

# **Standard Treatment Guidelines**

## **Snakebite**

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**Directorate General of Health Services  
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## Contents

1. THE NEED FOR STGs .....	5
Snakebite is a neglected Tropical disease .....	5
Antivenoms are essential medicines .....	6
<b>Determinants of snakebite incidence and severity of envenoming</b> .....	6
Existing variation in management of snakebite .....	7
<b>Classification of medically important species</b> .....	8
Sources of information on snakes .....	9
<b>2. THE PURPOSE OF THE STG</b> .....	9
3. DECLARATION OF INTEREST .....	10
4. THE FUNDING SOURCE .....	10
5. THE SCHEDULED REVIEW .....	10
6. SCOPE OF THE STG .....	10
7. LIST OF ALL RECOMMENDATIONS .....	11
8. METHODOLOGY .....	14
How the relevant guideline(s) were selected as source of recommendation .....	16
How recommendations were selected, adopted or adapted .....	18
9. STAGES OF MANAGEMENT .....	26
10. FIRST AID TREATMENT GUIDELINES .....	26
First aid: Bystanders/victim .....	26
At the community or village level (Warrell 2010) .....	27
At the PHC level .....	28
Important don'ts .....	29
Traditional methods to be discarded/ inappropriate methods .....	29
Tight Tourniquets .....	29
Pressure –immobilization .....	31
Cutting and Suction .....	32
Electrical Therapy and Cryotherapy .....	32
Traditional Remedies .....	32
Role of Snake Stones and Scarification .....	33
11. TRANSPORT TO HOSPITAL .....	33
<b>12. RECOMMENDATIONS</b> .....	34
<b>Clinical features of snakebite</b> .....	34
Treatment in the dispensary or hospital .....	34
At a health care facility .....	36
Asymptomatic (i.e., Non Venom Related Symptoms) .....	37
Dry Bite .....	37
Symptomatic Patients .....	37
Neuroparalytic (Progressive weakness; Elapid envenomation) .....	37
Vasculotoxic (Haemotoxic or Bleeding) .....	39
Locked-in syndrome (LIS) .....	40
Life threatening complications .....	40

Systemic capillary leak syndrome .....	40
Painful Progressive Swelling (PPS) .....	41
Myotoxic.....	42
Occult Snakebite .....	42
<b>Differential identification of type of snakebite based on the symptoms and signs .....</b>	<b>43</b>
CRITICAL ARRIVAL .....	44
Patient assessment: Non critical arrival and Critical patients after stabilization .....	46
Handling Tourniquets.....	47
Physical examination .....	47
<i>Examination of pregnant women</i> .....	49
Diagnosis Phase: Investigations.....	49
20 Minute Whole Blood Clotting Test (20WBCT) .....	49
Late-onset envenoming .....	52
13. ANTI SNAKE VENOM (ASV) .....	52
Monovalent vs. Polyvalent.....	53
ASV dosage forms .....	54
ASV administration .....	54
ASV Dosage.....	55
ASV dosage in victims requiring life saving surgery .....	56
What can ASV Do and more importantly what can it NOT Do? .....	57
Swelling and ASV.....	58
Monitoring of Patients on ASV therapy .....	58
Victims who arrive late .....	59
ASV and Pregnancy .....	59
ASV in Paediatric victims .....	60
ASV in Repeat bites.....	60
<b>ASV REPEAT DOSE .....</b>	<b>61</b>
Adverse Anti Snake Venom Reactions .....	61
Mechanism of the Reaction .....	62
Prediction of Adverse Reactions.....	62
Preventing Adverse Reactions.....	63
Treatment of Adverse Reactions .....	64
Contraindications to antivenom & Prophylaxis of high risk patients.....	65
Observation of the response to ASV.....	67
ASV in Recurrence of systemic envenoming .....	68
14. NEUROTOXIC ENVENOMATION .....	69
Airway Support Items .....	71
Bridging Devices.....	72
The Ideal Solution .....	72
15. HAEMOTOXIC ENVENOMATION, BLOOD PRODUCTS AND RENAL IMPAIRMENT .....	73
Persistent or Severe bleeding.....	74
Role of Anticoagulants .....	74
Dangers of venipuncture in patients with haemostatic abnormalities .....	74
Renal Failure .....	75

16.	PAIN, WOUND MANAGEMENT AND THE SURGICAL ASPECTS OF SNAKEBITE.....	78
	Pain and Wound Management .....	78
	Antibiotics and Tetanus .....	78
17.	SNAKE VENOM OPHTHALMIA .....	79
	Surgery and Snakebite .....	79
	Life Threatening Conditions Requiring Surgery.....	80
	Debridement of Necrotic Tissue.....	80
18.	COMPARTMENT SYNDROME .....	80
19.	DISCHARGE & FOLLOW-UP .....	82
	Follow-up.....	82
20.	REHABILITATION .....	83
21.	SNAKEBITE MANAGEMENT AT DIFFERENT LEVELS OF HEALTHCARE .....	83
	A. In basic or primary care facilities (PCF).....	83
	B. At a Primary health Care Center (PHC) .....	85
	C. At the district hospital.....	87
	D. At the tertiary care or medical college .....	88
22.	CONDITIONS AND EQUIPMENT ACCOMPANYING NEUROTOXIC REFERRAL .....	89
23.	EQUIPPING A BASIC HOSPITAL FOR EFFECTIVE SNAKEBITE MANAGEMENT .....	89
	Holding Quantities of ASV/ Stocks of ASV .....	90
24.	SNAKEBITE PREVENTION & OCCUPATIONAL RISK.....	91
25.	PATIENT INFORMATION SHEET .....	91
	ANNEXURE 1. SNAKE BITE EXAMINATION PERFORMA .....	95
	REFERENCES .....	97

## 1. THE NEED FOR STGs

Snakebite is an acute life threatening time limiting medical emergency (Kulkarni & Anees, 1994). It is a preventable public health hazard often faced by rural population in tropical and subtropical countries with heavy rainfall and humid climate (Warell DA 1992).

