismus, myoglobinuria (Fig. 51), hyperkalaemia, cardiac arrest, acute renal failure.

Figure 51: Patient bitten by a Russell's viper in Sri Lanka with signs of neurotoxicity. She began to pass dark brown urine containing myoglobin and haemoglobin 8 hours after the bite. (Copyright DA Warrell)



Renal (Viperidae, sea snakes)

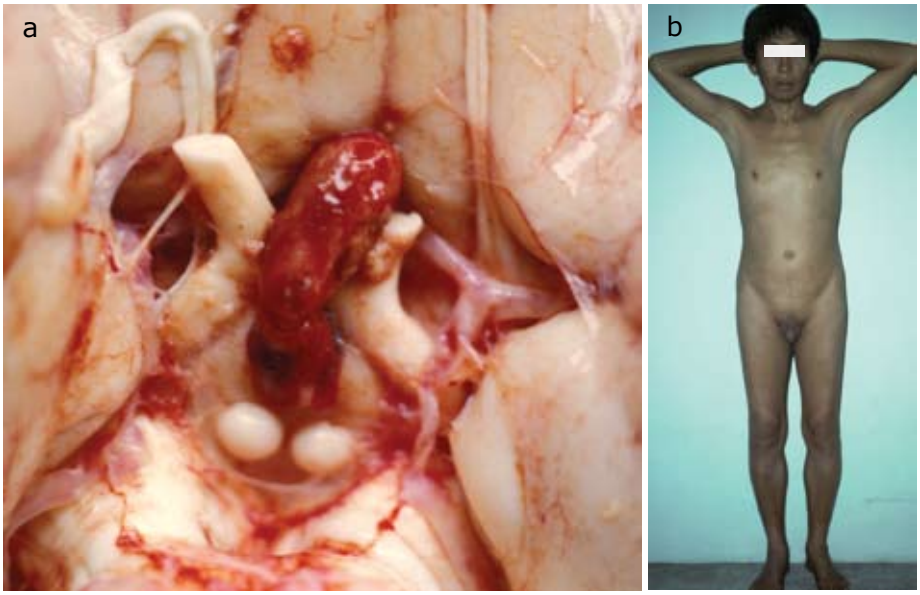
Loin (lower back) pain (Tin-Nu-Swe et al. 1993), haematuria, haemoglobinuria, myoglobinuria, oliguria/anuria, symptoms and signs of uraemia (acidotic breathing, hiccups, nausea, pleuritic chest pain etc., see below).

Endocrine (acute pituitary/adrenal insufficiency from infarction of the anterior pituitary – Fig. 52a) (Russell's viper in Myanmar and South India) (Tun-Pe et al., 1987)

Acute phase: Shock, hypoglycaemia

Chronic phase (months to years after the bite): Weakness, loss of secondary sexual hair, loss of libido, amenorrhoea, testicular atrophy, hypothyroidism etc (Fig. 52b)

Figure 52: Haemorrhagic infarction of the anterior pituitary resulting in Sheehan's-like syndrome (pan-hypopituitarism) after Russell's viper bite in Myanmar
(a) Appearances at the base of the brain at autopsy in a patient who died acutely after the bite (Copyright Dr U Hla Mon)
(b) Patient presenting with symptoms and signs of panhypopituitarism three years after severe envenoming by Russell's viper. There is loss of secondary sexual hair and testicular atrophy (Copyright DA Warrell)



Other: Generalised increase in capillary permeability is a feature of *D. siamensis* envenoming in Myanmar (Myint-Lwin et al., 1985); hyponatraemia has been observed in victims of krait bites in the area of Hanoi (Ha-Tran-Hung et al., 2009) and around Ho Chi Minh City in Viet Nam (*Bungarus candidus and B. multicinctus*), implying natriuretic hormone like activity in the venom.

6.3 Clinical syndromes of snake-bite in South-East Asia
(not including West Papua and Maluku Islands)

Limitations of syndromic approach: The more carefully the clinical effects of snake-bites are studied, the more it is realized that the range of activities of a particular venom is very wide. For example, some elapid venoms, such as those of Asian cobras, can cause severe local envenoming (Fig. 40d, 41, 42b), formerly thought to be an effect only of viper venoms. In Sri Lanka and South India, Russell's viper venom causes paralytic signs (ptosis, etc.) (Fig. 49b), suggesting elapid neurotoxicity, and muscle pains and dark brown urine (Fig. 51), suggesting sea snake rhabdomyolysis. Although there may be considerable overlap of clinical features caused by venoms of different species of snake, a "syndromic approach" may still be useful, especially

when the snake has not been identified and only monospecific antivenoms are available (see Annex 1) (Ariaratnam et al., 2009). In West Papua and the Maluku Islands, Australasian elapid snakes can cause Syndromes 4 and 5, associated with bleeding and clotting disturbances but with minimal local envenoming.

Syndrome 1

Local envenoming (swelling etc.) with bleeding/clotting disturbances = **Viperidae (all species)**

Syndrome 2

Local envenoming (swelling etc.) with bleeding/clotting disturbances, shock or acute kidney injury **= Russell's viper (hump-nosed pit viper in Sri Lanka and SW India)**

with conjunctival oedema (chemosis) and acute pituitary insufficiency **= Russell's viper, Myanmar**

with ptosis, external ophthalmoplegia, facial paralysis etc and dark brown urine **= Russell's viper, Sri Lanka and South India**

Syndrome 3

Local envenoming (swelling etc.) with paralysis **= cobra or king cobra**

Syndrome 4

Paralysis with minimal or no local envenoming
Bitten on land while sleeping on the ground **= krait**
Bitten in the sea, estuary and some freshwater lakes **= sea snake**

Syndrome 5

Paralysis with dark brown urine and acute kidney injury:

Bitten on land (with bleeding/clotting disturbance) **= Russell's viper, Sri Lanka or South India**

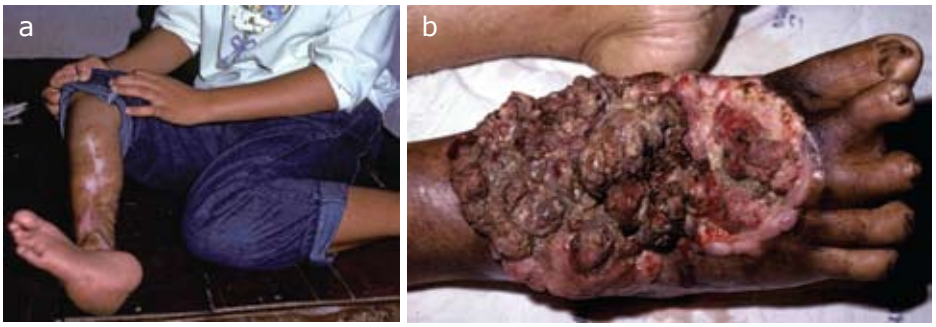
Bitten on land while sleeping indoors **= krait *(B. niger, B. candidus, B. multicinctus),* Bangladesh, Thailand**

Bitten in sea, estuary and some freshwater lakes (no bleeding/clotting disturbances) **= sea snake**

6.4 Long-term complications (sequelae) of snake-bite

At the site of the bite, loss of tissue may result from sloughing or surgical débridement of necrotic areas or amputation: chronic ulceration, infection, osteomyelitis, contractures, arthrodesis or arthritis may persist causing severe physical disability (Fig. 53a). Malignant transformation may occur in skin ulcers after a number of years (Fig. 53b).

Figure 53: Chronic physical handicap resulting from necrotic envenoming by Malayan pit vipers (Copyright DA Warrell)
(a) Deformity and dysfunction after a bite and subsequent necrosis of the calf.
(b) Squamous cell carcinoma arising at the site of a chronic skin ulcer with osteomyelitis 8 years after the bite.

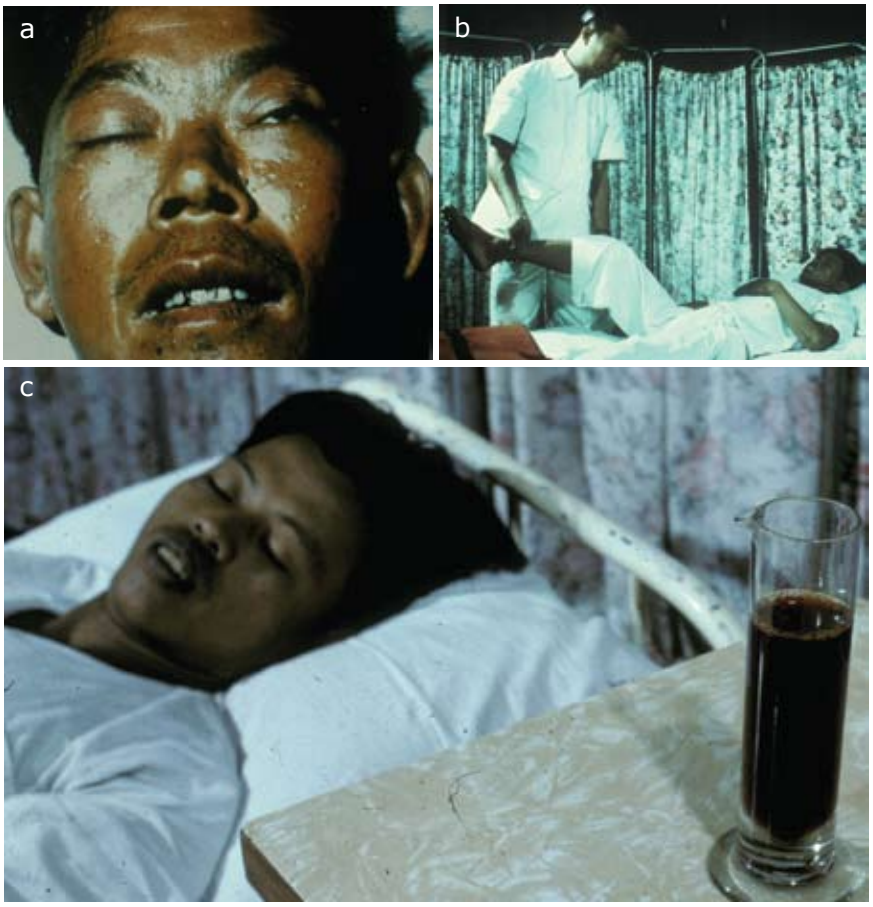


Chronic kidney disease (renal failure) occurs after bilateral cortical necrosis (Russell's viper and hump-nosed pit viper bites) and chronic panhypopituitarism or diabetes insipidus after Russell's viper bites in Myanmar and South India (Fig. 52b). Chronic neurological deficit is seen in the few patients who survive intracranial haemorrhages and thromboses (Viperidae).

6.5 Symptoms and signs of sea snake envenoming (Reid, 1979; Warrell, 1994)

Envenoming by sea snakes (Hydrophiinae) and sea kraits (Laticaudinae): the bite is usually painless and may not be noticed by the wader or swimmer. Fangs and other teeth may be left in the wound. There is minimal or no local swelling and the involvement of local lymph nodes is unusual. Generalized rhabdomyolysis is the dominant effect of envenoming by these snakes although patients without this feature have been described. 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 3½ hours after the bite. Trismus is common (Fig. 54a). Passive stretching of the muscles is painful (Fig. 54b). 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 3–8 hours after the bite (Fig. 54c)**.** These are suspected when the serum/plasma appears brownish and the urine dark reddish brown (Coca-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.

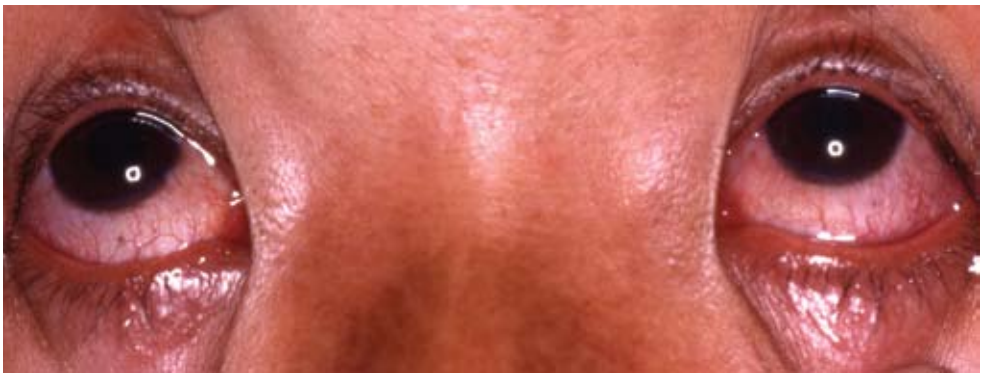
Figure 54: Sea snake bite in North-west Malaysia
(Copyright the late H Alistair Reid)
(a) Ptosis, facial paralysis and trismus
(b) Generalised myalgia making passive movement of the limbs extremely painful
(c) Myoglobinuria



6.6 Symptoms and signs of cobra-spit ophthalmia (eye injuries from spitting cobras)

If the "spat" venom enters the eyes, there is immediate and persistent intense burning, stinging pain, followed by profuse watering of the eyes with production of whitish discharge, congested conjunctivae, spasm and swelling of the eyelids, photophobia, clouding of vision and temporary blindness (Fig. 55). Corneal ulceration, permanent corneal scarring and secondary endophthalmitis are recognised complications of African spitting cobra venom but have not been described in Asia.

Figure 55: Bilateral conjunctivitis in a patient who had venom spat into both eyes by an Indo-Chinese spitting cobra *(Naja siamensis)* (Copyright DA Warrell)



7

Management of snake-bites in South-East Asia

7.1 Stages of management

The following steps or stages are often involved:

Management of snake-bite

- First aid treatment
- Transport to hospital
- Rapid clinical assessment and resuscitation
- Detailed clinical assessment and species diagnosis
- Investigations/laboratory tests
- Antivenom treatment
- Observing the response to antivenom
- Deciding whether further dose(s) of antivenom are needed
- Supportive/ancillary treatment
- Treatment of the bitten part
- Rehabilitation
- Treatment of chronic complications

7.2 First-aid treatment

Principles of first-aid

First-aid treatment is carried out immediately or very soon after the bite, before the patient reaches a dispensary or hospital. It can be performed by the snake-bite victim himself/herself or by anyone else who is present and able.

Unfortunately, most of the traditional, popular, available and affordable first-aid methods have proved to be useless or even frankly dangerous. These methods include: making local incisions or pricks/punctures ("tattooing") at the site of the bite or in the bitten limb, attempts to suck the venom out of the wound, use of (black) snake stones, tying tight bands (tourniquets) around the limb, electric shock, topical instillation or application of chemicals, herbs or ice packs. Local people may have great confidence in traditional

(herbal) treatments, but they must not be allowed to delay medical treatment or to do harm.

Aims of first-aid

- attempt to retard systemic absorption of venom.
- preserve life and prevent complications before the patient can receive medical care
- control distressing or dangerous early symptoms of envenoming.
- arrange the transport of the patient to a place where they can receive medical care.
- **ABOVE ALL, AIM TO DO NO HARM!**

The special danger of respiratory paralysis and shock

The greatest fear is that a snake-bite victim might develop fatal respiratory paralysis or shock before reaching a place where they may be resuscitated. This risk may be reduced by speeding up transport to hospital, for example by village-based motor- cyclist volunteers who transport the victim propped upright between the driver in front and a supporting pillion passenger behind. This has proved effective in villages in the Nepal Terai (S.K. Sharma, personal communication) (Fig. 56) [level of evidence O]. Medical workers can be trained in airway management and assisted ventilation (see below). The special danger of rapidly developing paralytic envenoming after bites by some elapid snakes has prompted the use of pressure-immobilization (Sutherland et al., 1979) (Annex 4) but this method requires equipment (long elasticated bandages and splints) (Canale et al., 2009) and skills that some have found hard to train health workers to acquire (see below) (Currie et al., 2008).

Figure 56: Evacuation of a snake bite victim showing early signs of paralysis by a village-based motorcycle volunteer. The victim is supported between the driver and a pillion passenger
(Copyright Dr Sanjib Sharma)

As far as the snake is concerned - do not attempt to kill it as this may be dangerous.

However, if the snake has already been killed, it should be taken to the dispensary or hospital with the patient in case it can be identified. However, **do not handle the snake with your bare hands as even a severed head can bite!**

MOST TRADITIONAL FIRST AID METHODS SHOULD BE DISCOURAGED : THEY DO MORE HARM THAN GOOD !

Recommended first-aid methods

- Reassure the victim who may be very anxious
- Immobilize the whole of the patient's body by laying him/her down in a comfortable and safe position and, especially, immobilize the bitten limb with a splint or sling. Any movement or muscular contraction increases absorption of venom into the bloodstream and lymphatics [level of evidence E].
- If the necessary equipment and skills are available, consider pressure-immobilization or pressure pad unless an elapid bite can be excluded (See Annex 4). In Myanmar, the pressure pad method has proved effective in victims of Russell's viper bite (Tun Pe et al., 1995) [level of evidence O].
- Avoid any interference with the bite wound (incisions, rubbing, vigorous cleaning, massage, application of herbs or chemicals) as this may introduce infection, increase absorption of the venom and increase local bleeding (Bhat, 1974) [level of evidence O].

Release of tight bands, bandages and ligatures: Ideally, these should not be released until the patient is under medical care in hospital, resuscitation facilities are available and antivenom treatment has been started (Watt et al., 1988).