The numbers of snakebite fatalities in India has long been controversial. There is a huge gap between the number of snakebite deaths reported from direct survey and official data. Only 7.23% snakebite deaths were officially reported (Majumdar et al, 2014; Mohapatra et al, 2011). Earlier hospital based reports estimated about 1,300 to 50,000 annual deaths from snakebites per year in India. The registrar General of India's Million Death Study 2001-2003 conducted to ascertain the cause of death based on interviews by medical personnel and social workers in over a million households in randomly selected locations around India. The Million Deaths Study reported 46,000 deaths by snakebite in India per year; non-fatal bites may be as high as 1.4 million per year (Mohapatra et al, 2011). This proportion represents about 45,900 annual snakebite deaths nationally or an annual age-standardized rate of 4.1/100,000, with higher rates in rural areas (5.4) and with the highest rate in the state of Andhra Pradesh (6.2). Annual snakebite deaths were greatest in the states of Uttar Pradesh (8,700), Andhra Pradesh (5,200), and Bihar (4,500). Other Indian states with high incidence of snakebites cases are Tamil Nadu, West Bengal, Maharashtra and Kerala (Hati et al, 1992; Gaitonde et al, 2008). Because a large proportion of global totals of snakebites arise from India, global snakebite totals might also be underestimated. (Mohapatra et al, 2011).

In a retrospective study conducted in one district of West Bengal only 22.19% of the snakebite victims attended the hospitals (Majumder et al, 2014). This is because even today most of the victims initially approach traditional healers for treatment and many are not even registered in the hospital. Singh et al reported among the snakebite victims, about 60.76% received first aid at the site of incident, and 20.25% of them sought hospital care after consulting the traditional healers (ozhas, or mantrik and tandrik). Time lapsed for seeking hospital treatment was less than 4 h in 55.69% of the cases and more than 12 h in 7.59% of the cases. Most (41.79%) patients were frightened, but no local or systemic symptoms had appeared when they reported the emergency (Singh A et al 2015).

Although total number of bites may be more than 5-6 lakhs but only 30% are venomous bites.

### **Snakebite is a neglected Tropical disease**

Though snakebite is a life threatening centuries old condition, it was included in the list of neglected tropical diseases by World Health Organization in the year 2009 (Warrell and WHO 2009; Bawaskar HS, 2014). Since snakebite is an environmental, occupational and climatic hazard and mostly affect farmers, plantation workers, herdsmen, fishermen, snake restaurant workers and other food

producers, resulting in tens of thousands of deaths each year and chronic physical handicap in many cases (WHO, 2007; Williams, 2010; Warrell et al, 2013; Gutierrez et al 2013; Bawaskar 2014).

### **Antivenoms are essential medicines**

The only specific antidotes to snake venoms are immunoglobulin antivenoms (Warrell, 2010) and are recognized as Essential medicines (19.2 Sera and immunoglobulins WHO Essential Medicines List) and should be included as Essential Medicines in the national and state Essential Medicines Lists

### **Determinants of snakebite incidence and severity of envenoming**

The incidence of snakebites depends critically on the frequency of the contact between snakes and humans. Two seasonal peaks of snakebite incidence usually coincide with increases in agricultural activity or seasonal rains. Epidemic of snake bite may occur from heavy floods or water logging or when the snakes' habitat is invaded by a large workforce involved in road building. Bites may be inflicted in the home by peridomestic species such as Cobra which may live in roof spaces or under the floor and by Kraits which enter human dwellings at night in search of their prey and may bite people who move in their sleep.

Most snake bites occur in rural areas, and more commonly among males than females except where the work force is predominantly female – tea and coffee picking and peaking at ages 15–29.

The risk of envenoming after bites by venomous snakes varies with the species but is on average only around 50%. Many bites are dry bites i.e., fangs though pierce the skin but no envenoming results due to either mechanical inefficiency of the venom apparatus striking at an angle or through clothing or voluntary retention of venom by the snake.

Morbidity and mortality depends on the age and size of victim (children receive larger envenomation relative to body size) as well as comorbid conditions such as elderly patients, anaemia, hypertension, diabetes mellitus and renal disease succumb more easily to snake venom (Alirol et al, 2010). In pregnant women, snakebite carries definite but unquantified risks to mother and foetus, mainly from bleeding and abortion (WHO 2015). Other factors affecting severity and outcome are listed in Table 1. Factors not contributing to outcome are size of the snake and time of bite (day/night) (Warrell, 1999)

Table 1. Factors contributing to severity and outcome in snakebite

<b>Factor</b>	<b>Effect on outcome</b>
Exercise	Exertion following snakebite has poor outcome due to enhanced systemic absorption of toxin

Factor	Effect on outcome
Individual sensitivity	Sensitivity of individual to venom (atopy or previous sensitization) modifies the clinical picture
Bite characteristics	Bite number; depth of bite; dry bite; bite through clothes, shoes, or other protection; amount of venom injected; condition of fangs; fed / hungry snake and duration for which snake clings to the victim, all affect outcome
Snake species	Different species have different lethal dose, lethal period, and aggressiveness
Secondary infection	Presence or absence of pathogenic organisms in the mouth of the snake
Treatment	Nature of first aid given and time elapsed before first dose of antivenom. Factors not contributing to outcome are size of the snake and time of bite (day/night).

Do NOT ignore or dismiss bites by small snakes. They should be taken just as seriously as bites by large snakes of the same species (WHO, 2015). Venom of smaller, younger vipers may be richer in some dangerous components such as those affecting hemostasis because of venom composition varies ontogenically with the snake's age and size (Tun-Pe et al, 1995a).

### Existing variation in management of snakebite

Currently, treatment quality is highly varied, ranging from good quality in some areas, to very poor quality treatment in others. Cobra bite leads to early death hence reported less in hospital statistics as victim may not reach medical facility. The high fatality due to Krait bite is attributed to the non-availability of antislake venom (ASV), delayed and inappropriate administration of ASV, lack of standard protocol for management and inexperienced doctors and non-availability of ventilator or bag and valve (Bawaskar et al, 2008). In India, there has always been a crisis of antivenom supply (Bawaskar et al, 2001) and non –availability of effective antivenom, poor potency, poor safety and the absence of published preclinical or well-designed clinical trial data for Indian antivenoms are other concerns. On one hand there is shortage of ASV but on the other hand scarce ASV is being wasted due to excessive dosage of ASV in the absence of a Standard Treatment Guideline. Victims are not only misdiagnosed as - abdominal colic, and vomiting due to indigestion, appendicitis, stroke, head injury, ischemic heart disease, food poisoning, trismus, hysteria and Guillain-Barre' syndrome but also subjected to unnecessary investigations including MRI scans of the brain and lumbar puncture thus causing undue delay in ASV therapy. Delayed administration of ASV or waiting until victim develops systemic manifestations i.e., a 6 h wait results in systemic envenoming and high fatality (Bawaskar et al, 2008).

Moreover chance of snakebite death being missed are more than for deaths occurring from several other causes. Thus recorded figures of snakebite deaths be regarded as under-estimates of the total fatality from this cause. Majority of the snakebites treatment has remained with the traditional, herbal or ayurvedic practitioners and thus majority of snakebite victims are not seen or recorded in the hospitals and dispensaries (Sharma et al 2004; Sharma et al 2005.).

The continuing inadequacies in the reporting of snakebite incidence, morbidity and mortality prompts the following recommendation (WHO 2015):

**Snakebite should be made a notifiable disease and death certification should use the specific International Classification of Disease Code 9 ICD code) T63.0 (Toxic effect of contact with venomous animals- snake venom and sea snake venom (ICD-10 version 2015**  
**<http://apps.who.int/classifications/icd10/browse/2015/en#/T63.0>**

### **Classification of medically important species**

The three major families of venomous snakes are the Elapidae, the Viperidae, and the Colubridae Hydrophiinae (Warrell, 2010).

**Elapidae (cobra, king cobra, krait, and coral snake):** These snakes have heads that are of about the same width as their necks. The head is covered with large scales but lack loreal shields. Their pupils are round and they are oviparous. These snakes have grooved fangs that are short, fixed, and covered by mucous membrane. 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.

**Viperidae (vipers):** The head of a viper is triangular, wider than the neck, and has loreal shields. They have vertically elliptical pupils and are ovi-viviparous. Their fangs are long, movable, and canalized like hypodermic needles. They are further subdivided into pit viper and pitless viper subfamilies. The Crotalinae (pit vipers) have a special sense organ, the pit organ, to detect their warm-blooded prey. This is situated between the nostril and the eye. 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.

**Hydrophiinae (sea snake):**

Sea snakes are found in the vicinity of the seacoast. They have a small head and a flattened tail that helps them swim. Though venomous, they seldom bite.

There are more than 2000 species of snakes in the world. About 300 species are found in India out of which 52 are venomous. and of these four “the Big Four”, namely common cobra (*Naja naja*), Russell’s viper (*Daboia russelii*), saw-scaled viper (*Echis carinatus*) and common krait (*Bungarus caeruleus*) are highly venomous and believed to be responsible for most of the venomous bites in



India (Warrell DA., 1999; Alirol et al, 2010). However, this assumption of great four, has led to non-identification of other venomous species which are going unnoticed and leading to deaths (Simpson 2007). But other species have now been proved important in particular areas, such as *Naja oxian* (North), *N. Kaouthi* (east), *Hypnale hypnale* (south-west coast and Western Ghats (Joseph et al, 2007), *Echis carinatus sochureki* (Rajasthan) (Kochar et al, 2007) and *Trimeresurus (Craspedocephalus) malabaricus* (Hassan District, Mysore). The recent discovery of the hump nosed pit viper, capable of causing life threatening symptoms has demonstrated this (Parikh 1996). This non-recognition has led the ASV manufacturers to produce antivenom only against these four species only (Simpson ID et al , 2007) Thus there is a need to abandon the old concept of “The Big Four” in order to determine all the medically significant species in India.

### Sources of information on snakes

There are many sources of information on the web on snakes inhabiting Indian continent, such as **World Health Organization** [WHO Venomous snakes and antivenoms search interface](http://apps.who.int/bloodproducts/snakeantivenoms/database/snakeframeset.html) : <http://apps.who.int/bloodproducts/snakeantivenoms/database/snakeframeset.html>:

**Indian Herpetological Society** <http://www.indianherps.org/>

Clinical effects of envenoming by same species of snake are almost similar except a few regional variations. Kraits are active during night hours, often biting a person sleeping on floor bed. Maximum Viper and Cobra bites occur during the day or early darkness, while watering the plantation or walking bare foot in grown grass or soybean crops.

### Snakes of Medical Significance

Indian venomous snakes of medical significance have usually been regarded as only four species: Russell’s Viper, Saw Scaled Viper, Cobra and Krait. These species were believed to be causing all fatalities in India. However this concept has led to some serious problems:

1. ASV Manufacturers only produce antivenom against these species
2. The assumption that only ‘The ‘Big 4’ can cause serious symptoms and death has led to mis-identification of species.
3. Other deadly snakes may be going un-noticed and causing death and disability! The recent discovery of the Hump-nosed Pitviper as a species capable of causing life threatening symptoms has demonstrated this.

In order to determine the actual list of medically significant species in India, the old concept of ‘The Big Four’ is to be abandoned for a newer more flexible model that enables better classification of species.

## 2. THE PURPOSE OF THE STG

The guidelines are comprehensive covering first aid, transport to a health facility, initial assessment, diagnosis and management and are targeted at doctors, health officials (nurses, dispensers and community health workers) and first aid providers involved in dealing with snakebite victims. The guidelines aim to provide sufficient practical information to allow medically trained personnel to assess and treat patients with snakebites at different levels beginning with first aid, to management at primary health care to tertiary care and referral centres.