Tight (arterial) tourniquets are not recommended! [level of evidence E]: Traditional tight (arterial) tourniquets are not recommended. To be effective, these had to be applied around the upper part of the limb so tightly that the peripheral pulse gets occluded. This method can be extremely painful and very dangerous if the tourniquet was left on for too long (more than about 40 minutes), as the limb might be damaged by ischaemia. Tourniquets have caused many gangrenous limbs.

7.3 Transport to hospital

The patient must be transported to a place where they can receive medical care (dispensary or hospital) as quickly, but as safely and comfortably, as

possible. Any movement especially movement of the bitten limb, must be reduced to an absolute minimum to avoid increasing the systemic absorption of venom [level of evidence O and E]. Any muscular contraction will increase the spread of venom from the site of the bite. A stretcher, bicycle, motorbike (Fig. 56), cart, horse, motor vehicle, train or boat should be used, or the patient can be carried (e.g. using the "fireman's lift" method). If possible, patients should be placed in the recovery position, in case they vomit..

7.4 Treatment in the dispensary or hospital*

Rapid primary clinical assessment and resuscitation

Cardiopulmonary resuscitation may be needed, including administration of oxygen and establishment of intravenous access.

Rapid primary clinical assessment and resuscitation: ABCDE approach

Airway
Breathing (respiratory movements)
Circulation (arterial pulse)
Disability of the nervous system (level of consciousness)
Exposure and environmental control (protect from cold, risk of drowning etc.)

Airway patency, respiratory movements, arterial pulse and level of consciousness must be checked immediately. However, the Glasgow Coma Scale cannot be used to assess the level of consciousness of patients paralyzed by neurotoxic venoms (see below).

Clinical situations in which snake-bite victims might require urgent resuscitation:

(a) Profound hypotension and shock resulting from direct cardiovascular effects of the venom or secondary effects, such as hypovolaemia, release of inflammatory vasoactive mediators, haemorrhagic shock or rarely primary anaphylaxis induced by the venom itself.

(b) Terminal respiratory failure from progressive neurotoxic envenoming that has led to paralysis of the respiratory muscles.

(c) Sudden deterioration or rapid development of severe systemic envenoming following the release of a tight tourniquet or compression bandage (**see Caution above**).

(d) Cardiac arrest precipitated by hyperkalaemia resulting from skeletal muscle breakdown (rhabdomyolysis) after bites by sea snakes, certain kraits and Russell's vipers.

* Warrell 1990; 1995

(e) If the patient arrives late: Late results of severe envenoming such as renal failure and septicaemia complicating local necrosis.

Detailed clinical assessment and species diagnosis

History

A precise history of the circumstances of the bite and the progression of local and systemic symptoms and signs is very important.

Four useful initial questions:

i. "In what part of your body have you been bitten?"

The doctor can immediately see evidence that the patient has been bitten by a snake (e.g. fang marks) and the nature and extent of signs of local envenoming.

ii. "When and under what circumstances were you bitten?"

Assessment of the severity of envenoming depends on how long ago the patient was bitten.

If the patient has arrived at the hospital soon after the bite, there may be few symptoms and signs even though a large amount of venom may have been injected. If the patient was bitten at night while asleep, a krait was probably implicated; if in a paddy field, a cobra or Russell's viper; if while tending fruit trees, a green pit viper; if while swimming or wading in water a cobra (fresh water) or sea snake (sea or estuary).

iii. "Where is the snake that bit you?"

If the snake has been killed and brought, its correct identification can be very helpful. If it is obviously a harmless species (or not a snake at all!), the patient can be quickly reassured and discharged from hospital.

iv. "How are you feeling now?"

The answer may direct the doctor to the system(s) involved.

A common early symptom of systemic envenoming is vomiting. Patients who become defibrinogenated or thrombocytopenic may begin to bleed from old, partially-healed wounds as well as bleeding persistently from the fang marks. The patient should be asked how much urine has been passed since the bite and whether it was of a normal colour. Patients who complain of sleepiness, drooping eyelids or blurred or double vision may have neurotoxic envenoming. An important early symptom of sea snake envenoming that may develop as soon as 30 minutes after the bite is generalized pain, tenderness and stiffness of muscles and trismus.

Early clues that a patient has severe envenoming:

- Snake identified as a very dangerous one.
- Rapid early extension of local swelling from the site of the bite.
- Early tender enlargement of local lymph nodes, indicating spread of venom in the lymphatic system.
- Early systemic symptoms: collapse (hypotension, shock), nausea, vomiting, diarrhoea, severe headache, "heaviness" of the eyelids, inappropriate (pathological) drowsiness or early ptosis/ophthalmoplegia.
- Early spontaneous systemic bleeding.
- Passage of dark brown/black urine.

Physical examination

This should start with careful assessment of the site of the bite and signs of local envenoming.

Examination of the bitten part: The extent of swelling, which is usually also the extent of tenderness to palpation (start proximally), should be recorded. Lymph nodes draining the limb should be palpated and overlying ecchymoses and lymphangitic lines noted. A bitten limb may be tensely oedematous, cold, immobile and with impalpable arterial pulses. These appearances may suggest intravascular thrombosis, which is exceptionally rare after snake-bite, or a compartmental syndrome, which is uncommon. If possible, intracompartmental pressure should be measured (see Annex 5) and the blood flow and patency of arteries and veins assessed (e.g. by doppler ultrasound). Early signs of necrosis may include blistering, demarcated darkening (easily confused with bruising) (Fig. 40b, 41) or paleness of the skin, loss of sensation and a smell of putrefaction (rotting flesh).

General examination: Measure the blood pressure (sitting up and lying to detect a postural drop indicative of hypovolaemia) and heart rate. Examine the skin and mucous membranes for evidence of petechiae, purpura, discoid haemorrhages (Fig. 48), ecchymoses and, in the conjunctivae, for haemorrhages (Fig. 47) and chemosis (Fig. 43). Thoroughly examine the gingival sulci, using a torch and tongue depressor, as these may show the earliest evidence of spontaneous systemic bleeding (Fig. 44). Examine the nose for epistaxis. Abdominal tenderness may suggest gastrointestinal or retroperitoneal bleeding. Loin (low back) pain and tenderness suggests acute renal ischaemia (Russell's viper bites). Intracranial haemorrhage is suggested by lateralising neurological signs, asymmetrical pupils, convulsions or impaired consciousness (in the absence of respiratory or circulatory failure).

Neurotoxic envenoming: Bulbar and respiratory paralysis

To exclude early neurotoxic envenoming, ask the patient to look up and observe whether the upper lids retract fully (Fig. 57). Test eye movements for evidence of early external ophthalmoplegia (Fig. 50). Check the size and reaction of the pupils. Ask the patient to open his/her mouth wide and protrude his/her tongue; early restriction in mouth opening may indicate trismus (sea snake envenoming) or more often paralysis of pterygoid muscles (Fig. 58).

Figure 57: Examination for ptosis in a patient with neurotoxic envenoming by a Papuan taipan. This is usually the earliest sign of neurotoxic envenoming (Copyright DA Warrell)

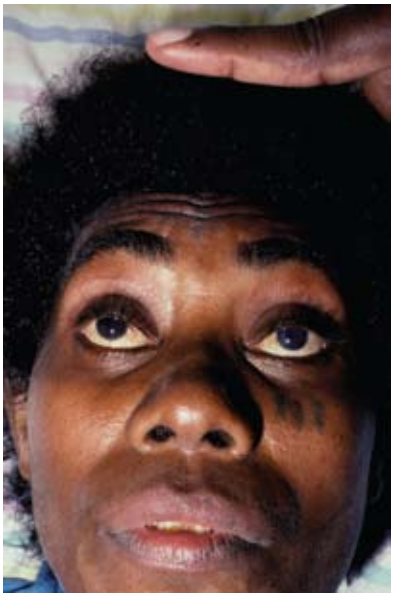
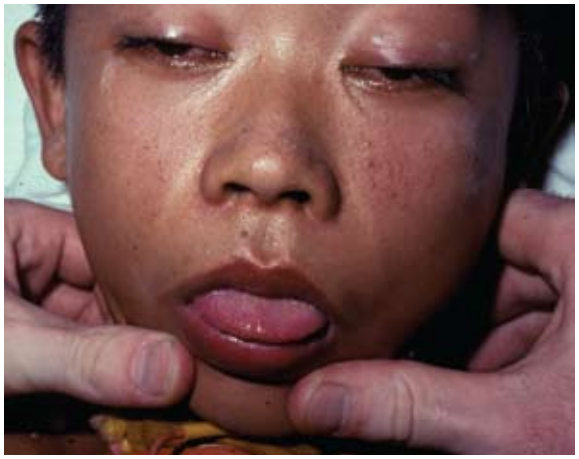


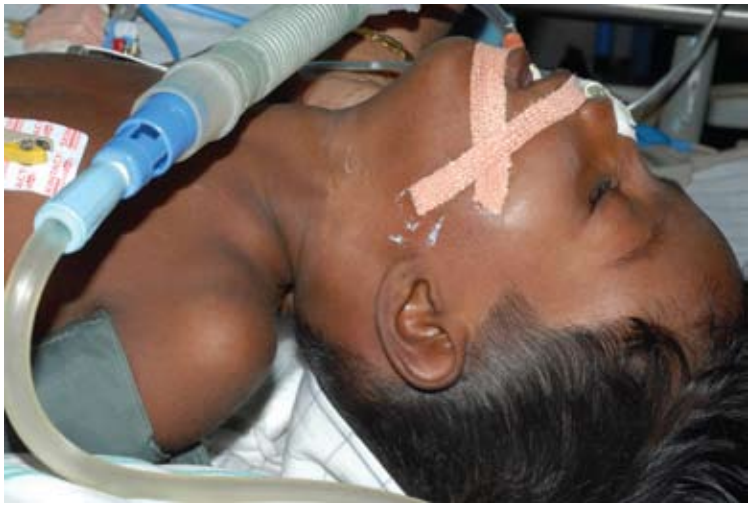
Figure 58: Examination for ability to open the mouth and protrude the tongue in a patient with neurotoxic envenoming from the Malayan krait (note bilateral ptosis and facial paralysis) (Copyright DA Warrell)



Check other muscles innervated by the cranial nerves (facial muscles, tongue, gag reflex etc).

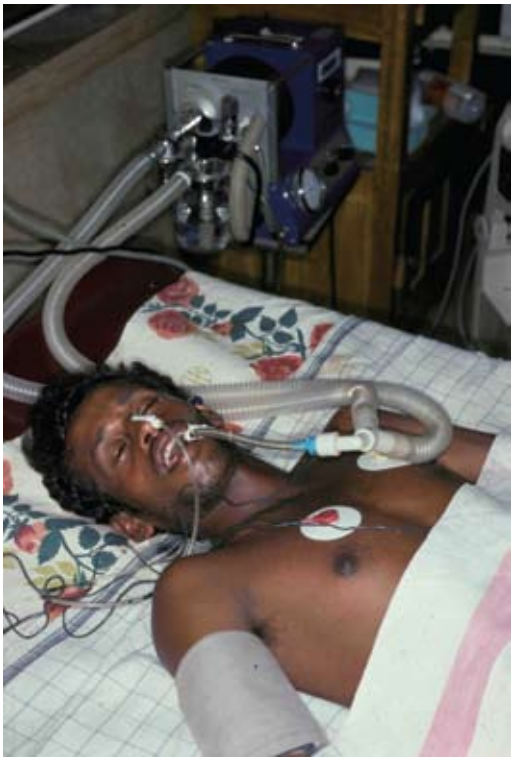
The muscles flexing the neck may be paralysed, giving the "broken neck sign" (Fig. 59). Can the patient swallow or are secretions accumulating in the pharynx, an early sign of bulbar paralysis? Ask the patient to take deep breaths in and out. "Paradoxical respiration" (abdomen expands rather than the chest on attempted inspiration) indicates that the diaphragm is still contracting but that the intercostal muscles and accessory muscles of inspiration are paralysed.

Figure 59: Broken neck sign in a child envenomed by a krait in Sri Lanka (Copyright DA Warrell)



Objective measurement of ventilatory capacity is very useful. Use a peak flow metre, spirometer (FEV1 and FVC) or ask the patient to blow into the tube of a sphygmomanometer to record the maximum expiratory pressure (in mmHg). Remember that, provided their lungs are adequately ventilated, patients with profound generalised flaccid paralysis from neurotoxic envenoming are fully conscious (Fig. 60). Lifting their paralysed upper eyelids allows them to see their surroundings which they find very reassuring. If asked, they may still be able to flex a finger or toe, allowing simple communication. However, because their eyes are closed and they do not move or speak, they are commonly assumed to be unconscious or even dead. A child with snake-bite paralysis in Bangladesh was almost put on a funeral pyre and there are reports of snake-bite victims being almost buried alive.

Figure 60: Generalised flaccid paralysis in a patient envenomed by a common krait in Sri Lanka (Copyright DA Warrell)



Do not assume that snake bitten patients are unconscious or even irreversible "brain dead" just because their eyes are closed, they are unresponsive to painful stimuli, are areflexic, or have fixed dilated pupils. They may just be paralysed!

Generalised rhabdomyolysis

In victims of envenoming by sea snakes, some species of kraits (*B. niger* and *B. candidus*), some Australasian elapids and Russell's vipers in Sri Lanka and South India, muscles, especially of the neck, trunk and proximal part of the limbs, may become tender and painful on active or passive movement and later may become paralysed. In sea snake-bite envenoming, there is pseudotrismus that can be overcome by sustained pressure on the lower jaw. Myoglobinuria may be evident three hours after the bite (Figs. 51, 54c).

Examination of pregnant women

There will be concern about fetal distress (revealed by fetal bradycardia), vaginal bleeding and threatened abortion (Hanprasertpong and Hanprasertpong, 2008). Monitoring of uterine contractions and fetal heart rate is useful. Lactating women who have been bitten by snakes should be encouraged to continue breast feeding.

8

Species diagnosis

If the dead snake has been brought, it may be possible to identify it but this requires skill and even experienced medical personnel may mistake harmless mimics for venomous snakes or they may confuse different venomous species (Viravan et al., 1992; Ariaratnam et al., 2009). A consequence may be that the patient is given antivenom pointlessly, as in the case of hump-nosed pit viper (*Hypnale hypnale*) bites mistaken for saw-scaled viper (*Echis carinatus)* bites in South-West India (Joseph et al., 2007) or mistaken for Russell's viper (*Daboia russelii*) bites in Sri Lanka, since available polyvalent antivenoms do not cover the venom of *H. hypnale*. Otherwise, the species responsible must be inferred indirectly from the patient's description of the snake, circumstances of the bite (e.g. nocturnal bites by kraits in people sleeping on the ground, Ariaratnam et al., 2008) and the clinical syndrome of symptoms and signs (see above and Annex 1). This was specially important in Thailand where, until recently, only monospecific antivenoms were available.

9

Investigations/laboratory tests

9.1 20-minute whole blood clotting test (20WBCT) *

This very useful and informative bedside test requires very little skill and only one piece of apparatus – a new, clean, dry, glass vessel (tube or bottle).

20-minute whole blood clotting test (20WBCT)

- Place 2 mls of freshly sampled venous blood in a small, new or heat cleaned, dry, glass vessel.
- Leave undisturbed for 20 minutes at ambient temperature.
- Tip the vessel once.
- If the blood is still liquid (unclotted) and runs out, the patient has hypofibrinogenaemia ("incoagulable blood") as a result of venom-induced consumption coagulopathy (Fig. 61).
- In the South-East Asia region, incoagulable blood is diagnostic of a viper bite and rules out an elapid bite*.
- **If the vessel used for the test is not made of ordinary glass, or if it has been cleaned with detergent, its wall may not stimulate clotting of the blood sample (surface activation of factor XI – Hageman factor) and test will be invalid**
- If there is any doubt, repeat the test in duplicate, including a "control" (blood from a healthy person such as a relative)

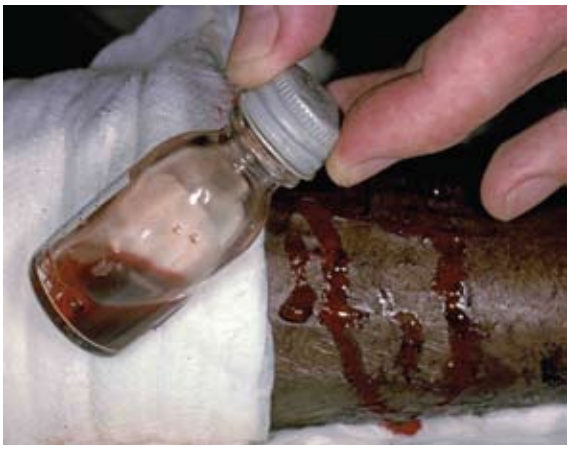
* Note - in West Papua and the Maluku Islands, envenoming by Australasian elapids can cause incoagulable blood

9.2 Other tests

Haemoglobin concentration/haematocrit: A transient increase indicates haemoconcentration resulting from a generalized increase in capillary permeability (e.g. in Russell's viper bite). More often, there is a decrease reflecting blood loss or, in the case of Indian, Thai and Sri Lankan Russell's viper bite, intravascular haemolysis.

* Warrell et al., 1977; Sano-Martins et al., 1994

Figure 61: 20 minute whole blood clotting test in a patient envenomed by a Papuan taipan who is still beeding from incisions made at the site of the bite. The blood is incoagulable indicating venom-induced consumption coagulopathy (Copyright DA Warrell)



Platelet count: This may be decreased in victims of envenoming by vipers and Australasian elapids.

White blood cell count: An early neutrophil leucocytosis is evidence of systemic envenoming from any species.

Blood film: Fragmented red cells ("helmet cell", schistocytes) are seen when there is microangiopathic haemolysis.

Plasma/serum: May be pinkish or brownish if there is gross haemoglobinaemia or myoglobinaemia.

Biochemical abnormalities: Aminotransferases and muscle enzymes (creatine kinase, aldolase etc) will be elevated if there is severe local muscle damage or, particularly, if there is generalized muscle damage (sea snake, some krait, Australasian elapid and Sri Lankan and South Indian Russell's viper bites). Mild hepatic dysfunction is reflected in slight increases in other serum enzymes. Bilirubin is elevated following massive extravasation of blood. Potassium, creatinine, urea or blood urea nitrogen levels are raised in the renal failure of Russell's viper, hump-nosed viper bites and sea snake-bites. Early hyperkalaemia may be seen following extensive rhabdomyolysis in sea snake-bites. Bicarbonate will be low in metabolic acidosis (e.g. renal failure). Hyponatraemia is reported in victims of krait bites in northern Viet Nam (*Bungarus candidus and B. multicinctus*).

Arterial blood gases and pH may show evidence of respiratory failure (neurotoxic envenoming) and acidaemia (respiratory or metabolic acidosis).

Warning: Arterial puncture is contraindicated in patients with haemostatic abnormalities (Viperidae and some Australasian Elapidae)

Desaturation: Arterial oxygen saturation can be assessed non-invasively in patients with respiratory failure or shock using a finger oximeter.

Urine examination: The colour of the urine (pink, red, brown, black) should be noted and the urine should be tested by dipsticks for blood or haemoglobin or myoglobin. Standard dipsticks do not distinguish blood, haemoglobin and myoglobin. Haemoglobin and myoglobin can be separated by immunoassays but there is no easy or reliable test. Microscopy will confirm whether there are erythrocytes in the urine.

Red cell casts indicate glomerular bleeding. Massive proteinuria is an early sign of the generalized increase in capillary permeability in Russell's viper envenoming and an early indicator of acute kidney injury.

10

Antivenom treatment

Antivenom is the only specific antidote to snake venom. A most important decision in the management of a snake-bite victim is whether or not to administer antivenom.

10.1 What is antivenom?

Antivenom treatment for snake-bite was first introduced by Albert Calmette at the Institut Pasteur in Saigon in the 1890s (Bon and Goyffon 1996). Antivenom is immunoglobulin [usually pepsin-refined $F(ab')_2$ fragment of whole IgG] purified from the plasma of a horse, mule or donkey (equine) or sheep (ovine) that has been immunized with the venoms of one or more species of snake. "Specific" antivenom, implies that the antivenom has been raised against the venom of the snake that has bitten the patient and that it can therefore be expected to contain specific antibody that will neutralise that particular venom and perhaps the venoms of closely related species (paraspecific neutralization). Monovalent (monospecific) antivenom neutralizes the venom of only one species of snake. Polyvalent (polyspecific) antivenom neutralizes the venoms of several different species of snakes, usually the most important species, from a medical point of view, in a particular geographical area.

For example, the Indian antivenom manufacturers' "polyvalent anti-snake venom serum" is raised in horses using the venoms of the four most important venomous snakes in India (Indian cobra, *Naja naja*; Indian krait, *Bungarus caeruleus*; Russell's viper, *Daboia russelii*; saw-scaled viper, *Echis carinatus*), although the validity of the concept of "the big four" is increasingly challenged by the discovery that other species are also important in certain regions [e.g. *H. hypnale* in South-West India (Joseph et al., 2007); *Trimeresurus malabaricus* in southern India; *Echis carinatus sochureki* in Rajasthan (Kochar et al., 2007)]. Antibodies raised against the venom of one species may have

cross-neutralizing activity against other venoms, usually from closely related species. This is known as paraspecific activity. For example, the manufacturers of Haffkine polyvalent anti-snake venom serum claim that this antivenom also neutralizes venoms of two Trimeresurus species.

Recently, the Thai Red Cross Society began to manufacture two polyvalent antivenoms to cover the venoms of neurotoxic Elapidae (*Naja kaouthia, O. hannah, Bungarus candidus, B. fasciatus*) and haematotoxic Viperidae (*Daboia siamensis, Calloselasma rhodostoma, Cryptelytrops-Trimeresurus-albolabris*).

10.2 Indications for antivenom treatment

(see also Annex 1)

Antivenom should be given only to patients in whom its benefits are considered likely to exceed its risks. Since antivenom is relatively costly and often in limited supply, it should not be used indiscriminately. The risk of reactions should always be taken into consideration [level of evidence E].

10.3 Inappropriate use of antivenom

In some parts of the world, a small standard dose of antivenom is given to any patient claiming to have been bitten by a snake, irrespective of symptoms or signs of envenoming. Sometimes the local community are so frightened of snake-bite that they compel the doctor to give antivenom against medical advice to the patient with such a claim.

These practices should be strongly discouraged as they expose patients who may not need treatment to the risks of antivenom reactions; they also waste valuable and scarce stocks of antivenom.

Indications for antivenom [level of evidence O,E]

Antivenom treatment is recommended if and when a patient with proven or suspected snake-bite develops one or more of the following signs:

Systemic envenoming

- *Haemostatic abnormalities:* Spontaneous systemic bleeding **(clinical)**, coagulopathy **(20WBCT or other laboratory tests such as prothrombin time)** or thrombocytopenia (<100 x 10^9/litre or 100 000/cu mm) **(laboratory)**.
- Neurotoxic signs: ptosis, external ophthalmoplegia, paralysis etc **(clinical)**.
- *Cardiovascular abnormalities:* hypotension, shock, cardiac arrhythmia **(clinical)**, abnormal ECG.

- *Acute kidney injury (renal failure):* oliguria/anuria **(clinical)**, rising blood creatinine/ urea **(laboratory)**.
- *(Haemoglobin-/myoglobin-uria:)* dark brown urine (clinical), urine dipsticks, other evidence of intravascular haemolysis or generalised rhabdomyolysis (muscle aches and pains, hyperkalaemia) **(clinical, laboratory)**.
- Supporting laboratory evidence of systemic envenoming (see above).

Local envenoming

- Local swelling involving more than half of the bitten limb (in the absence of a tourniquet) within 48 hours of the bite. Swelling after bites on the digits (toes and especially fingers).
- Rapid extension of swelling (for example, beyond the wrist or ankle within a few hours of bite on the hands or feet).
- Development of an enlarged tender lymph node draining the bitten limb

10.4 How long after the bite can antivenom be expected to be effective?

Antivenom treatment should be given as soon as it is indicated. It may reverse systemic envenoming even when this has persisted for several days or, in the case of haemostatic abnormalities, for two or more weeks. It is, therefore, appropriate to give antivenom for as long as evidence of the coagulopathy persists. Whether antivenom can prevent local necrosis remains controversial, but there is some clinical evidence that, to be effective in this situation, it must be administered within the first few hours after the bite (Warrell et al., 1976; Tilbury 1982) [level of evidence T, O, E].

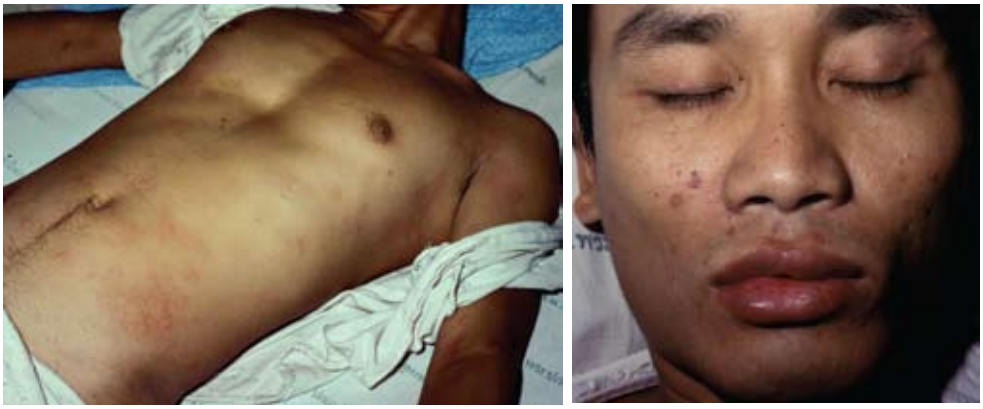
10.5 Antivenom reactions

A proportion of patients, usually more than 10%, develop a reaction either early (within a few hours) or late (five days or more) after being given antivenom. The risk of reactions is dose-related, except in rare cases in which there has been sensitization (IgE-mediated Type I hypersensitivity) by previous exposure to animal serum, for example, to equine antivenom, tetanus-immune globulin or rabies-immune globulin.

(1) ***Early anaphylactic reactions***: Usually within 10-180 minutes of starting antivenom, the patient begins to itch (often over the scalp) and develops urticaria (Fig. 62), dry cough, fever, nausea, vomiting, abdominal colic, diarrhoea and tachycardia. A minority of these patients may develop severe life-threatening anaphylaxis: hypotension, bronchospasm and angio-oedema.

Fatal reactions have probably been under-reported as death after snake-bite is usually attributed to the venom and patients may not be monitored carefully after treatment.

Figure 62 (a), (b): Early anaphylactic reaction to antivenom: urticaria and pruritus of the trunk and face (Copyright DA Warrell)



In most cases, these reactions are not truly "allergic". They are not IgE-mediated type I hypersensitivity reactions to horse or sheep proteins as there is no evidence of specific IgE, either by skin testing or radioallergosorbent tests (RAST). Complement activation by IgG aggregates or residual Fc fragments or direct stimulation of mast cells or basophils by antivenom protein are more likely mechanisms for these reactions.

(2) ***Pyrogenic (endotoxin) reactions:*** Usually these develop 1-2 hours after treatment. Symptoms include shaking chills (rigors), fever, vasodilatation and a fall in blood pressure. Febrile convulsions may be precipitated in children. These reactions are caused by pyrogen contamination during the manufacturing process. They are commonly reported.

(3) ***Late (serum sickness type) reactions:*** Develop 1-12 (mean 7) days after treatment. Clinical features include fever, nausea, vomiting, diarrhoea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy, periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis and, rarely, encephalopathy. Patients who suffer early reactions and are treated with antihistamines and corticosteroid are less likely to develop late reactions.

Prediction of antivenom reactions

Skin and conjunctival "hypersensitivity" tests will reveal IgE mediated Type I hypersensitivity to horse or sheep proteins. However, since the majority of early (anaphylactic) or late (serum sickness type) antivenom reactions result from direct complement activation rather than from IgE-mediated hypersensitivity, these tests are not predictive. Since they may delay treatment and can in themselves be sensitising, these tests should not be used [level of evidence T].

Contraindications to antivenom: Prophylaxis of high risk patients

There is no absolute contraindication to antivenom treatment, but patients who have reacted to horse (equine) or sheep (ovine) serum in the past (for example, after treatment with equine anti-tetanus serum, equine anti-rabies serum or equine or ovine antivenom) and those with a strong history of atopic diseases (especially severe asthma) are at high risk of severe reactions and should therefore be given antivenom only if they have signs of systemic envenoming.

In the absence of any prophylactic regimen that has proved effective in clinical trials (see below), these high risk patients may be pre-treated **empirically** with subcutaneous epinephrine (adrenaline), intravenous antihistamines (both anti-H_1, such as promethazine or chlorphenamine; and anti-H_2, such as cimetidine or ranitidine) and corticosteroid. In asthmatic patients, prophylactic use of an inhaled adrenergic β_2 agonist such as salbutamol may prevent bronchospasm.

Prevention of antivenom reactions

In the sole systematic review carried out in the field of snake-bite treatment, Nuchpraryoon and Garner (2000) concluded that routine prophylactic adrenaline for antivenom known to have high adverse event rates seemed sensible, based on only one trial (Premawardhena et al., 1999) and that antihistamine appeared to be of no obvious benefit, again based on one trial (Fan et al., 1999) [level of evidence S]. Since then, more data have become available.

(1) Prophylactic drugs (adrenaline, antihistamine anti-H_1 blockers, corticosteroids)

Adrenaline (epinephrine) is the most effective treatment for anaphylactic reactions, by reducing bronchospasm and capillary permeability. However, the risks of adrenaline make it less attractive for prophylaxis (Rusznak and Peebles, 2002). Premawardhena et al. (1999) used premedication with subcutaneous adrenaline in 105 snakebite victims and found a reduction from 43% to 11% ($p=0.04$) in the incidence of acute adverse reactions compared to placebo. No adverse reactions to the adrenaline were observed in this study. However, a subsequent fatality (Dassanayake et al., 2002) raised concerns about intracranial bleeding (a known complication of systemic envenoming following bites by vipers and Australian elapid snakes), hypertension and arrhythmias if adrenaline prophylaxis were to be used routinely especially in children, pregnant women and in patients with heart disease who had been excluded from the trial. Gawarammana et al. (2004) tested parallel pre-antivenom infusion of placebo, hydrocortisone alone, or hydrocortisone plus chlorphenamine in 52 patients. Reactions

were reduced from approximately 80% in the first two groups to 52% in the premedicated group though the results did not achieve statistical significance and the study was underpowered.

A randomized placebo-controlled trial of 101 patients in Brazil by Fan et al. (1999) showed that premedication with intramuscular promethazine had no significant effect on the high rate (68%) of anaphylactic reactions to antivenom. A review of 10 years of experience with various premedication regimens in Papua New Guinea (Williams et al., 2007) further illustrates the heterogeneity and lack of standardization of snakebite victim care in developing countries where most venomous snakebites occur but suggested efficacy of some prophylactic regimes, as did the study of Caron et al., 2009 in Ecuador. Recently data were presented comparing premedication of 1007 Sri Lankan snake-bite victims with promethazine, hydrocortisone, and low dose adrenaline, alone and in various combinations (de Silva et al., 2008). The only statistically significant reduction in the overall high rate of early adverse reactions (77%) was found in the promethazine alone group where a 33% reduction in pruritus, urticaria, facial oedema and bronchospasm was observed.

(2) Speed and dilution of intravenous antivenom administration

The in vitro anticomplementary activity of several commercial antivenoms led Sutherland (1977) and others to advocate dilution and slow infusion of antivenom (Reid, 1980; WHO, 1981). However, although a trial is in progress, no convincing clinical evidence has yet been published demonstrating that this strategy reduces the risk of reactions. In a small randomized study, Malasit et al. (1986) found no difference in rate or severity of reactions in patients given diluted antivenom over 30 minutes compared to those in whom intravenous push injection over 10 minutes was used. In Ecuador, Caron et al., 2009 found a strikingly lower incidence of reactions in a group of patients premedicated with intravenous hydrocortisone and diphenhydramine and given antivenom by infusion over 60 minutes compared to a group of historical controls who had been given no prophylaxis and in whom antivenom had been injected intravenously over 10 minutes.

At the earliest sign of a reaction:

- Antivenom administration must be temporarily suspended.
- Epinephrine (adrenaline) (0.1% solution, 1 in 1,000, 1 mg/ml) is the effective treatment for early anaphylactic and pyrogenic antivenom reactions.

Since no prophylactic drug regimen has proved effective in reducing the incidence or severity of early antivenom reactions, these drugs should not be used except in high risk patients (see above). All patients should be watched carefully for two hours after the completion of antivenom administration and should be treated with epinephrine/adrenaline at the first sign of a reaction [level of evidence T].

Treatment of antivenom reactions

Early anaphylactic and pyrogenic antivenom reactions: Epinephrine (adrenaline) is given intramuscularly (into upper lateral thigh) in an initial dose of 0.5 mg for adults and 0.01 mg/kg body weight for children. Because severe, life-threatening anaphylaxis can evolve so rapidly, epinephrine (adrenaline) should be given at the very first sign of a reaction, even when only a few spots of urticaria have appeared or at the start of itching, tachycardia or restlessness. The dose can be repeated every 5-10 minutes if the patient's condition is deteriorating.

Additional treatment: After epinephrine (adrenaline), an antihistamine anti-H_1 blocker such as chlorphenamine maleate (adults 10 mg, children 0.2 mg/kg by intravenous injection over a few minutes) should be given followed by intravenous hydrocortisone (adults 100 mg, children 2 mg/kg body weight). The corticosteroid is unlikely to act for several hours, but may prevent recurrent anaphylaxis [level of evidence O].

In pyrogenic reactions the patient must also be cooled physically and with antipyretics (for example paracetamol by mouth or suppository). Intravenous fluids should be given to correct hypovolaemia.

Treatment of late (serum sickness) reactions: Late (serum sickness) reactions may respond to a 5-day course of oral antihistamine. Patients who fail to respond in 24-48 hours should be given a 5-day course of prednisolone.

Doses: Chlorphenamine: adults 2 mg six hourly, children 0.25 mg/kg / day in divided doses.

Prednisolone: adults 5 mg six hourly, children 0.7 mg/kg/day in divided doses for 5-7 days

10.6 Selection, storage and shelf life of antivenom

Antivenom should be given only if its stated range of specificity and paraspecific neutralization includes the species known or suspected to have been responsible for the bite. Liquid antivenoms that have become opaque

should not be used as precipitation of protein indicates loss of activity and an increased risk of reactions.

To retain their full potency within the limits of stated expiry dates, lyophilized antivenoms (shelf life about 5 years) should be stored at below 25ºC and liquid antivenoms (shelf life 2-3 years) should be stored at 2-8 ºC and not frozen. Ideally, antivenoms should be used before the stated expiry dates but, provided that they have been properly stored, they can be expected to retain useful activity for months or even years after these dates (WHO, 1981; O'Leary et al., 2009). In patients with severe envenoming, recently expired antivenoms may be used if there is no alternative [level of evidence E].