### **3. DECLARATION OF INTEREST**

None

### **4. THE FUNDING SOURCE**

The development of the guidelines was supported from Ministry of Health & family Welfare through National Health System Resource Centre (NHSRC) in technical collaboration with National Institute of Health and Care Excellence (NICE) International.

### **5. THE SCHEDULED REVIEW**

The review is scheduled after 2 years or earlier in case of any break through advance in therapy or level of evidence for major recommendations

### **6. SCOPE OF THE STG**

The guidelines covers all clinical issues and aspects of management of snakebite including clinical features, community interventions measures (first aid, transport and referral criteria), snakebite diagnostic features, treatment with and with antsnake venom, snakebite complications and snakebite management in primary, community health care centres up to tertiary care. These guidelines provide brief guidance about follow-up and rehabilitation of the snakebite victims. The guidelines also cover all populations and age groups including pregnant women. Though community education on snakebite is outside the terms of reference of this guideline but prevention of snakebite is an essential component of any community education programme it is covered as part of the patient education leaflet.

These guidelines do not cover detailed management of complications of snakebite such as hypotension, shock, dissemination intravascular coagulopathy, acute kidney injury, detailed ICU care as well as management of chronic complications of snakebite due to restrictions on the length of this document.

## 7. LIST OF ALL RECOMMENDATIONS

### 1. First aid and transport

- i. Quick transport to Hospital in an ambulance equipped with transport ventilator. Situational adaptation; Ambulance with Transport ventilators are ideal, but very rarely available in Rural India, Recommendation may DELAY transfer to Base Hospital. The patient must be quickly transported to a place where they can receive medical care (dispensary or hospital) as quickly, but as safely, passively 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. Motorbike is a practical alternative especially in rural areas for rapid transport but third person must sit behind the patient to support on bike.
- ii. If ASV available must be administered in appropriate dose before shifting victim to higher centre.
- iii. Immobilization of the bitten limb with situational adaptation in case splint for immobilization is not available use bandages or cloth to hold the splints (wooden stick), but do NOT block the blood supply or apply pressure.
- iv. Tight (arterial) Tourniquets should NOT be used for snakebite first aid as it may cause gangrenous limbs. Situational adaptation
- v. Pressure immobilization (Sutherland method) modified in case victim is expected to reach the hospital in more than 30 minutes but less than 3 hours crepe bandage may be applied by qualified medical personnel only till the patient is shifted to the hospital. The bandage is wrapped over the bitten area as well as the entire limb with the limb placed in a splint. It should be capable of admitting a finger beneath it. If trained personnel is not present, Must not be tried)
- vi. Release of tight bands, bandages and ligatures: In case of venomous envenomation, tourniquet/light band, bandages/ligatures should be removed only after patient has reached the hospital, medical staff and resuscitation facilities are available and antsnake venom has been started in the presence of the doctor by the bedside of the patient and keep Atropine Neostigmine injection ready.
- vii. If envenomation is confirmed on local examination and bite is non-venomous tourniquet, if any can be removed after establishing IV line. In case of multiple ligatures, all the ligatures can be released in Emergency Room with doctor on the bed side of the patient EXCEPT the most proximal one; which should only be released after admission and all preparations for resuscitation facilities are available and antivenom treatment has been started. Expert consensus -
- viii. Avoid any interference with the bite wound (incision, rubbing, vigorous cleaning, massage, application of herbs or chemicals)
- ix. Electrical therapy has no role in snakebite first aid and cryotherapy may do more harm
- x. No role of black stones and scarification No role of Traditional Remedies
- xi. No role of local ASV

### 2. Diagnosis of snake bite

- i. 20 WBCT Added Accepting that the 20WBCT may remain negative (clotting) in patients with evolving venom-induced DIC, the test should be repeated frequently and antivenom

treatment should not be delayed if there is other evidence of anti-haemostatic disturbances (e.g., spontaneous systemic bleeding distant from the bite site. Added-frequency of 20 WBCT specified. If clotted, the test should be carried out every 1 h from admission for three hours and then 6 hourly for 24 hours. In case test is non-clotting, repeat 6 hour after administration of loading dose of ASV

- ii. In case where the 20WBCT result is inconsistent with the patients' clinical condition, normal control blood is used for comparison.

### 3. Management of snakebite

- i. **Resuscitation: Adapted** as per American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care 2015: **CABDE approach**
  - ii. **Removal of tourniquet-** If envenomation is confirmed on local examination and bite is non-venomous, tourniquet, if any can be removed after establishing IV line in the presence of the doctor. In case of multiple ligatures, all the ligatures can be released in Emergency Room EXCEPT the most proximal one; which should only be released after admission and all preparations.
  - iii. **Antivenom treatment** should not be delayed if there is other evidence of spontaneous systemic bleeding distant from the bite site. In case test is non-clotting, repeat 6 hour after administration of loading dose of ASV. In case of neurotoxic envenomation repeat clotting test after 6 hours. Expert Consensus in case with a history of Bite; known or unknown, if there is spontaneous abnormal bleeding beyond 20 minutes from time of bite, ASV is to be started, do NOT wait for 20 WBCT report.
  - iv. **REPEAT dose of ASV** should also be given if abnormal bleeding does not stop one hour after completion of 1<sup>st</sup> 10 vials.
  - v. **A trial of anticholinesterase ("AN 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.
  - vi. Added criteria for continuing or stopping Stop Atropine Neostigmine (AN) dosage schedule if:
  - vii. Patient has complete recovery from neuromuscular paralysis. Rarely patient can have recurrence, carefully watch patients for recurrence.
  - viii. Patient shows side effects in the form of fasciculations or bradycardia.
  - ix. If there is no improvement after 3 doses.
  - x. No response to 3 doses of AN test Adapted In case of no improvement after 3 doses of atropine neostigmine, indicating probable Krait bite. Krait affects pre-synaptic fibres where calcium ion acts as neurotransmitter. Give Inj. Calcium gluconate 10ml IV (in children 1-2 ml/kg (1:1 dilution) slowly over 5-10 min every 6 hourly and continue till neuromuscular paralysis recovers which may last for 5-7 days.
4. **Differential identification of type of snakebite based on the symptoms and signs** Identification of the type of snake should not hold the treatment though to a large extent the manifestation of snakebite depends upon the species of snake. Take One smart phone photograph of the snake, dead or alive, if available, for confirmation by an expert.
5. **Routine use of ASV to any patient** claiming to have bitten by a snake should be strongly discouraged as they expose patients who may not need treatment to the risks of antivenom reactions. Adopted and added the patient may have reaction to any horse serum preparation

like antirabies immunoglobulin sensitizing patient to any future use of Horse serum product; they also waste valuable and scarce stocks of antivenom.