If the biting species is known, the ideal treatment may be with a monovalent (monospecific) antivenom, as this may be less expensive and may involve administration of a lower dose of antivenom protein than with a polyvalent (polyspecific) antivenom. However, immunization of a horse or sheep with venoms of several related species of snakes (e.g. Viperidae) may produce an enhanced antibody response to common antigens, making the resulting polyvalent antivenom more rather than less potent than a monovalent antivenom (WHO, 2010).

Polyvalent (polyspecific) antivenoms are preferred in many countries because of the difficulty in identifying species responsible for bites and they can be just as effective as monovalent (monospecific) ones.

10.7 Administration of antivenom

- **Epinephrine (adrenaline) should always be drawn up in readiness before antivenom is administered.**
- **Antivenom should be given by the intravenous route whenever possible.**

Freeze-dried (lyophilized) antivenoms are reconstituted, usually with 10 ml of sterile water for injection per ampoule. If the freeze-dried protein is difficult to dissolve, it may have been denatured by inadequate freeze-drying technique (WHO, 2010).

Two methods of administration are recommended:

(1) *Intravenous "push" injection*: Reconstituted freeze-dried antivenom or neat liquid antivenom is given by slow intravenous injection (not more than 2 ml/minute). This method has the advantage that the doctor, nurse or dispenser administering the antivenom must

remain with the patient during the time when some early reactions may develop. It is also economical, saving the use of intravenous fluids, giving sets, cannulae etc.

(2) *Intravenous infusion*: Reconstituted freeze-dried or neat liquid antivenom is diluted in approximately 5-10 ml of isotonic fluid per kg body weight (i.e. 250-500 ml of isotonic saline or 5% dextrose in the case of an adult patient) and is infused at a constant rate over a period of about one hour.

Patients must be closely observed *for at least one hour* after starting intravenous antivenom administration, so that early anaphylactic antivenom reactions can be detected and treated early with epinephrine (adrenaline).

Local administration of antivenom at the site of the bite is not recommended: Although this route may seem rational, it should not be used as it is extremely painful, may increase intracompartmental pressure and has not been shown to be effective.

Intramuscular injection of antivenom: Antivenoms are large molecules ($F(ab')_2$ fragments or sometimes whole IgG) which, after intramuscular injection, are absorbed slowly via lymphatics. Bioavailability is poor, especially after intragluteal injection, and blood levels of antivenom never reach those achieved rapidly by intravenous administration. Other disadvantages are the pain of injection of large volumes of antivenom and the risk of haematoma formation in patients with haemostatic abnormalities.

The only situations in which intramuscular administration might be considered:

(1) At a peripheral first aid station, before a patient with obvious envenoming is put in an ambulance for a journey to hospital that may last several hours (Win-Aung et al., 1996);

(2) On an expedition exploring a remote area very far from medical care;

(3) When intravenous access has proved impossible.

Antivenom must never be given by the intramuscular route if it could be given intravenously.

Antivenom should never be injected into the gluteal region (upper outer quadrant of the buttock) as absorption is exceptionally slow and unreliable and there is always the danger of sciatic nerve damage when the injection is given by an inexperienced operator.

Although the risk of antivenom reactions is less with intramuscular than intravenous administration, epinephrine (adrenaline) must be readily available.

Under these unusual circumstances, the dose of antivenom should be divided between a number of sites in the upper anterolateral region of both thighs. A maximum of 5-10 ml should be given at each site by deep intramuscular injection followed by massage to aid absorption. Local bleeding and haematoma formation is a problem in patients with incoagulable blood. Finding enough muscle mass to contain such large volumes of antivenom is particularly difficult in children.

10.8 Dose of antivenom (Table 1 and Annex 2)

Manufacturers' recommendations are usually based on assays in which venom and antivenom are incubated *in vitro* before being injected into the test animal. This may not reflect the dose required to cure a human patient. The recommended dose is often the amount of antivenom required to neutralize the average venom yield when captive snakes are milked of their venom. In practice, the choice of an initial dose of antivenom is usually empirical.

Since the neutralizing power of antivenoms varies from batch to batch, the results of a particular clinical trial may soon become obsolete if the manufacturers change the strength of their antivenom.

Suggested initial doses of some of the available antivenoms are given in Annex 3 (classified by country of manufacture) and Table 1 (by species of snake) For choice of antivenom, see also WHO venomous snakes and antivenoms web-site http://apps.who.int/bloodproducts/snakeantivenoms/database/.

Snakes inject the same dose of venom into children and adults. Children must therefore be given exactly the same dose of antivenom as adults.

Antivenom manufacturers, health institutions and medical research organizations should encourage and promote the proper clinical testing of antivenoms as with other therapeutic agents. This is the only reliable guide to the initial dose (and safety) of an antivenom.

Table 1: Guide to initial dosage of some antivenoms for treating bites by medically important snakes in the SEARO region

Species

Latin name	English name	Manufacturer, antivenom	Approximate average initial dose
Acanthophis species	Death adder	CSL[1] Death Adder or Polyvalent Antivenom	1-3 vials
Bungarus caeruleus	Common krait	Indian manufacturers[4] polyvalent	100 ml
Bungarus candidus	Malayan krait	QSMI[5] Malayan Krait Antivenin[7]	50 ml
Bungarus multicinctus	Chinese krait	Shanghai Vaccine & Serum Institute	5 vials
		NIPM Taipei *Naja-Bungarus* antivenin	5 vials
Calloselasma (Agkistrodon) rhodostoma	Malayan pit viper	QSMI[5], Malayan Pit Viper Antivenin monovalent[6]	100 ml
Cryptelytrops (Trimeresurus) albolabris, C. macrops	Green pit vipers	QSMI[5] Green Pit Viper Antivenin[6]	100 ml
Daboia russelii	Western Russell's viper	Indian manufacturers[4] polyvalent	100 ml
Daboia siamensis	Eastern Russell's viper	Myanmar Pharmaceutical Industry monovalent	80ml
		QSMI[5], Russell's Viper Antivenin monovalent[6]	50ml
Echis carinatus India	saw-scaled viper	Indian manufacturers[4] polyvalent	50 ml
Gloydius (Agkistrodon) (brevicaudus)	Chinese Mamushi	Shanghai Vaccine & Serum Institute Mamushi antivenom	1 vial
Hydrophiinae	Sea snakes	CSL[1]Sea Snake Antivenom	1-10 vials
Micropechis ikaheka	New Guinean small-eyed snake	CSL[1] Polyvalent Antivenom	?2 vials
Naja kaouthia	Monocellate Thai cobra	QSMI[5], monovalent[7]	100 ml
Naja naja, N oxiana	Indian cobras	Indian manufacturers[4] polyvalent	100 ml
Oxyuranus scutellatus	Australian/Papuan taipans	CSL[1] Taipan or Polvalent Antivenom	1-6+ vials
Pseudonaja species	Australian brown snakes	CSL[1] Brown Snake or Polyvalent Antivenom	1-2 vials
Pseudechis species	Australian black snakes	CSL[1] Black Snake Antivenom	1-3 vials
Rhabdophis tigrinus, R. subminiatus	Japanese yamakagashi, SE Asian red-necked keelback	Japanese Snake Institute, Nitta-gun Yamakagashi antivenom	1-2 vials

[1] Commonwealth Serum Laboratories, Parkville, Australia

[2] South African Vaccine Producers, formerly SAIMR, Johannesburg

[3] National Guards Hospital, Riyadh, KSA

[4] Indian Manufacturers: Bharat Serums & Vaccines, Mumbai; Vins Bioproducts, Hyderabad; Biologicals E, Hyderabad

[5]Queen Saovabha Memorial Institute (Thai Red Cross Society)

[6]Also the new QSMI Haemato-polyvalent snake antivenom

[7]Also the new QSMI Neuro-polyvalent snake antivenom

Observation of the response to antivenom: If an adequate dose of appropriate antivenom has been administered, the following responses may be observed.

(a) *General*: The patient feels better. Nausea, headache and generalised aches and pains may disappear very quickly. This may be partly attributable to a placebo effect.

(b) *Spontaneous systemic bleeding* (e.g. from the gums): This usually stops within 15-30 minutes.

(c) *Blood coagulability* (as measured by 20WBCT): This is usually restored in 3-9 hours. Bleeding from new and partly healed wounds usually stops much sooner than this.

(d) *In shocked patients*: Blood pressure may increase within the first 30-60 minutes and arrhythmias such as sinus bradycardia may resolve.

(e) *Neurotoxic envenoming* of the post-synaptic type (cobra bites) may begin to improve as early as 30 minutes after antivenom, but usually takes several hours. Envenoming with presynaptic toxins (kraits and sea snakes) will not respond in this way.

(f) *Active haemolysis and rhabdomyolysis* may cease within a few hours and the urine returns to its normal colour.

10.9 Recurrence of systemic envenoming

In patients envenomed by vipers, after an initial response to antivenom (cessation of bleeding, restoration of blood coagulability) signs of systemic envenoming may recur within 24-48 hours.

This is attributable to:

(1) Continuing absorption of venom from the "depot" at the site of the bite, perhaps assisted by improved blood supply following correction of shock, hypovolaemia etc, after elimination of antivenom (range of elimination half-lives: IgG 45 hours; $F(ab')_2$ 80-100 hours; Fab 12-18 hours) (Ho et al., 1986; Ho et al., 1990)

(2) Redistribution of venom from the tissues into the vascular space, as the result of antivenom treatment (Rivière et al., 1997).

Recurrent neurotoxic envenoming after treatment of cobra bite has also been described.

10.10 Criteria for repeating the initial dose of antivenom

Criteria for giving more antivenom [level of evidence O, E]**:**

- Persistence or recurrence of blood incoagulability after 6 hours or of bleeding after 1-2 hours.
- Deteriorating neurotoxic or cardiovascular signs after 1-2 hours.

If the blood remains incoagulable (as measured by 20WBCT) six hours after the initial dose of antivenom, the same dose should be repeated. This is based on the observation that, if a large dose of antivenom (more than enough to neutralize the venom procoagulant enzymes) is given initially, the time taken for the liver to restore coagulable levels of fibrinogen and other clotting factors is 3-9 hours [level of evidence O, T].

In patients who continue to bleed briskly, the dose of antivenom should be repeated within 1-2 hours [level of evidence E].

In case of deteriorating neurotoxicity or cardiovascular signs, the initial dose of antivenom should be repeated after 1-2 hours, and full supportive treatment must be considered [level of evidence E].

11

Conservative treatment when no antivenom is available

This will be the situation in many parts of the SEA Region, where supplies of antivenom run out or where the bite is known to have been inflicted by a species against whose venom there is no available specific antivenom.

The following conservative measures are suggested:

Neurotoxic envenoming with respiratory paralysis: Assisted ventilation with room air or oxygen has proved effective, and has been followed by complete recovery, even after being maintained for periods of more than one month. Manual ventilation (anaesthetic bag) by relays of doctors, medical students, relatives and nurses has been effective where no mechanical ventilator was available. Anticholinesterases should always be tried (see below).

Haemostatic abnormalities: Strict bed rest to avoid even minor trauma; transfusion of clotting factors and platelets; ideally, fresh frozen plasma (FFP) and cryoprecipitate with platelet concentrates or, if these are not available, fresh whole blood. Intramuscular injections should be avoided.

Shock, myocardial damage: Hypovolaemia should be corrected with colloid/crystalloids, controlled by observation of the central venous pressure. Ancillary pressor drugs (dopamine or epinephrine-adrenaline) may also be needed. Patients with hypotension associated with bradycardia should be treated with atropine.

Acute kidney injury: Conservative treatment or dialysis (see below).

Dark brown urine (myoglobinuria or haemoglobinuria): Correct hypovolaemia with intravenous fluid, correct acidosis with a slow intravenous infusion of 50-100 mmol of sodium bicarbonate and, by analogy with crush syndrome, consider a single infusion of mannitol. 200 ml of 20% mannitol may be infused intravenously over

20 minutes, but this must not be repeated as there is a danger of inducing dangerous fluid and electrolyte imbalance.

Severe local envenoming: Local necrosis, intracompartmental syndromes and even thrombosis of major vessels is more likely in patients who cannot be treated with antivenom. Surgical intervention may be needed but the risks of surgery in a patient with consumption coagulopathy, thrombocytopenia and enhanced fibrinolysis must be balanced against the life threatening complications of local envenoming. Prophylactic broad spectrum antimicrobial treatment is justified (see below).

12

Supportive/ancillary treatment

Antivenom treatment can be expected to neutralize free circulating venom, prevent progression of envenoming and allow recovery. However, these processes take time and the severely envenomed patient may require life support systems such as treatment of shock, assisted ventilation and renal dialysis until the severely damaged organs and tissues have had time to recover.

13

Treatment of neurotoxic envenoming

13.1 Introduction

Antivenom treatment alone cannot be relied upon to save the life of a patient with bulbar and respiratory paralysis.

Death may result from aspiration, airway obstruction or respiratory failure. A clear airway must be maintained. Once there is loss of gag reflex and pooling of secretions in the pharynx, failure of the cough reflex or respiratory distress, a cuffed endotracheal tube or laryngeal mask airway should be inserted. If this is impossible for any reason, a tracheostomy should be performed and a snugly-fitting or cuffed tracheostomy tube inserted.

Although artificial ventilation was first suggested for neurotoxic envenoming 135 years ago, patients continue to die of asphyxiation because some doctors believe that antivenom alone is sufficient treatment.

13.2 Practical guide to airway management and respiratory support**

The following guidelines have been produced specifically to aid health care workers in the acute management of snakebite patients. However, it is important to recognize that the techniques described below are applicable to the care of all critically ill patients.

Importance of training

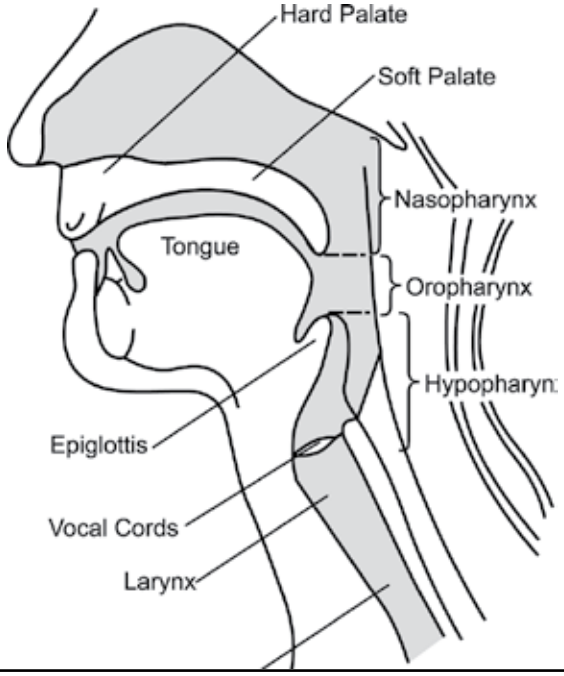
The techniques discussed below are not complicated. However, expert instruction is desirable, ideally from a fully trained doctor, nurse, first-aid worker or other health professional, with experience in resuscitation,

**With a contribution by Dr Simon D. Jensen

airway management, use of the necessary equipment, intubation and assisted ventilation. These techniques must be practised frequently, under supervision, using a manikin (dummy/model – see Fig 63a) or, but only where appropriate and culturally acceptable, a dead body in the mortuary, to acquire essential understanding of the anatomy of the upper airway and the techniques themselves, and to maintain an adequate baseline level of skill (Fig 63b).

Figure 63a: Training health workers in techniques of endrotracheal intubation and airway management in Papua New Guinea using a manikin (Copyright DJ Williams)

Figure 63b: Anatomy of the upper airway



Resuscitation

This follows the general principles of life support given below:

DRABCDE

D - DANGER

R - RESPONSE

A - AIRWAY

B – BREATHING

C - CIRCULATION

D - DISABILITY

E – EXPOSE THE PATIENT

(Only DRAB are discussed here)

D - DANGER - Scene safety: The rescuer should ensure that there is no risk of exposure to danger of a further snake bite to the victim, to themselves, or to other helpers by observing *standard precautions* possible under the circumstances (e.g. removing the victim from undergrowth and, in the case of sea snake-bite, removal from the water to avoid drowning) and by making sure that any snake brought to hospital with the patient, for identification, will not bite another person.

R - RESPONSE -The rescuer checks responsiveness of the victim (e.g. vocal - "Are you all right?", with gentle shaking). If there is no response, or limited response, summon assistance. Call out for help, send someone for medical assistance, or make a very quick telephone call.

Making an emergency call

If the victim does not respond:

(1) In a field situation: emergency medical services (EMS) are activated by calling the local emergency number (either by a second rescuer or by the first rescuer him/her self). The response team (ambulance) is asked to bring the necessary resuscitation equipment (also termed "code cart" or "code blue cart" in some hospitals/clinics), including an automated external defibrillator (AED).