6. For vasculotoxic snakebite - Two regimens low dose infusion therapy and high dose intermittent bolus therapy can be used. Adopted Low dose infusion therapy is as effective as high dose intermittent bolus therapy and also saves scarce ASV doses.

#### 7. ASV Therapy and maximum dose of ASV

- i. Max dose of ASV for neuromuscular snakebite – ASV 10 vials stat as infusion over 30 minutes followed by 2<sup>nd</sup> dose of 10 vials if no improvement within 1<sup>st</sup> hour. Repeat 2<sup>nd</sup> dose even after 2-3 hours; if relapse of signs of Neurotoxicity is noted; may be due to delayed absorption). Expert consensus.
- ii. In vasculotoxic envenomation - Envenomation by the Hump-nosed Pit viper does not respond to normal Indian polyvalent ASV and coagulopathy may continue for up to 3 weeks. If 30 vials of ASV have been administered reconsider whether continued administration of ASV is serving any purpose, particularly in the absence of proven systemic bleeding. If large doses have been administered and the coagulation abnormality persists, give fresh frozen plasma (FFP) or cryoprecipitate (fibrinogen, factor VIII), fresh whole blood, if FFP not available

8. **Criteria for repeat dose of ASV-** Persistence or recurrence of blood coagulability after 6 h or of bleeding after 1-2 h and deteriorating neurotoxic or cardiovascular signs after 1-2 hours.

9. **Dose in children and pregnancy** Snakes inject the same dose of venom into children and adults. Children and pregnant women must therefore be given exactly the same dose of antivenom as adults.

#### 10. Skin and conjunctival “hypersensitivity” tests should not be used.

11. **Routine use of prophylactic adrenaline** is recommended before ASV, except in known hypertensive, and if patient presents with blood pressure more than 140/90 in adult victims or if evidence of suspicion of underlying cardiovascular disease. The adult dose of adrenaline (epinephrine) is 0.25 mg of 0.1% solution by subcutaneous injection (Children 0.005 mg/kg body weight of 0.1% solution).

- i. Use of histamine, anti-H1 and anti-H2 blockers, corticosteroids and the rate of intravenous infusion of antivenom between 10 and 120 minutes), do not affect the incidence or severity of early antivenom reactions.
- ii. 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.

#### 12. Severe Hypersensitivity reaction to ASV For high risk patients

- i. In patients with history of hypersensitivity or exposure to animal serum such as equine ASV, tetanus-immune globulin or rabies-immune globulin in past, severe atopic conditions:
- ii. Give ASV only if they have signs of systemic envenoming.
- iii. Subcutaneous epinephrine (adrenaline) 0.25 mg of 0.1% solution to be given just before antivenom treatment is started

- iv. Give Inj. Hydrocortisone 200 mg and Chlorpheniramine maleate 22.75 mg prior to the administration of ASV.

### 13. No Role of anticoagulants and coagulants in vasculotoxic envenomation

### 14. Criteria for fasciotomy in snake-bitten limbs

- i. Haemostatic abnormalities should be corrected (antivenom with or without clotting factors)
- ii. Clinical evidence of an intracompartmental syndrome
- iii. Intracompartmental pressure >40 mmHg (in adults)
- iv. Early treatment with antivenom remains the best way of preventing irreversible muscle damage. In any case, fasciotomy should not be contemplated until haemostatic abnormalities have been corrected, otherwise the patient may bleed to death. Intracompartmental pressure >40 mmHg of normal saline (in adults). This can be confirmed by vascular Doppler and rising CPK in thousands. Bedside Compartment pressure measurement procedure.

**15. Management of snake bite patients at basic or Primary healthcare facilities** Adapted – referral criteria added - referral to a higher centre depending on availability of ASV, ventilation facility, hemodialysis facility and infrastructure.

### 16. Equipping a Basic Hospital for Effective Snakebite Management

## 8. METHODOLOGY

An Indian guideline on the management of snakebite has been evolved through intensive discussions and workgroups amongst 12 invited experts from India, plus a review and discussion of relevant research publications and papers (list of experts enclosed).

The invited experts comprised a select group of professionals drawn from the fields of clinical medicine, toxicology, & pharmacology. The participants came from a wide variety of leading institutions, States, representing different levels of healthcare in the public as well as private sector.

Facilitator	<b>Dr. Sangeeta Sharma,</b> Professor & Head, Department of Neuropsychopharmacology Institute of Human Behaviour and Allied Sciences, Delhi
Co-Facilitator	<b>Dr. Ashoo Grover</b> Scientist , Indian Council for Medical Research , New Delhi
Expert	<b>Dr. D. B. Kadam</b> Professor & Head, Dept. of Medicine, B. J. Medical College, Pune <b>Dr. Himmat Bawaskar,</b> Bawaskar Hospital & Research Centre, Raigad,