(2) In a health centre: emergency cart and defibrillator are summoned

Once the EMS/emergency cart has been summoned, the rescuer starts airway management

A – AIRWAY PROTECTION AND MANAGEMENT

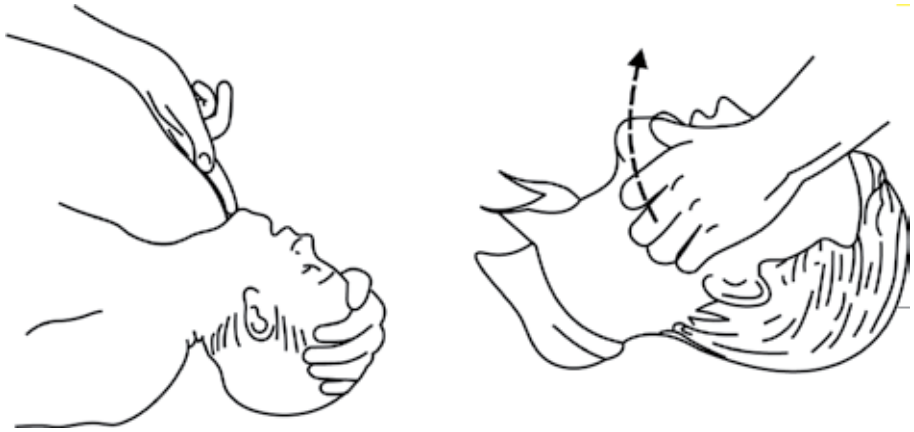
Basic Airway Management (BAM)

Opening and maintaining the airway:

The airway can be opened using the "head tilt - chin lift" manoeuvre (**Fig 63c**), bringing the patient's head into the "sniffing" position.

If this does not improve air flow, the "jaw thrust" manoeuvre (**Fig 63c**) should be performed as the tongue may have fallen or been sucked backwards, obstructing the oropharynx. "Jaw thrust" helps to lift the tongue forward, and is often effective in improving air flow as lifting the patient's chin and extending their neck serves to dislodge the tongue and reopen the upper airway.

Figure 63c: Head-tilt, chin-lift (left) and jaw-thrust manoeuvres (right)



Next look inside the victim's mouth. There may be blood, vomit or excessive oral secretions contributing to airway obstruction and putting the patient at risk of aspirating (inhaling) this material into their lungs. Remove any foreign material by suction, using a suitable suction catheter, such as a Yankeur suction catheter (attempts should not be longer than 10 seconds) or by using forceps. Use of a gloved finger is discouraged as this may push the material or object further down the airway and may put the rescuer at risk of being bitten.

Finally, insert an oropharyngeal (Guedel) airway (OPA), measured to suit the patient (from the corner of the mouth to the angle of the jaw), being sure to avoid causing trauma to the lips and mouth, especially if there is evidence of bleeding or the if the patient has been bitten by a snake which causes bleeding abnormalities. While nasopharyngeal airway (NPA) devices are better tolerated by semi-conscious patients, who may still have a gag reflex, or in those who have trismus, they are more likely to cause nasal bleeding, and so are not preferred.

If an OPA device cannot be inserted because of trismus (rigidity of the chewing muscles, preventing opening of the mouth), the patient may have one of the following life-threatening conditions, which must be urgently treated:

- Severe hypoxia;
- Hypoglycaemia;
- Seizure;

- Active rhabdomyolysis affecting the masseter muscles (e.g. in sea snake bite envenoming)
- Or they may, in fact, be awake and simply resisting you.

Advanced Airway Management (AAM)

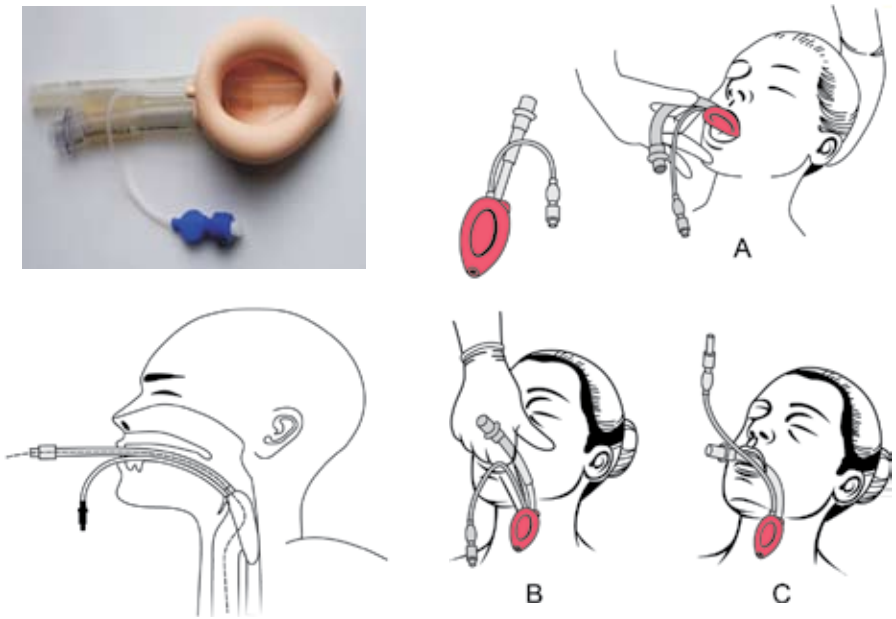
AAM is defined as the use of more advanced techniques in airway management. It may be used in the following circumstances:

- To maintain (keep open) the airway over long periods;
- To protect the airway (prevent the inhalation/pulmonary aspiration of saliva, vomit or blood):
- To ventilate a paralysed patient (such as after a bite by a snake with neurotoxic venom);
- To allow high concentrations of oxygen (up to 100%) to be delivered;
- To remove, and control the concentration of, carbon dioxide in the blood.

The devices used for this type of airway management are divided into 2 categories:

Supraglottic (above the larynx) devices (**Fig 63d**)

Figure 63d: Laryngeal mask airway, introduction and position



These include the various types of laryngeal mask airways. Many models with different features, benefits and disadvantages are now available, depending on the country in which you work. They do not require special

equipment to insert them, and even medically untrained people can be taught to insert them successfully after minimal (as little as one hour's) tuition, making them potentially ideal in a low-skill setting. However, they do not provide good protection of the airway as, potentially, fluids can still leak past them into the patient's lungs. They do not permit high ventilation/airway pressures, and require a gastric tube to reduce the risk of gastric insufflation (distension with gas) and the risk of gastro-oesophageal reflux.

Infraglottic (extending below the larynx) devices:

The most familiar, and by far the most readily available, is the endotracheal tube (ETT), typically a cuffed tube for adults and an uncuffed tube for children, though the use of cuffed (low pressure, high volume) tubes for children is becoming more acceptable.

These do provide protection of the lower airway (the lungs) against contamination by fluids and also permit higher ventilation pressures and the highest inspired oxygen concentrations.

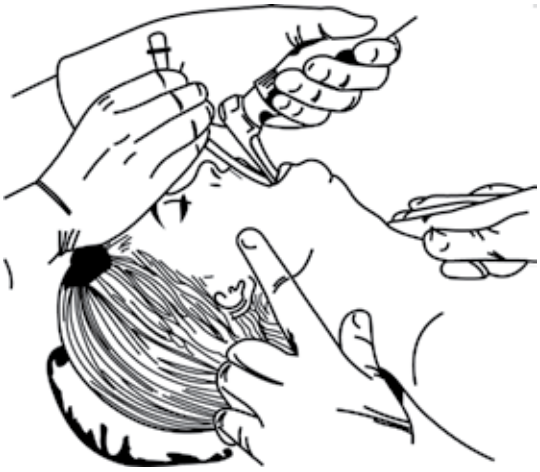
However, they require a laryngoscope of some sort to permit visualization of the laryngeal structures, and even the most basic of these are not available in small health centres.

To insert these devices safely and quickly (to reduce the period of no ventilation, and hence the risk of hypoxia) experience is required.

Induction/intubation drugs should be used, though these may not be available or the staff may not be experienced in their safe use.

Discussion of the actual techniques involved is beyond the scope of this document. However, essentially an endotracheal tube is inserted under laryngoscopic vision between the vocal cords so that its tip lies in the mid trachea (**Fig 63e**).

Figure 63e: Insertion of an endotracheal tube



Intubation is more invasive than supra-glottic devices and needs laryngoscopy and more skill to perform.

Surgical airway devices (tracheostomy)

These are discouraged and are rarely necessary because:

Patients rarely require ventilation beyond a week, once the correct type and dose of antivenom has been given;

Patients with venom-induced bleeding disorders, for example after bites by Australasian elapids (West Papua and Maluku Islands), and will bleed excessively from any such intervention. Therefore, "tracheostomy" is a term that should be removed from snakebite management protocols.

B – BREATHING

Assessing breathing: Place your ear near the victim's mouth and nose, keeping your gaze towards the victim's chest. Look for chest to rise and fall, listen for air escaping during exhalation, feel for the flow of air against your cheek. Take at least 5 seconds but no more than 10 seconds to make this assessment.

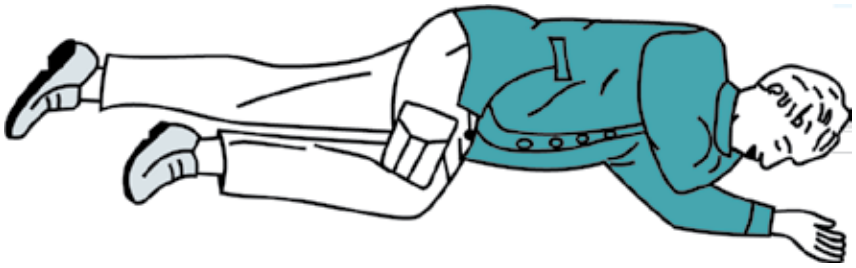
If oxygen is available, it should be administered by any available means (nasal prongs/catheters, mask, bag-valve-mask etc.) between each suctioning attempt (which should not be prolonged). [Arterial Peripheral oxygen saturation (SpO2) should be monitored by digital oximeter, if available.]

Positioning the patient to protect airway patency (Dangers of vomiting and aspiration)

If breathing is present and adequate (with or without airway opening manoeuvres), put the victim in the *recovery position* **(Fig 63f)** and keep checking for breathing every 2 minutes. This position and a chin-up tilt can be maintained using pillows, sand bags or an assistant, often the patient's relative. The recovery position is especially important in envenomed patients because vomiting is such a common early symptom, oral bleeding is common if there is a bleeding disorder, there may be hypersalivation and, since patients with neurotoxicity cannot cough or swallow, they are at increased risk of inhaling any of these secretions and fluids. However, when the patient is placed in the correct recovery position, these fluids will drain harmlessly from their mouth. The recovery position will also help to stop the tongue from falling back and blocking the airway.

If breathing stops at any time, make the victim supine, go through the airway opening manoeuvres again, and then provide breathing artificially, if required.

Figure 63f: The recovery position



If breathing is absent or inadequate, such as if:

- No breathing is discernable within 10 seconds (or 5 seconds in a child, 2 seconds in a baby);
- The respiratory rate is low (a general idea of normal ranges of age-related respiratory rates and other basic physiological parameters is required of all health care workers, or this information should be readily available to them);
- The depth of respiration is inadequate (shallow)(the tidal volume is low);
- The patient is taking agonal (gasping) breaths;
- The patient is cyanosed centrally (blue lips, ears, or tongue) (this might not be visible if the patient is very anaemic, such as from malnutrition, chronic malaria or chronic gastrointestinal parasite infestation), or
- The measured blood peripheral oxygen saturation is low (a poor trace, and so a potentially low reading, may be obtained if the patient has cold peripheries or a low blood pressure -shock);
- The end-tidal CO_2, by whichever method is being used, is high, or climbing;

ASSISTED VENTILATION IS REQUIRED!

How this is delivered will depend on:

- The clinical circumstances, ie. whether the patient is in the bush, in an small health centre or in a hospital;
- The skills of the rescuer;
- The availability of assistants;
- Equipment available.

Methods for providing assisted ventilation

Expired Air Resuscitation (EAR) (no health facilities immediately available):

Deliver 2 initial "rescue breaths" as follows (**Fig 63g**): close the patient's nose with one hand and pull the jaw down with the other, and place your mouth over the patient's mouth and deliver a breath over a second, enough to see the chest rise, and allowing 4 seconds for exhalation before giving a second breath. In the case of a small child the mouth and nose may be covered by the rescuer's mouth.

Figure 63g: Technique of giving "rescue breaths"

Assisted ventilation by this means will provide a maximum of approximately only 16% inspired oxygen concentration (FIO_2 0.16).

The risk of communicable disease transmission to the rescuer is low, but can be diminished further by the use of:

- A special EAR face shield, manufactured for this purpose;
- A mask of the type used with Bag-Valve-Mask (devices);
- A piece of cloth thin enough to allow for the free passage of air.

If the patient does not begin to breathe, or to breathe more effectively, at this point, the decision will need to be made about how long to continue this method of assisted ventilation.

This will depend on:

- The clinical circumstances, e.g. the likely diagnosis, the age of the patient (the rescuer might reasonably persist for longer if the patient is a small child), or the distance from medical assistance or from more advanced health care facilities;

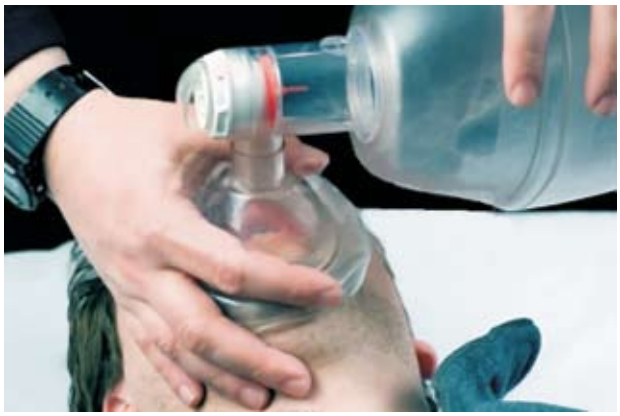
- The presence of effective cardiac activity; as determined by the presence of a carotid pulse (palpate on both sides before determining that this is absent), more advanced tests such as auscultation of audible heart sounds, or visible cardiac contraction on ultrasound; are supportive tests which may be available.

The presence of electrical activity, as determined using a cardiac monitor of some kind, with no demonstrable cardiac output or pulse (so-called "pulse-less electrical activity") usually carries a very poor prognosis, though there is a list of potentially reversible conditions which may cause this. This topic is not covered in these guidelines, but should be covered in any advanced life support course material.

Non-invasive ventilation:

Bag-mask/Bag-mask-valve ventilation: In a health care centre, a commonly used method for providing initial respiratory assistance is with a bag-mask/Bag-Valve-Mask (BVM) (resuscitator bag) (**Fig. 63h**). Even the simplest health care centre should have these, with different sizes required for different ages of patients, and the staff should be well versed in how to check that the device is functioning correctly and know how to use it correctly and safely.

Figure 63h: Bag-valve-mask ventilation



The rescuer positions him/her self at the victim's head end. Holding the bag with one hand, he/she places the mask on the victim's face with the apex of the mask on the bridge of the nose and its base on the groove over the chin. With the other hand, he/she seals the mask around the victim's nose and mouth, tilts (extends) the victim's head, lifts the jaw forward and gives breaths at approximately the normal respiratory rate for the patient by squeezing/pressing the bag, looking for visible chest rise. Any chest movement is usually adequate, especially in children.

If chest movement is inadequate, a correctly-sized OPA should be inserted. This will usually assist with air flow in and out of the lungs. If there is no bleeding disorder, an NPA (or 2) may be used instead of, or in addition to, an OPA.

Bag-mask breathing suffices for short- term respiratory support but if there is no breathing or inadequate breathing that needs longer term support, the airway needs to be secured more definitively and even the bag may have to be replaced with a ventilator. However, many snakebite patients around the developing world have been kept alive for days, or week, using simply an OPA and a BVM, or with an ETT and a BVM, using relatives to squeeze the bag, though this is far from ideal.

Invasive Ventilation:

This includes the use of supraglottic or infraglottic devices to open the airway and assist with both the supply of oxygen to the lungs and removal of carbon dioxide from the lungs. Generally, and where possible, endotracheal intubation (insertion of an ETT) should be performed and the patient placed on a ventilator, attended constantly by a suitably qualified nurse, with a suitably qualified doctor always on call to provide additional assistance, if required.

Adequacy of respiratory assistance can be assessed by reversal of clinical signs of inadequate respiration and stabilization of SpO_2 and end-tidal CO_2 (where available) and improvement in the victim's level of consciousness if respiratory failure was the sole cause of his/her unresponsiveness. However, assessing the level of consciousness of a patient with neurotoxic envenoming can be difficult because of their often generalized flaccid paralysis, such that the normal method of ascertaining the level of consciousness (the Glasgow Coma Scale – GCS) is irrelevant since the patient is unable to open their eyes, unable to speak and often unable to obey commands. They are, contrary to common belief, awake, able to hear everything which is said around them. They should be sedated during the period of their ventilation.

Other important aspects of the care of a ventilated patient include:

- Adequate hydration, monitoring of renal function and of fluid balance;
- Nutrition (in addition to the minimal nutrition contained in normal IV fluids);
- Physiotherapy (including chest physiotherapy, regular turning to prevent pressure areas and lung collapse, and maintenance of the range of motion of paralysed, immobile joints and muscles, as

well as limbs where significant cytotoxicity and tissue damage has occurred).

- Safe and effective weaning from ventilation.

Always be careful to minimize trauma to the airway of a snakebite patient; this includes the insertion of basic airway devices, advanced airway devices and gastric tubes. Orogastric tubes are much preferred over nasogastric ones – the latter often lead to bleeding which is difficult to deal with in the patient who has a coagulopathy, and may even lead inexperienced staff to give more antivenom or blood products when these are not necessary.

Such care also applies to the insertion of intravenous catheters and urinary (urethral) catheters.