	Maharashtra <b>Dr. Dayal Bandhu Majumdar</b> Senior MO, National Medical College, Kolkata <b>Dr. S. Ragunathanan</b> Professor & Head Poison Centre, Madras Medical College <b>Dr. Arvind Mathur</b> Professor , Jhodhpur Medical College <b>Dr. Rakesh Lodha</b> Additional Professor, Paediatrics, AIIMS, New Delhi <b>Dr. Anurag Agrawal</b> Assistant Professor, Paediatrics, MAMC, New Delhi <b>Dr. J. N. Srivastava</b> Advisor, Quality Improvement, NHSRC
Physician	<b>Dr. Rajiv Kapil</b> Consultant Physician, Lal Bahadur Shastri Hospital, Delhi
Private Practitioner	<b>Dr. Sadanand Raut</b> Vighnagar Nursing Home, Narayangaon, Pune
Paramedic /Nurse/Rehabilitation Experts	<b>Mrs. Sunita Bisht,</b> ICU Nurse, GTB Hospital Delhi
Primary Care Practitioners	<b>Dr. Sanjay Bajaj,</b> SMO, State Health Services, Himachal Pradesh
ASV Manufacturer	<b>Dr. M.V. Khadilkar</b> Premium Laboratories, Pune
Project Manager/Quality Professional	<b>Dr. Nikhil Prakash</b> Senior Consultant, Quality Improvement, NHSRC

The guidelines have been reviewed by experts having ground experience of handling snakebite cases including those from Indian Society of Toxicology and manufacturer of the antisnake venom.

1. Dr Jeevan Kuruvilla, Gandhi Health Centre, Bardwah
2. Dr Omesh Bharti, Government of Himachal Pradesh
3. Dr DP Punde, Senior Physician, Punde Hospital, Nanded, Maharashtra
4. Dr Joseph K Joseph, President Toxicological Society of India, Kochi
5. Dr VK Himgire, Nanded

The guidelines have also been reviewed by Global Snakebite Initiative (GSI) group. The Global Snakebite Initiative is an internationally-active non-profit organisation, registered in Australia, and led by snakebite experts who are dedicated to improving access to good quality, robustly tested, safe, effective antivenoms in the world's poorest communities.

### How the relevant guideline(s) were selected as source of recommendation

Much of snakebite treatment is not based on clinical trials as very few have been carried out by experts in the past. Although it is desirable to have good quality evidence from clinical trials in support of the recommendations made for the management of snakebite. Feasibility of conducting randomized controlled trials (RCT) to assess the comparative efficacy of various treatment options in snakebite is limited. Yet at the same time there is an urgent need for recommendations on snakebite since waiting for a good quality evidence before publication of the guidelines would be neither helpful nor realistic as meanwhile snakebite victims would continue to die in absence of good effective first aid and guidelines on use of antsnake venom (i.e., indications, dosage etc). Moreover victim first reach the primary health centre, the medical officer who never treated snakebite victims earlier is in-charge of the health facility, therefore, standard treatment guidelines and practical training of the doctors in providing first aid and early management of snakebite is urgently required.

Search for existing guidelines on snakebite was conducted through Pub med and grey literature and the following guidelines for management of snakebite were identified:

Available guidelines and articles in the literature	Selected guidelines for adoption/adaptation of recommendations	Rationale for selection of source
1. A2 Snakebite Management in Asia & Africa Guidelines produced by: Pakistan Medical Research Council, Pakistan Medical Association; National Program for Family Planning and Primary Health Care and Indian Journal of Emergency Pediatrics, 2011.		<ul style="list-style-type: none"><li>• Recent guidelines</li><li>• Pertinent to Asian region</li><li>• Developed based on syndromic approach based on available Evidence</li></ul>
2. Guidelines for the management of snake-bites by Warrell, David A. World Health Organization 2010.		Pertinent to Asian region based on available evidence
3. Guidelines for the clinical management of		<ul style="list-style-type: none"><li>• Currency of the guidelines</li><li>• Pertinent to Asian region based</li></ul>



snakebite in the South East Asian Region, 2015 (Draft		on available evidence
4. A Module on the “Management of Snake Bite Cases” For Medical Officers. Developed By PUBLIC Health Branch Of The Directorate Of Health Services & Institute Of Health & Family Welfare Kolkata. Department Of Health & Family Welfare. Government of West Bengal.		<ul style="list-style-type: none"> <li>• Recent State specific guidelines (West Bengal)</li> <li>• Based on syndromic approach</li> <li>• Adopted/adapted to Indian situation</li> </ul>
5. Handbook on Treatment Guidelines For Snake Bite And Scorpion Sting 2008 - TNHSP Publication. Tamil Nadu Health Systems Project Health and Family Welfare Department, Government of Tamil Nadu, Chennai.		
6. Surjit Singh and Gagandeep Singh. Snake Bite: Indian Guidelines and Protocol. Page 424-428		
7. Draft national snakebite management Protocol. Dte General of Health Services. Ministry of Health and family Welfare. Government of India 2009 developed with technical support from WHO Country Office, India.		<ul style="list-style-type: none"> <li>• Draft guidelines developed by multidisciplinary expert group</li> <li>• Pan India specific based on available evidence adopted/adapted to Indian situation</li> </ul>
8. Snakebite & Spider bite Clinical Management Guidelines. Nsw Ministry Of Health 2014. Third		For management followed identification of snake approach

Edition		
9. Syed Moied Ahmed, Mohib Ahmed, Abu Nadeem, Jyotsna Mahajan, Adarash Choudhary, and Jyotishka Pal. Emergency treatment of a snakebite: Pearls from literature J Emerg Trauma Shock. 2008 Jul-Dec; 1(2): 97– 105. doi: 10.4103/0974- 2700.43190.		
10. High Dose versus low- dose antivenom in the treatment of poisonous snakebites: A systematic review. Rashmi Ranjan Das, Jhuma Sankar, Nishanth Dev. IJCCM 2015; 19: 340-349.		

### How recommendations were selected, adopted or adapted

Recommendations given in draft national guidelines, Warrell 2010, WHO draft 2015 and A2 snakebite management in Asia and Africa guidelines are largely adopted following deliberations of the group of experts. Diagnosis of the species of snake responsible for the bite is important for optimal clinical management which could be achieved by identifying dead snake or by inference from the “clinical syndrome” of envenoming. In the draft national guidelines (2009) the line of treatment were largely decided on the basis of the identification of the snake (Elapid or Viperine). The expert group decided to develop guidelines largely focusing on the syndromic approach since catching of snake is not only dangerous but also may cause undue delay in approaching medical care besides identification of snake requires skills which may not be available at the lower levels of health care. Moreover, neither bite marks nor clinical manifestations may correlate with the species of snake brought as evidence. Lastly there may be overlapping of the symptoms of envenomation.

Symptoms and signs vary according to the species of snake responsible for the bite and the amount of venom injected. The Guideline Development Group recognises the limitations of syndromic approach though as more careful study of the clinical effects of snakebites shows that the range of activities of particular venom is very wide. For example some elapid venoms such as those of Asian Cobra, can cause severe local envenoming formerly thought to be an effect only of viper venoms.

Also Russell's viper venom cause paralytic signs suggesting elapid neurotoxicity and muscle pains and dark brown urine suggesting sea snake rhabdomyolysis. There may be a considerable overlap of clinical features on presentation still a "Syndromic approach" may still be useful, especially when the snake has not been identified.

Management of snakebite		Remarks
<b>First aid and transport</b>		
Quick transport to Hospital in an ambulance equipped with transport ventilator	WHO 2015	<p>Adapted – situational adaptation Ambulance with Transport ventilators are ideal, but very rarely available in Rural India, Recommendation may DELAY transfer to Base Hospital. The patient must be quickly transported to a place where they can receive medical care (dispensary or hospital) as quickly, but as safely, passively 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.</p> <p>Motorbike is a practical alternative especially in rural areas for rapid transport but third person must sit behind the patient to support on bike.</p> <p>If ASV available must be administered in appropriate dose before shifting victim to higher centre.</p>
Immobilization of the bitten limb	WHO 2015	<p>Adapted – situational adaptation in case splint for immobilization is not available use bandages or cloth to hold the splints (wooden stick), but do NOT block the blood supply or apply pressure.</p>
Tight (arterial) Tourniquets should NOT be used for snakebite first aid as it may cause gangrenous limbs.	WHO 2015	<p>Situational adaptation Pressure immobilization (Sutherland method) modified in case victim is expected to reach the hospital in more than 30 minutes but less than 3 hours crepe bandage may be applied by qualified medical personnel only till the patient is shifted to the hospital. The bandage is wrapped over the bitten area as well as the entire limb with the limb placed in a splint. It should be capable of admitting a finger</p>

		beneath it. If trained personnel is not present, Must not be tried)
Release of tight bands, bandages and ligatures – ideally these should not be released until the patient is under medical care in hospital, hospital staff and resuscitation facilities are available and antivenom treatment has been started.	WHO 2015	<p><b>Adapted.</b> In case of venomous envenomation, <b>tourniquet/light band, bandages/ligatures should be removed only after patient has reached the hospital,</b> medical staff and resuscitation facilities are available <b>and antsnake venom has been started in the presence of the doctor by the bedside of the patient and keep Atropine Neostigmine injection ready.</b></p> <p>Expert consensus - If envenomation is confirmed on local examination and bite is non-venomous tourniquet, if any can be removed after establishing IV line. In case of multiple ligatures, all the ligatures can be released in Emergency Room with doctor on the bed side of the patient EXCEPT the most proximal one; which should only be released after admission and all preparations for resuscitation facilities are available and antivenom treatment has been started.</p>
<p>Avoid any interference with the bite wound (incision, rubbing, vigorous cleaning, massage, application of herbs or chemicals)</p> <p>Electrical therapy has no role in snakebite first aid and Cryotherapy may do more harm</p> <p>No role of black stones and scarification No role of Traditional Remedies</p>	A2, WHO 2015	Adopted
No role of local ASV	WHO 2015	Adopted
<b>Presentation and examination of snakebite victims</b>		
Examination of Pregnant women	WHO 2015	Adopted
Signs and Symptoms of Snakebite Asymptomatic/non venom related symptoms of snake bite	A2, WHO 2015	Adapted – signs and symptoms have been arranged in order of appearance to guide the treating doctors in diagnosis and monitoring of the patient.
<b>Diagnosis of snake bite</b>		
20 WBCT	WHO 2015	Added- frequency of 20 WBCT specified. If

Accepting that the 20WBCT may remain negative (clotting) in patients with evolving venom-induced DIC, the test should be repeated frequently and antivenom treatment should not be delayed if there is other evidence of anti-haemostatic disturbances (e.g., spontaneous systemic bleeding distant from the bite site.		clotted, the test should be carried out every 1 h from admission for three hours and then 6 hourly for 24 hours. In case test is non-clotting, repeat 6 hour after administration of loading dose of ASV
In case where the 20WBCT result is inconsistent with the patients' clinical condition, normal control blood is used for comparison.		Adopted
<b>Management of snakebite</b>		
<b>ABCDE approach</b> <b>A</b> irway <b>B</b> reathing (respiratory movements) <b>C</b> irculation (arterial pulse) <b>D</b> isability of the nervous system (level of consciousness) <b>E</b> xposure and environmental control (protect from cold etc.)	WHO 2015	<b>Adapted</b> as per American Heart Association Guidelines for cardiopulmonary resuscitation and emergency cardiovascular care 2015 <b>CABDE approach</b> <b>C</b> irculation (arterial pulse) <b>A</b> irway <b>B</b> reathing (respiratory movements) <b>D</b> isability of the nervous system (level of consciousness) <b>E</b> xposure and environmental control (protect from cold etc.)
In case of venomous envenomation, tourniquet should be removed only after completion of loading dose of ASV in the presence of the doctor.	WHO 2015	Adapted - If envenomation is confirmed on local examination and bite is non-venomous, tourniquet, if any can be removed after establishing IV line in the presence of the doctor. In case of multiple ligatures, all the ligatures can be released in Emergency Room EXCEPT the most proximal one; which should only be released after admission and all preparations.
Antivenom treatment should not be delayed if there is other evidence of spontaneous systemic bleeding distant from the bite site. In case test is non-clotting, repeat 6 hour after administration of loading dose of ASV. In case of neurotoxic envenomation repeat clotting test after 6 hours.		Expert Consensus in case with a history of Bite; known or unknown, if there is spontaneous abnormal bleeding beyond 20 minutes from time of bite, ASV is to be started, do NOT wait for 20 WBCT report. REPEAT dose of ASV should also be given if abnormal bleeding does not stop one hour after completion of 1 <sup>st</sup> 10 vials.