Central venous lines may be inserted, if required and possible, but the insertion site will depend on the presence or absence of a bleeding disorder.

Intra-arterial lines may be useful in many respects, but, again, are discouraged in the presence of a bleeding disorder.

13.3 Trial of anticholinesterase

Anticholinesterase drugs have a variable, but potentially very useful effect in patients with neurotoxic envenoming, especially those bitten by cobras (Banerji et al., 1972; Watt et al., 1986; Watt et al., 1989).

A trial of anticholinesterase (eg "Tensilon test") should be performed in every patient with neurotoxic envenoming, as it would be in any patient with suspected myasthenia gravis. However, this should not delay antivenom treatment or endotracheal intubation. Patients must be observed closely as they may deteriorate while the trial of anticholinesterase is being carried out

Procedure

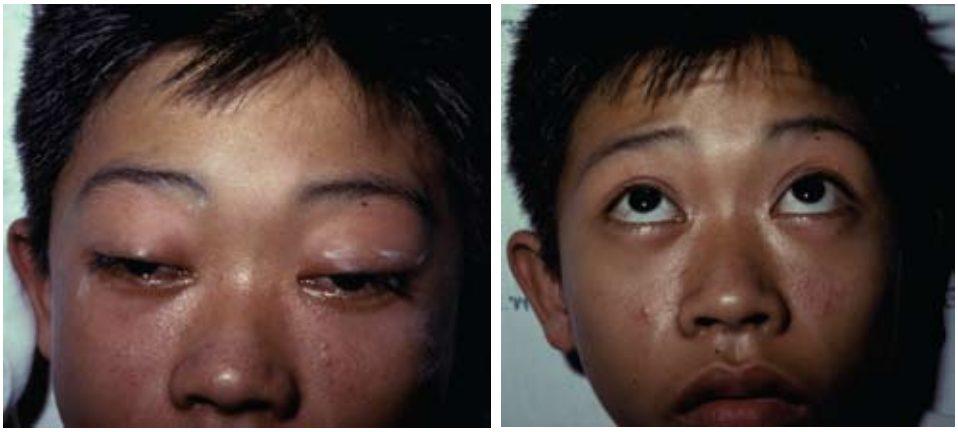
(1) Baseline observations or measurements are made against which to assess the effectiveness of the anticholinesterase.

(2) Atropine sulphate (0.6 mg for adults; 50 µg/kg for children) or glycopyrronium is given by intravenous injection followed by neostigmine bromide or methylsulphate (Prostigmin) (or distigmine, pyridostigmine, ambenomium etc. in appropriate doses) by intramuscular injection 0.02 mg/kg for adults, 0.04 mg/kg for children. Short acting edrophonium chloride (Tensilon) is ideal for

this test but is rarely available in the region. It is given by slow intravenous injection in an adult dose of 10 mg, or 0.25 mg/kg for children.

(3) The patient is observed over the next 30-60 minutes (neostigmine) or 10-20 minutes (edrophonium) for signs of improved neuromuscular transmission. Ptosis may disappear (**Fig 64**) and ventilatory capacity (peak flow, FEV-1 or maximum expiratory pressure) may improve.

Figure 64: (a) Before and (b) after intravenous atropine followed by intravenous edrophonium chloride in a patient envenomed by a Malayan krait *(Bungarus candidus)* (Copyright DA Warrell)



(4) Patients who respond convincingly can be maintained on neostigmine methylsulphate, 0.5-2.5 mg every 1-3 hours up to 10 mg/24 hours maximum for adults or 0.01-0.04 mg/kg every 2-4 hours for children by intramuscular, intravenous or subcutaneous injection together with atropine to block muscarinic side effects. Patients able to swallow tablets may be maintained on atropine 0.6 mg twice each day, neostigmine 15 mg four times each day or pyridostigmine 60 mg four times each day.

Anticholinesterase (e.g. "Tensilon") test

- Baseline observations
- Give atropine intravenously
- Give anticholinesterase drug (e.g. neostigmine intramuscularly)
- Observe effect
- If positive, institute regular atropine and neostigmine

The "ice test" as a possible alternative to the Tensilon test (Golnik et al., 1999)

In patients with myasthenia gravis who have bilateral ptosis, application of an ice-filled plastic glove to one eye for 2 minutes resulted in improvement in ptosis on that side, possibly due to inhibition of anticholinesterase. This quick and simple test might obviate the need for the Tensilon test. However, it has not yet been evaluated in patients with neurotoxic envenoming.

14

Treatment of hypotension and shock

This is usually the result of (1) hypovolaemia from loss of circulating volume into the swollen limb, as a result of generalised increase in capillary permeability (e.g. Russell's viper envenoming in Myanmar) or internal/external haemorrhage, (2) venom-induced vasodilatation or (3) direct myocardial effects with or without arrhythmias. Ideally, treatment with plasma expanders (colloids or crystalloid) should be controlled by observation of the central venous pressure (jugular venous pressure or direct measurement of pressure in the superior vena cava via a catheter connected to a saline manometer, see Annex 4). Excessive volume replacement may cause pulmonary oedema when plasma extravasated in the bitten limb and elsewhere is reabsorbed into the circulation.

In patients with evidence of a generalized increase in capillary permeability, a selective vasoconstrictor such as dopamine may be given by intravenous infusion, preferably into a central vein (starting dose 2.5-5 mcg/kg/minute).

Snake-bite: Causes of hypotension and shock

- Anaphylaxis
- Vasodilatation
- Cardiotoxicity
- Hypovolaemia
- Antivenom reaction
- Respiratory failure
- Acute pituitary adrenal insufficiency
- Septicaemia

In victims of Russell's viper bites in Myanmar and South India, acute pituitary adrenal insufficiency resulting from haemorrhagic infarction of the anterior ituitary may contribute to shock (Tin-Pe et al., 1987) (Fig. 52a). Hydrocortisone is effective in these cases.

15

Treatment of oliguria and acute kidney injury*

Detection of kidney injury:

- dwindling or no urine output
- rising blood urea/creatinine concentrations
- clinical "uraemia syndrome":
  - nausea, vomiting,
  - hiccups, fetor,
  - drowsiness, confusion, coma,
  - flapping tremor, muscle twitching, convulsions
  - pericardial friction rub,
  - signs of fluid overload.

In patients with any of the above features, the following should be monitored:

- pulse rate,
- blood pressure, lying and sitting, to detect postural hypotension,
- respiratory rate,
- temperature,
- height of jugular venous pulse,
- auscultation of lung bases for crepitations,

15.1 Oliguric phase of renal failure

Most, but not all, patients with acute renal failure are oliguric, defined as a urine output of less than 400 ml/day or less than 20 ml/hour. Conservative management may avoid the need for dialysis.

* Sitprija and Boonpucknavig 1979; Chugh 1989

If the patient has intravascular volume depletion, indicated by supine or postural hypotension, or empty neck veins, proceed as follows:

(1) Establish intravenous access.

(2) Give fluid challenge: An adult patient can be given two litres of isotonic saline over one hour or until the jugular venous pressure/ central venous pressure has risen to 8-10 cm above the sternal angle (with the patient propped up at 45º). The patient must be closely observed while this is being done. The fluid challenge must be stopped immediately if pulmonary oedema develops. If the urine output does not improve it is reasonable to try a furosamide and/ or mannitol challenge, but these are not of proven benefit.

In some patients it can be difficult to determine the height of the central venous pressure by clinical examination. Direct measurement of central venous (superior vena caval) pressure through a long catheter, preferably inserted at the antecubital fossa (see Annex 4), can be helpful in this circumstance. The catheter is connected to a saline manometer, the 0 point of which must be placed at the same level as the right atrium (that is, at the sternal angle when the patient is propped up at 45º). However, in someone who is obviously volume-depleted, resuscitation should start immediately, and not be delayed until a central venous line has been inserted.

(3) Insert a urethral catheter with full sterile precautions

(4) Furosemide (frusemide) challenge: 100 mg of furosemide is injected slowly (4-5 mg/minute). If this does not induce a urine output of 40 ml/hour, give a second dose of furosemide of 200 mg. If urine output does not improve, try conservative management.

(5) Conservative management: If the urine output does not improve, despite these challenges no further diuretics should be given and fluid intake should be restricted to a total of the previous day's output plus "insensible losses" (500-1000 ml/day). If possible, the patient should be referred to a renal unit. The diet should be bland, high on calories (1700/day), low in protein (less than 40g/day), low in potassium (avoid fruit, fruit juices and potassium-containing drugs) and low in salt. Infections will cause tissue breakdown and increase urea levels. They should be prevented or treated promptly with non-nephrotoxic antibiotics (i.e. avoid aminoglycosides such as gentamicin).

(6) Biochemical monitoring: Serum potassium, urea, creatinine and, if possible, pH, bicarbonate, calcium and phosphate should be monitored frequently. If this is not possible the electrocardiogram

(ECG) should be examined for evidence of hyperkalaemia, especially following bites by sea snakes, or Sri Lankan or South Indian Russell's vipers, or if the patient is passing dark brown urine, indicating rhabdomyolysis or intravascular haemolysis.

(7) Detection and management of hyperkalaemia: ECG evidence of hyperkalaemia: tall peaked T waves, prolonged P-R interval, absent P waves, wide QRS complexes. Emergency treatments, which will control hyperkalaemia for 3-6 hours only, should be given if serum potassium >6.0 mmol/l or ECG changes

- Give 10 ml of 10% calcium gluconate intravenously over 2 minutes (with ECG monitoring if possible) repeated up to three times
- Give 50 ml of 50% dextrose with 10 units of soluble insulin intravenously
- Sodium bicarbonate (40 ml of 8.4%) by slow intravenous infusion and a β_2 agonist aerosol by inhaler (e.g. salbutamol - "Ventolin" 5-10 mg) may also be used

(8) Management of severe acidosis: If the patient is hypotensive and profoundly acidotic (deep sighing "Kussmaul" respirations, very low plasma bicarbonate concentration or very low pH - <7.10), sodium bicarbonate should be given. Based on volume of distribution of bicarbonate which is 40% of body weight, bicarbonate deficit can be calculated. Usually 2-3 ampoules (40 ml of 8.4% sodium bicarbonate equivalent to 1 mmol/ml) in 5% dextrose water, or half of the calculated deficit can be replaced in 3-4 hours. Severe acidosis in snake-bite is usually associated with acute renal failure. Volume expansion by sodium bicarbonate can cause fluid overload. Therefore, if there is no clinical improvement dialysis is required. Intravenous bicarbonate may precipitate profound hypocalcaemia and fits, especially in patients with rhabdomyolysis.

(9) Dialysis (Fig. 65a,b)

Indications for dialysis

(a) Clinical uraemia

(b) Fluid overload

(c) Blood biochemistry-one or more of the following
creatinine >4 mg/dl (500 µmol/l)
urea >130 mg/dl (27 mmol/l)
potassium >7 mmol/l (or hyperkalaemic ECG changes)
symptomatic acidosis

Figure 65: Dialysis for treatment of acute kidney injury
(Copyright DA Warrell)
(a) Peritoneal dialysis in a township hospital in Myanmar
(b) Haemodialysis in a district hospital in India

15.2 Prevention of renal damage in patients with myoglobinuria or haemoglobinuria

To minimize the risk of renal damage from excreted myoglobin and/or haemoglobin:

- Correct hypovolaemia (see above) and maintain saline diuresis (if possible)
- Correct severe acidosis with bicarbonate (see above)
- Give a single infusion of mannitol (200 ml of 20% solution over 20 minutes) (not of proven benefit)

15.3 Diuretic phase of kidney injury

This is as important and as life-threatening as the oliguric phase. Urine output increases to 5-10 litres/24 hours following the period of anuria. The patient may become polyuric and volume depleted so that salt and water must be carefully replaced. Hypokalaemia may develop, in which case a diet rich in potassium (fruit and fruit juices) is recommended.

15.4 Renal recovery phase

The diuretic phase may last for months after Russell's viper bite. In Myanmar and South India, hypopituitarism may complicate recovery of Russell's viper bite victims. Corticosteroid, fluid and electrolyte replacement may be needed in these patients.

15.5 Persisting renal dysfunction

In Myanmar, persistent tubular degenerative changes were observed in Russell's viper bite victims who showed continuing albuminuria, hypertension and nocturia for up to 11 months after the bite, despite apparent recovery in renal function. In India, 20%-25% of patients referred to renal units with acute renal failure following Russell's viper bite suffered oliguria for more than four weeks suggesting the possibility of bilateral renal cortical necrosis. This can be confirmed by renal biopsy or contrast enhanced CT scans of the kidneys. In Sri Lanka, some patients envenomed by hump-nosed pit vipers develop chronic kidney dysfunction requiring dialysis or renal transplantation but these options are not open to impoverished rural people. Patients with patchy cortical necrosis show delayed and partial recovery of renal function but those with diffuse cortical necrosis require regular maintenance dialysis and eventual renal transplantation.

16

Haemostatic disturbances

Bleeding and clotting disturbances usually respond satisfactorily to treatment with specific antivenom, but the dose may need to be repeated several times, at six hourly intervals, before blood coagulability (assessed by the 20WBCT) is finally and permanently restored.

Heparin is ineffective against venom-induced thrombin and may cause bleeding on its own account. It should never be used in cases of snake-bite.

Antifibrinolytic agents are not effective and should not be used in victims of snake-bite.

In exceptional circumstances, such as severe bleeding or imminent urgent surgery, once specific antivenom has been given to neutralise venom procoagulants and other antihaemostatic toxins, restoration of coagulability and platelet function can be accelerated by giving fresh frozen plasma, cryoprecipitate (fibrinogen, factor VIII), fresh whole blood or platelet concentrates.

16.1 Dangers of venipuncture in patients with haemostatic abnormalities

In patients with incoagulable blood, any injection (subcutaneous, intramuscular) and, particularly venepuncture, carries a risk of persistent bleeding and haematoma formation.

Arterial puncture is contraindicated in such patients.

Repeated venipuncture can be avoided by using an indwelling cannula and three-way tap system. When blood coagulability has been restored, the dead space should be filled with heparinised saline, but if this is not flushed out before blood sampling, misleading results will be obtained in clotting tests, including the 20WBCT.

In patients with coagulopathy, sites of venous access and placement of intravenous cannulae or catheters should be chosen where haemostasis by external pressure is most likely to be effective, e.g. the antecubital fossa. If possible, avoid jugular, subclavian and femoral vein puncture. A pressure pad must be applied at the site of any venipuncture.

17

Treatment of the bitten part

The bitten limb, which may be painful and swollen, should be nursed in the most comfortable position, but not excessively elevated as this may reduce arterial perfusion pressure in a tensely swollen limb and increase the risk of intra-compartmental ischaemia. Bullae may be large and tense but they should be aspirated only if they seem likely to rupture.

17.1 Bacterial infections

Infection at the time of the bite with organisms from the snake's venom and buccal cavity is a problem with some species such as the Malayan pit viper (Theakston et al., 1990) but prophylactic antibiotics were not effective in a controlled study in Brazil (Jorge et al., 2004) [level of evidence T]. Interference with the wound (incisions made with an unsterilised razor blade/knife etc) creates a risk of secondary bacterial infection and justifies the use of immediate broad spectrum antibiotics (e.g. amoxycillin or a cephalosporin plus a single dose of gentamicin plus metronidazole) and tetanus prophylaxis. Later infections include nosocomial pneumonias and urinary tract infections.

17.2 Compartmental syndromes and fasciotomy

(Fig. 65) (Matsen 1980; Mars and Hadley 1998; Mars et al., 1991)

The appearance of an immobile, tensely-swollen, cold and apparently pulseless snake-bitten limb may suggest to surgeons the possibility of increased intracompartmental pressure, especially if the digital pulp spaces or the anterior tibial compartment are involved. Swelling of envenomed muscle within such tight fascial compartments could result in an increase in tissue pressure above the venous pressure, resulting in ischaemia. However, the classical signs of an intracompartmental pressure syndrome may be difficult to assess in snake-bite victims and many unnecessary, dangerous and debilitating fasciotomies are performed, especially where surgeons rather than physicians have the primary responsibility for managing snake-bite cases (Fig. 66).

Clinical features of a compartmental syndrome

- Disproportionately severe pain.
- Weakness of intracompartmental muscles.
- Pain on passive stretching of intracompartmental muscles.
- Hypoaesthesia of areas of skin supplied by nerves running through the compartment.
- Obvious tenseness of the compartment on palpation.

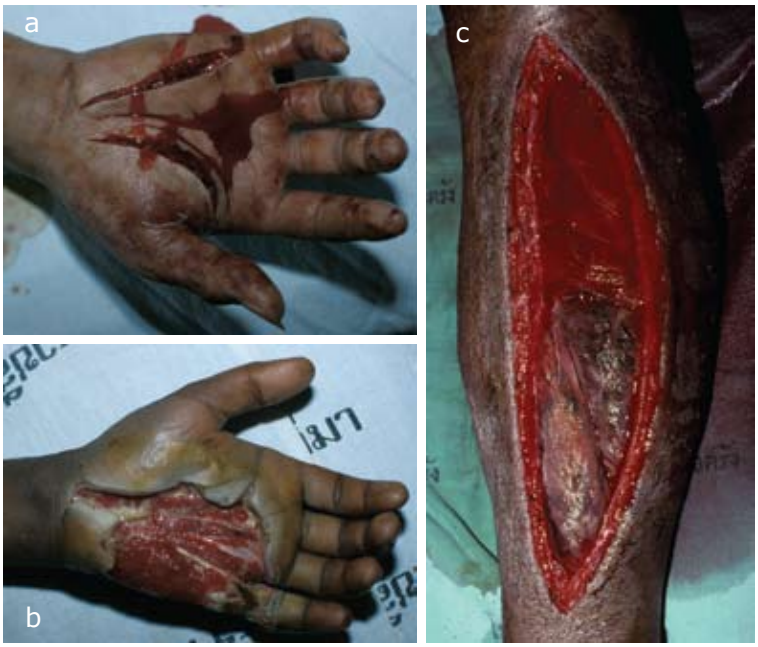
Detection of arterial pulses by palpation or doppler ultrasound probes, does not exclude intracompartmental ischaemia. The most reliable test is to measure intracompartmental pressure directly through a cannula introduced into the compartment and connected to a pressure transducer or manometer (Annex 5). In orthopaedic practice, intracompartmental pressures exceeding 40 mmHg (less in children) may carry a risk of ischaemic necrosis (e.g. Volkmann's ischaemia or anterior tibial compartment syndrome). However, envenomed muscle may not be saved by fasciotomy. Animal studies have suggested that muscle sufficiently envenomed and swollen to cause intracompartmental syndromes, may already be irreversibly damaged by the direct effects of the venom (Garfin et al., 1984). In any case, fasciotomy should not be contemplated until haemostatic abnormalities have been corrected, otherwise the patient may bleed to death (Fig. 66c). Not only in reversing coagulopathy, antivenom may also be helpful in reducing severe limb oedema (Rojnuckarin et al., 2006) [level of evidence T]. However, corticosteroids are not effective in ameliorating local effects of envenoming and, since they carry the risk of side-effects, they should not be used (Reid et al., 1963; Nuchprayoon et al., 2008) [level of evidence T].

Early treatment with antivenom remains the best way of preventing irreversible muscle damage.

Criteria for fasciotomy in snake-bitten limbs

- Haemostatic abnormalities have been corrected (antivenom with or without clotting factors)
- Clinical evidence of an intracompartmental syndrome
- Intracompartmental pressure >40 mmHg (in adults)

Figure 66: Results of unnecessary fasciotomies in snake bite victims in Thailand
(a) Profuse bleeding in a patients with mild local envenoming but severe coagulopathy following a bite by green pit viper (*Cryptelytrops albolabris*) (Copyright the late Sornchai Looareesuwan)
(b) Residual skin loss and exposure of tendons following fasciotomy for mild local envenoming in a patient bitten by a green pit viper (Cryptelytrops albolabris) (Copyright Sornchai Looareesuwan)
(c) Persistent bleeding for 10 days, resulting in haemorrhagic shock despite transfusion of 20 unites of blood, in a victim of Malayan pit viper bite in whom fasciotomy was performed before adequate antivenom treatment had been given to correct the coagulopathy (Copyright DA Warrell)



17.3 Rehabilitation

In patients with severe local envenoming, the limb should be maintained in a functional position. For example, in the leg, equinus deformity of the ankle should be prevented by application of a back slab.

Functional effects of local envenoming range from persistent stiffness and induration due to sclerosis of veins, lymphatics and tissue planes through which the venom has spread, to severe deformity, tissue loss, especially dermonecrosis, and requiring skin grafting and gangrene requiring debridement and amputation. Restoration of normal function in the bitten part should be started by simple exercises while the patient is still in hospital. After the patient has been discharged from hospital rehabilitation is rarely supervised but relatives can be instructed and given a time table of rehabilitation activities. Conventional physiotherapy may accelerate functional recovery of the bitten limb.

18

Management of cobra spit ophthalmia*

Management of venom ophthalmia consists of: (1) urgent decontamination by copious irrigation (2) analgesia by vasoconstrictors with weak mydriatic activity (e.g. epinephrine) and limited topical administration of local anesthetics (e.g. tetracaine) (3) exclusion of corneal abrasions by fluorescein staining with a slit lamp examination and application of prophylactic topical antibiotics 4) prevention of posterior synechiae, ciliary spasm and discomfort with topical cycloplegics and (5) antihistamines in case of allergic kerato-conjunctivitis. Topical or intravenous antivenom and topical corticosteroids are contraindicated [level of evidence E]. First aid consists of irrigating the affected eyes and other mucous membranes with liberal quantities of water or any other available bland liquid. Instillation of 0.5% adrenaline drops relieves pain and inflammation. Topical anaesthetic drops such as tetracaine may help to relieve pain but should be used only once as they render the eye vulnerable to trauma. In view of the risk of corneal abrasion, fluorescein staining or slit lamp examination is essential. Otherwise, topical antimicrobials (tetracycline or chloramphenicol) should be applied to prevent endophthalmitis or blinding corneal opacities. Topical cycloplegic drops such as atropine, scopolamine and homatropine 2% may be beneficial in several ways. Some ophthalmologists recommend the use of a dressing pad to close the eye. The instillation of diluted antivenom may cause local irritation and is of uncertain benefit. It is not recommended.

* Chu et al., 2010

19

Management of snake-bites at different levels of the health service

All levels of the health service can contribute to the management of patients with suspected snake-bite. Since the treatment of severe envenoming is a medical emergency that may require a range of medical skills, equipment, antivenom and other medicines, referral should be to the highest level of care that is readily available. However, in the rural areas where snake-bites are most frequent, transfer to a hospital may not be feasible within the reasonable time frame of a few hours. In that case, a lower level of health facility services must cope with the emergency as suggested below.

A. At the community or village level

(1) Check history of snake-bite and look for obvious evidence of a bite (fang puncture marks, swelling of the bitten part etc.).

(2) Immobilize the patient as far as possible by laying him/her down in a relaxed but safe position (e.g. the recovery position), immobilize especially the bitten limb and give reassurance.

(3) Arrange transport of the patient to medical care as quickly, safely and passively as possible by vehicle, boat, bicycle, motorbike, stretcher etc. Ideally the patient should lie in the recovery position (prone, on the left side) with his/her airway protected to minimise the risk of shock and inhalation of vomit.

(4) Discourage time-wasting and potentially dangerous traditional treatments such as tight ligatures (tourniquets), incisions, suction and application of herbs, ice, chemicals, "snakestones" etc.

(5) If the snake responsible has already been caught or killed take it with the patient but ensure safety by avoiding direct contact.

B. At the rural clinic, dispensary or health post

(1) Carry out a simple medical assessment including history and simple physical examination – local swelling, painful tender and enlarged

local lymph glands, persistent bleeding from the bite wound, blood pressure, pulse rate, bleeding (gums, nose, vomit, stool or urine), level of consciousness, drooping eyelids (ptosis) and other signs of paralysis, 20 minute whole blood clotting test, urine examination (appearance, sticks testing for blood etc). Identify the snake (if brought).

(2) Assess the need and feasibility of transporting the patient to a higher level of the health service (see A above).

(3) Give analgesia by mouth if required: Paracetamol (acetaminophen) (adult dose 500 mg to 1 gm maximum 4 gm in 24 hours; children 10-15 mg/kg/day maximum 100mg/kg/day) or codeine phosphate (adult dose 30-60 mg maximum 240 mg in 24 hours; children more than 2 years old, 0.5 mg/kg, maximum 2 mg/kg/day) can be administered every 4-6 hours by mouth as required (not aspirin or non-steroidal anti-inflammatory drugs which can cause bleeding).

(4) If the necessary skills, equipment, antivenom and other drugs are available, give intravenous fluid to correct hypovolaemic shock. If the patient fulfils criteria for antivenom treatment, give antivenom. These skills include ability to diagnose local and systemic envenoming, set up intravenous infusion or intravenous injection, identify the early signs of anaphylaxis and treat it with intramuscular adrenaline/epinephrine. If no antivenom is available, transfer to a hospital.

(5) If the patient has evidence of respiratory paralysis, give oxygen by mask and transfer to a hospital. It is assumed that assisted ventilation other than by a tight-fitting face mask connected to an anaesthetic (Ambu) bag will not be possible at this level.

(6) Discourage the use of ineffective and potentially harmful drugs (e.g. corticosteroids, antihistamines, and heparin).

C. At the district hospital

Proceed as in B above in addition to the followings:

(1) Carry out a more detailed clinical and laboratory assessment including biochemical and haematological measurements, ECG or radiography, as indicated.

(2) If no antivenom is available, transfer to a hospital that has antivenom or treat conservatively; this may require transfusion of blood or fresh frozen plasma (see below).

(3) Reassess analgesia (see B above) and, if required, consider stronger parenteral opioid drugs as required all with great caution (e.g. subcutaneous, intramuscular or even intravenous pethidine, initial adult dose 50-100 mg; children 1-1.5 mg/kg; or morphine, initial adult dose 5-10 mg; children 0.03-0.05 mg/kg,).

(4) If the patient has evidence of local necrosis (gangrene), give tetanus toxoid booster, antibiotics and consider surgical debridement of dead tissue.

(5) If the patient has evidence of bulbar or respiratory paralysis, insert endotracheal tube or laryngeal mask airway. If there is evidence of respiratory failure, assist ventilation manually by anaesthetic (Ambu) bag or mechanical ventilator.

(6) If the patient has evidence of acute renal failure, treat with peritoneal dialysis. If this is not available, transfer to a specialized hospital.

(7) If the patient is bleeding severely or is already seriously anaemic, consider blood transfusion.

(8) Implement simple rehabilitation (exercising of bitten limb).

D. At the referral (specialized) hospital

Proceed as in B and C above in addition to the followings:

(1) More advanced surgical management of local necrosis (e.g. split skin grafting).

(2) More advanced investigations including bacterial cultures and imaging (CT scans) as indicated.

(3) If the patient has evidence of acute renal failure peritoneal or haemodialysis or haemofiltration.

(4) Implement rehabilitation by physiotherapists.

20

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annex 1

Algorithm: Diagnosis of snake-bite cases based on clinical data

Algorithms should be created based on local data so that they can be relevant for local use. The example below is intended for use in Sri Lanka (Ariaratnam et al., 2009).

Clinical spectrum of syndromes of snake-bites, Sri Lanka

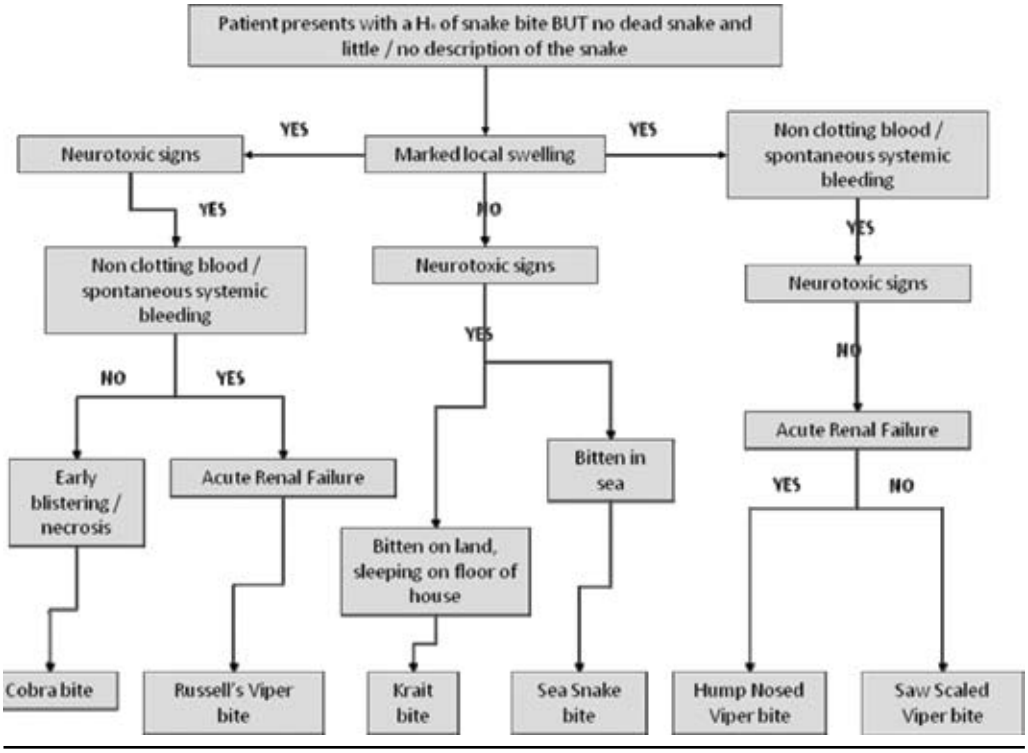
Species	No.	Local effects (%)	Coagulo-pathy (%)	Neurotoxi-city (%)	Renal toxicity (%)	Myotoxicity (%)
Russell's viper	319	96	76	59	19	24
Hump-nosed viper	302	91	39	–	10	–
Common krait	88	9	–	95	–	–
Cobra	45	91	–	80	–	–

Sensitivity and specificity of clinical syndromes as a screening test in identifying snake-bites, Sri Lanka

Snake	Sensitivity (%)	Specificity (%)
Russell's viper	14	100
Cobra	78	96
Common krait	66	100
Hump-nosed viper	10	97

Figure 67: Syndromic approach to snake bite management in Sri Lanka: venomous snakes of Sri Lanka (Ariaratnam et al., 2009)

Figure 68: Algorithm for diagnosis of the snake responsible for a bite in Sri Lanka (Ariaratnam et al., 2009)



annex 2

Antivenoms for treatment of bites by South East Asian snakes

(Listed by country of manufacture) (Theakston and Warrell 1991)

2.1 Production of anti snake venom in countries of South-East Asia Region

A. India

Polyvalent antivenoms raised in equines against venoms of *Bungarus caeruleus*, *Naja naja, Daboia/Vipera russelli, Echis carinatus*

Antivenoms are lyophilised (reconstituted to 10ml per vial) or liquid.

Recommended initial dosage for all these antivenoms is:

Bungarus caeruleus: 10-20 vials

Naja naja: 10-20 vials

Daboia/Vipera russelli: 10 vials

Echis carinatus: 5 vials (10 vials for *E. c. sochureki* in N and NW India)

Note: venoms of other species (e.g. hump-nosed pit-viper *Hypnale hypnale* – South-West India and Sri Lanka) are not covered, nor are venoms by Naja, Daboia or Echis species or other species from outside India.

(i) Bharat Serums & Vaccines, Mumbai (production capacity 600,000 – 800,000 vials/year)

Hoechst House, 16th Floor,
Nariman Point,
Mumbai – 400021.
Maharashtra, India.
Tel. No. : 91-22-66560900
Fax. No. : 91-22-66560901
E-mail : export@bharatserums.com factory@bharatserums.com

ASVS –ASIA SNAKE VENOM ANTISERUM IP

(ii) Biological E (Evans). Limited (production capacity 40,000 vials/year)

18/1&3, Azamabad,
Hyderabad - 500 020,
A.P., India.
Phone 91-40-30213999 , 91-40-27617831 / 27617835 / 27615134
Fax 91-40-27615309 / 27616715 / 27630307
E-mail: info@biologicale.co.in

Anti-Snake Venom (ASVS)

(iii) VINS Bioproducts Ltd. (production capacity 800,000 – 1,100,000 vials/year)

806, Essjay House, Road No.: 3,
Banjara Hills,
Hyderabad - 500 034
Phone: 91-40-23354550, 23353540, 55622962
Fax: 91-40-23350410
email (General): info@vinsbio.in
email (Marketing): vinsbio@gmail.com
Web: www.vinsbio.in

VINS - Snake Venom Antiserum I.P.

B. Indonesia

Perum Bio Farma (Pasteur Institute), Jl Pasteur 28, Post Box 1136, Bandung 40161 (production capacity 40,000 vials/year)

(liquid antivenom, 5 ml/ampoule)

(Tel ++ 6222-83755; Fax ++ 6222-210299; Telex 28432 BIOFAR IA)

Polyvalent antivenom serum *(Calloselasma rhodostoma, B fasciatus, N sputatrix)*

C. Myanmar

Myanmar Pharmaceutical Factory, Yangon (production capacity 52,000 vials/year)

(lyophilized and liquid antivenoms, 10 ml/ampoule)

Viper antivenom *(V. russelli = Daboia siamensis)*

Cobra antivenom (*N. kaouthia*)

Recommended initial dose: 8-10 vials

D. Thailand

The Thai Red Cross Society (production capacity 75,000 – 82,000 vials/ year)

Queen Saovabha Memorial Institute, 1871 Rama VI Road,

Bangkok 10330 (Tel ++ 662-2520161-4; Fax ++ 662-2540212; Telex 82535 THRESCO TH)

(freeze dried monovalent antivenoms, 10 ml/ampoule)

(1) Cobra antivenom (*Naja kaouthia*)
(2) King cobra antivenin (*Ophiophagus hannah*)
(3) Banded krait antivenin (*Bungarus fasciatus*)
(4) Russell's viper antivenin (*Daboia siamensis*)
(5) Malayan pit viper antivenin (*Calloselasma rhodostoma*)
(6) Green pit viper antivenin *(Cryptelytrops – Trimeresurus-albolabris)*
(7) Malayan Krait Antivenin (*Bungarus candidus*)

Neuro polyvalent (raised against 1-3 and 7)

Haemato polyvalent (raised against 4-6)

Recommended initial dose: 5-10 vials

2.2 Antivenoms for treatment of envenoming by snakes in the SEA region that are manufactured outside the region

A. Australia

Commonwealth Serum Laboratories
45 Poplar Rd
Parkville
Victoria 3052
Australia
Phone: +61 3 9389 1911
Fax: +61 3 9389 1434
customerservice@csl.com.au
Phone: +61 39389 1204

Black snake (Pseudechis spp.), brown snake (Pseudonaja spp.), death adder (Acanthophis spp.), polyvalent, sea snake antivenoms.

Recommended initial dose: 1-3 vials

B. China

Shanghai Institute of Biological Products,
Ministry of Health, 1262 Yan An Road (W),
Shanghai 200052, China (Tel ++ 8621-62803189;
Fax ++ 8621-62801807).
Contact: Ms Minzhi Lu, Manager, International Affairs & Trade Department (Tel ++ 8621-62805234)

(liquid antivenoms, 10-15 ml/ampoule)

"*Agkistrodon" acutus* antivenin (purified) (= *Deinagkistrodon acutus*, found in North Viet Nam).

Recommended initial dose: 8,000 IU (= 4 ampoules)

"*Agkistrodon halys*" (= *Gloydius brevicaudus*) antivenin (purified) (said to be active against venoms of *Protobothrops/Trimeresurus mucrosquamatus* and *Viridovipera/Trimeresurus stejnegeri*).

Recommended initial dose: 6,000 IU (= 1 ampoule)

Bungarus multicinctus antivenin (purified) (said to be effective against the venom of *Ophiophagus hannah*).

Recommended initial dose; for bites by both species 10,000 IU (= 1.25 ampoules)

"*Naja naja*" antivenom (purified) (= *Naja atra*).

Recommended initial dose: 2,000 IU (= 2 ampoules)

C. Iran

State Serum & Vaccine Institute, Razi Hessarek, bP 656, Teheran

(liquid antivenoms, 10 ml/ampoule)

(Tel ++ 98 2221 2005)

Polyvalent snake antivenom (equine) (said to neutralise the venoms of two South East Asian species – *Naja oxiana* and *Echis carinatus* (probably *E sochureki*), *Vipera lebetina* (= *Macrovipera lebetina*) and *Pseudocerastes persicus*

Recommended initial dose: ?

D. Japan

Japan Snake Institute
Nihon Hebizoku Gakujutsu Kenkyujo

3318 Yunoiri Yabuzuka
Yabuzukahonmachi Nittagun Gunmaken 379-2301
Tel 0277 785193 Fax 0277 785520
Snake-c@sunfield.ne.jp
www.sunfield.ne.jp/~snake-c/

Yamakagashi (*Rhabdophis tigrinus*) antivenom (also effective against red-necked keelback *R. subminiatus* venom)

E. Pakistan

National Institute of Health, Biological Production Division, Islamabad (Tel ++ 9251-240946; Fax ++ 9251-20797; Telex 5811-NAIB-PK)

Dr. Birjees Mazher Kazi, Executive Director National Institute of Health, Islamabad
Tel: (051) 9255117
Fax: (051) 9255099, 9255125
Email: edoffice@isb.apollo.net.pk webmaster@nih.org.pk
Contact: Shahid Akhtar

(liquid and lyophilized antivenoms, 10 ml/ampoule)

Polyvalent anti-snake venom serum (*B. caeruleus, E. carinatus, N. naja, V. lebetina (=Macrovipera lebetina), V. russelli (= Daboia russelii*)

Recommended initial dose: 5 vials for *Echis carinatus*, 10 vials for other species.

F. Taiwan

National Institute of Preventive Medicine, 161 Kun-Yang Street, Nan-Kang, Taipei, ROC 11513 (Tel ++ 8862-7859215; Fax ++ 8862-7853944).
Contact: Dr Gong-Ren Wang, Director

(lyophilised antivenoms, 10 ml/ampoule)

Bungarus multicinctus and *N atra* bivalent antivenom

Trimeresurus mucrosquamatus (= Protobothrops mucrosquamatus) and *Trimeresurus grammineus* (= *Viridovipera stejnegeri*) bivalent antivenom

Recommended initial dose: 5 vials

Agkistrodon acutus (= *Deinagkistrodon acutus*) antivenom

Recommended initial dose: ?

annex 3

Pressure-immobilisation and pressure pad

Bites by cobras, king cobras, kraits, Australasian elapids or sea snakes may lead, on rare occasions, to the rapid development of life-threatening respiratory paralysis. This paralysis might be delayed by slowing down the absorption of venom from the site of the bite. The following techniques are currently recommended:

Pressure-immobilisation method*

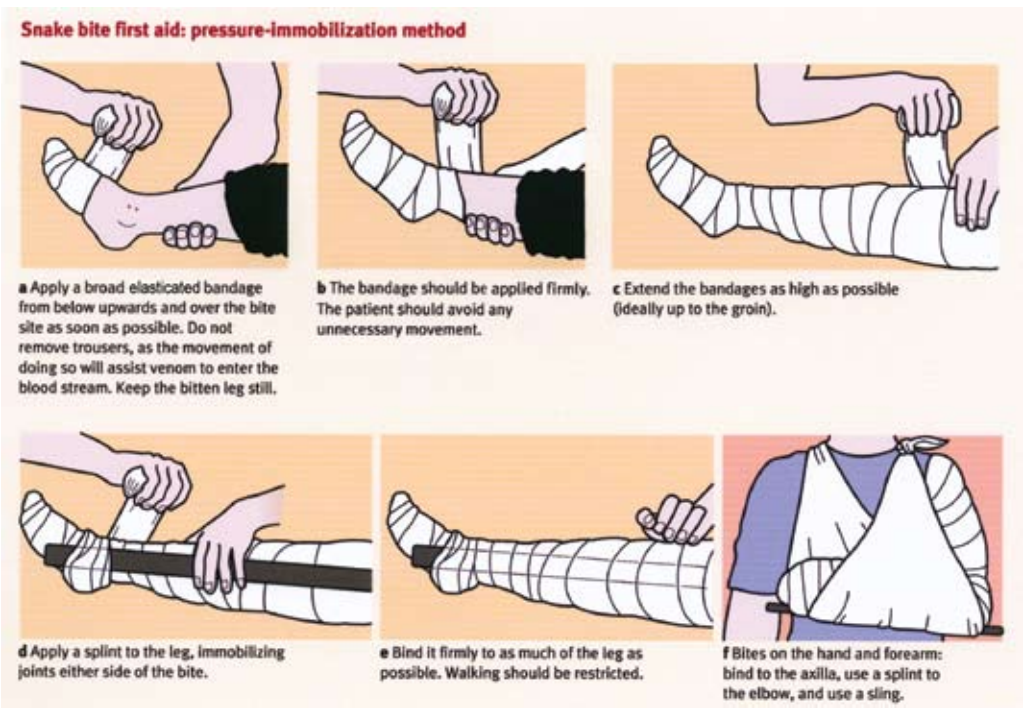
Ideally, an elasticated bandage, approximately 10 – 15 cm wide and at least 4.5 metres long should be used (Canale et al., 2009). If that it not available, any long strips of material can be used. The bandage is bound firmly around the entire bitten limb, starting distally around the fingers or toes and moving proximally, to include a rigid splint (Fig. 69). The bandage is bound firmly (at a pressure of 50-70 mmHg), but not so tightly that the peripheral pulse (radial, posterior tibial, dorsalis pedis) is occluded or that the patient develops severe (ischaemic) pain in the limb.

Pressure pad**

A rubber and/or folded material pad approximately 5 cm square and 2-3 cm thick is placed directly over the bite site anywhere on the body and bound in place with a non-elastic bandage at a pressure of at least 70 mmHg.

* Sutherland et al., 1979
** Anker et al., 1982; Tun-Pe et al., 1995

Figure 69: Pressure immobilisation method. Recommended first-aid for bites by neurotoxic elapid snakes (by courtesy of the Australian Venom Research Unit, University of Melbourne)



annex 4

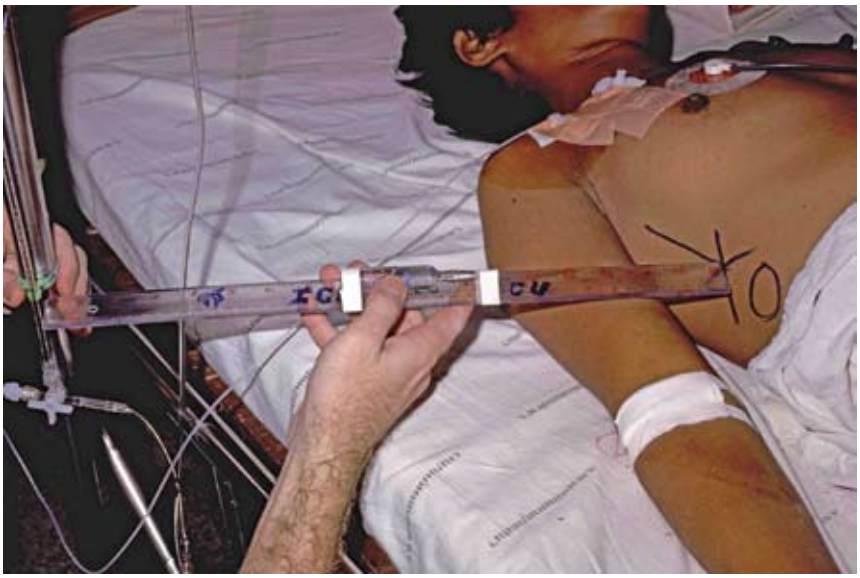
Measurement of central venous pressure

In seriously ill patients with shock or renal failure in whom clinical assessment of the jugular venous pressure is difficult or considered inaccurate, a central venous catheter should be inserted percutaneously. In those with no haemostatic problems, a catheter may be inserted into the jugular or subclavian vein provided adequate facilities for a sterile procedure and subsequent nursing are available. However, patients who have been bitten by vipers may have obvious haemostatic problems or may develop coagulopathy. In these cases, the antecubital approach is by far the safest as haemostasis can be achieved by local pressure. A long catheter (at least 50-70 cm for an adult) is required (Fig. 70a). The catheter is connected via a three-way tap and pressure tubing to a manometer. The whole system is filled with sterile isotonic saline. Before readings can be taken, the zero on the manometer must be aligned as accurately as possible with the horizontal plane of the left atrium. A simple spiritlevel (e.g. a 20 ml glass ampoule with bubble, taped to a ruler) can be used to locate the manometer zero at the same height as an appropriate chest-wall landmark, such as the midaxillary line, in the supine patient (Fig. 70b) or the sternal angle in a patient sitting up at 45º.

There should be strict attention to asepsis. Infection and thrombosis are potential complications; especially if the catheter remains in place for a long time.

Figure 70a: Central venous pressure monitoring in a patient with shock after Russell's viper bite, in a township hospital in rural Myanmar. A 70 cm long catheter was inserted into an antecubital vein (Seldinger percutaneous guidewire technique) and advanced until its tip was in the superior vena cava. An extension tube connects with a simple saline manometer whose zero point is at the level of the mid-axillary line (Copyright DA Warrell)

Figure 70b: Adjusting the zero point of the central venous pressure manometer to the midaxillary line, using a home-made ruler-plus-glass-ampoule "spirit level" (Copyright DA Warrell)



annex 5

Measurement of intracompartmental pressure in tensely swollen snake-bitten limbs

To confirm a clinical suspicion of intracompartmental syndrome [see 5.8 (2)] the pressure inside the particular compartment should be measured directly (Matsen 1980; Mars and Hadley 1998; Mars et al., 1991).

The threshold pressure required to initiate the flow of liquid into the fascial compartment is a measure of the tissue pressure inside that compartment. With full sterile precautions and after infiltrating local anaesthetic, a 21 or 22 gauge cannula, approximately 3-4 cm long, is inserted into the compartment through or around an introducing 20 or 21 gauge needle. The cannula is connected through narrow pressure tubing to a syringe or low speed infusion pump. Through a three-way tap, the system is connected, through a side arm to a blood pressure transducer or saline or mercury manometer (Fig. 71a). The system is filled with sterile isotonic saline. If a syringe-type infusion pump and arterial blood pressure transducer with monitor is used, the pressure can be measured continuously at a very slow rate of infusion (e.g. 0.7 ml/day). If a saline or mercury manometer is used, a much higher rate of infusion is required to initiate flow into the compartment. These systems are not suitable for continuous intracompartmental pressure monitoring.

Alternatively, the simple but expensive Stryker pressure monitor can be used (Fig. 71b). Whatever system is employed, the zero point in the pressure measuring device must be aligned to the level at which the cannula enters the fascial compartment.

Figure 71a: Infusion pump, saline manometer system in use for measuring the tissue pressure inside the anterior tibial compartment (Copyright DA Warrell)

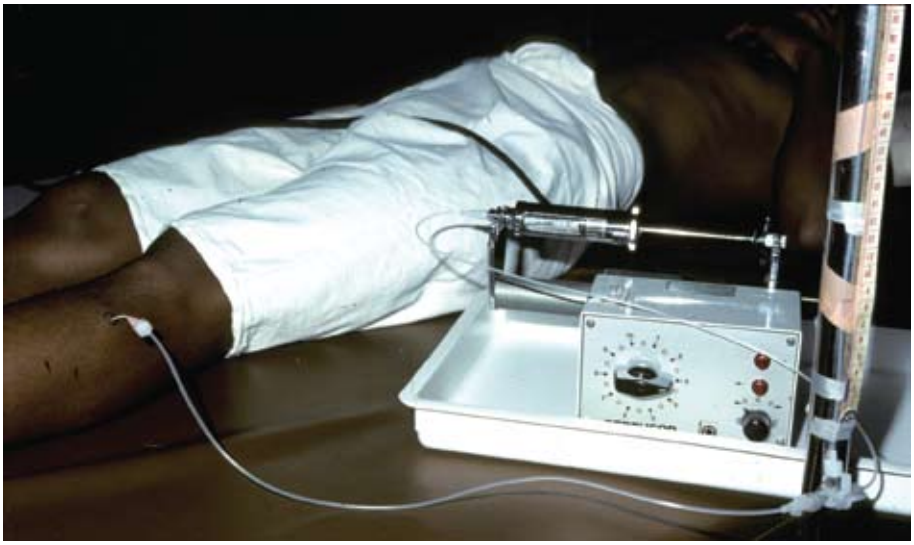
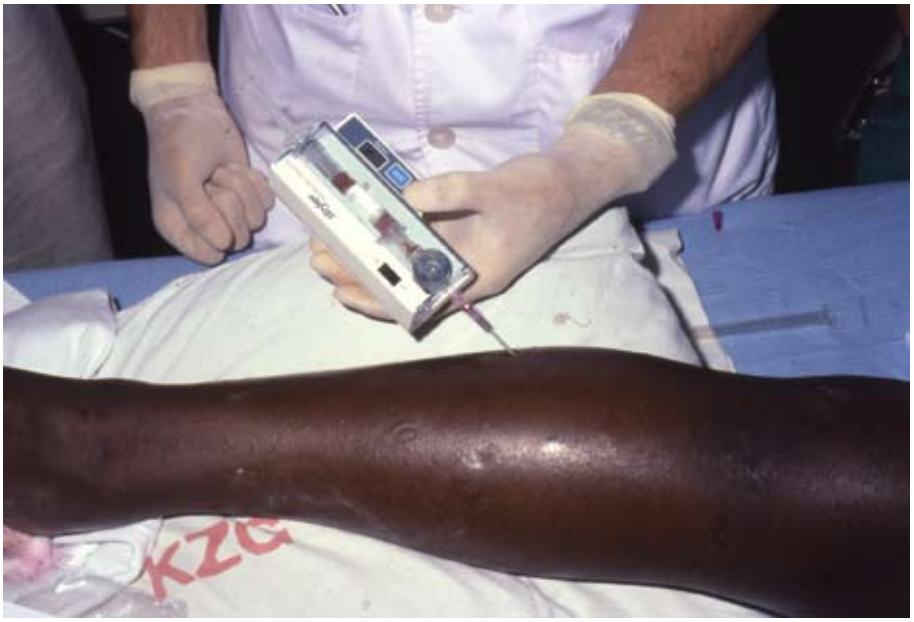


Figure 71b: Stryker pressure monitor in use for measurement of intracompartmental pressure (Copyright DA Warrell)



annex 6

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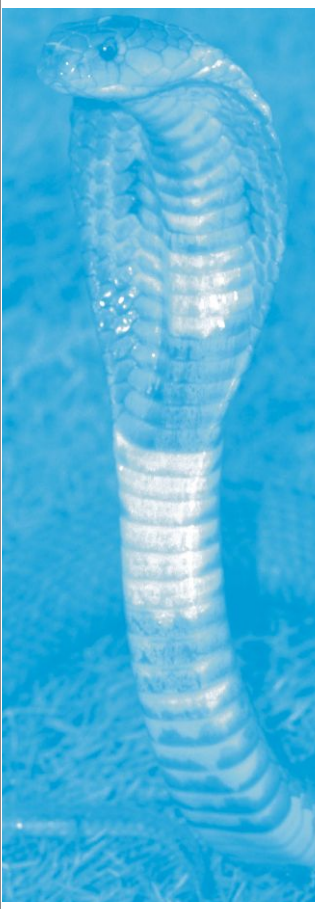

Snake-bites are well-known medical emergencies in many parts of the world, especially in rural areas. Agricultural workers and children are the most affected. The incidence of snake-bite mortality is particularly high in South-East Asia. Rational use of snake anti-venom can substantially reduce mortality and morbidity due to snake bites. These Guidelines are a revised and updated version of similar guidelines published by the WHO Regional Office in South-East Asia in 1999. These guidelines aim to promote the rational management of snake-bite cases in various health facilities where trained health functionaries and quality snake antivenom are available.

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