A trial of anticholinesterase ("AN 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.	WHO 2015	Adopted. Added criteria for continuing or stopping Stop Atropine Neostigmine (AN) dosage schedule if: <ol style="list-style-type: none"> <li>1. Patient has complete recovery from neuromuscular paralysis. Rarely patient can have recurrence, carefully watch patients for recurrence.</li> <li>2. Patient shows side effects in the form of fasciculations or bradycardia.</li> <li>3. If there is no improvement after 3 doses.</li> </ol>
No response to 3 doses of AN test		Adapted In case of no improvement after 3 doses of atropine neostigmine, indicating probable Krait bite. Krait affects pre-synaptic fibres where calcium ion acts as neurotransmitter. Give Inj. Calcium gluconate 10ml IV (in children 1-2 ml/kg (1:1 dilution) slowly over 5-10 min every 6 hourly and continue till neuromuscular paralysis recovers which may last for 5-7 days.
Differential identification of type of snakebite based on the symptoms and signs	WHO 2015	Identification of the type of snake should not hold the treatment though to a large extent the manifestation of snakebite depends upon the species of snake, unfortunately, <ul style="list-style-type: none"> <li>• Catching of snake is not only dangerous</li> <li>• Undue delay in approaching medical care</li> <li>• Identification of snake requires skills</li> <li>• Neither bite marks nor clinical manifestations may correlate with the species of snake brought as evidence.</li> <li>• Overlapping of the symptoms of envenomation.</li> <li>• Take One smart phone photograph of the snake, dead or alive, if available, for confirmation by an expert.</li> </ul>
Routine use of ASV to any patient claiming to have bitten by a snake should be strongly discouraged as they expose patients who may not need treatment to the risks of antivenom reactions	WHO 2010	Adopted and added the patient may have reaction to any horse serum preparation like antirabies immunoglobulin sensitizing patient to any future use of Horse serum product; they also waste valuable and scarce stocks of antivenom.

For vasculotoxic snakebite - Two regimens low dose infusion therapy and high dose intermittent bolus therapy can be used.	WHO 2015	Adapted. Low dose infusion therapy is as effective as high dose intermittent bolus therapy and also saves scarce ASV doses.
ASV Therapy and maximum dose of ASV Not specified in WHO SEARO 2015 document. mentions “....Medical personnel must usually rely in manufacturers’ recommendations stated in the package insert.	WHO 2015	Expert consensus. Max dose of ASV for neuroparalytic snakebite – ASV 10 vials stat as infusion over 30 minutes followed by 2 <sup>nd</sup> dose of 10 vials if no improvement within 1 <sup>st</sup> hour. Repeat 2nd dose even after 2-3 hours; if relapse of signs of Neurotoxicity is noted; may be due to delayed absorption).  In vasculotoxic envenomation - Envenomation by the Hump-nosed Pit viper does not respond to normal Indian polyvalent ASV and coagulopathy may continue for up to 3 weeks. If 30 vials of ASV have been administered reconsider whether continued administration of ASV is serving any purpose, particularly in the absence of proven systemic bleeding. If large doses have been administered and the coagulation abnormality persists, give fresh frozen plasma (FFP) or cryoprecipitate (fibrinogen, factor VIII), fresh whole blood, if FFP not available
Criteria for repeat dose of ASV Persistence or recurrence of blood coagulability after 6 h or of bleeding after 1-2 h and deteriorating neurotoxic or cardiovascular signs after 1-2 hours.	WHO 2015	Adopted
Snakes inject the same dose of venom into children and adults. Children must therefore be given exactly the same dose of antivenom as adults.	WHO 2015	Adopted
Skin and conjunctival “hypersensitivity” tests should not be used.	WHO 2010 & 2015	Adopted
Routine use of prophylactic adrenaline is recommended before	WHO 2015	Adopted

ASV, except in known hypertensive, and if patient presents with blood pressure more than 140/90 in adult victims or if evidence of suspicion of underlying cardiovascular disease. The adult dose of adrenaline (epinephrine) is 0.25 mg of 0.1% solution by subcutaneous injection (Children 0.005 mg/kg body weight of 0.1% solution).		
Use of histamine, anti-H1 and anti-H2 blockers, corticosteroids and the rate of intravenous infusion of antivenom between 10 and 120 minutes), do not affect the incidence or severity of early antivenom reactions.	WHO 2015	Adopted
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.	WHO 2015	Adapted Added history of reaction to treatment with equine anti-tetanus serum and antirabies immunoglobulin, equine anti-rabies serum or equine or ovine antivenom)
<p>Severe Hypersensitivity reaction to ASV</p> <p><b>For high risk patients</b></p> <p>In patients with history of hypersensitivity or exposure to animal serum such as equine ASV, tetanus-immune globulin or rabies-immune globulin in past, severe atopic conditions:</p> <ol style="list-style-type: none"> <li>1. Give ASV only if they have signs of systemic envenoming.</li> <li>2. Subcutaneous epinephrine (adrenaline) 0.25 mg of 0.1% solution to be given just before antivenom treatment is started</li> </ol>		<p>Expert consensus - Desensitization procedure only in case of severe anaphylaxis reaction with shock and generalised anasarca after injection of very few ml of ASV usually less than 5 ml of diluted ASV despite reaction occurring after prophylaxis of adrenaline.</p> <p>Change the batch of ASV</p>



3. Give Inj. Hydrocortisone 200 mg and Chlorpheniramine maleate 22.75 mg prior to the administration of ASV.		
No Role of anticoagulants and coagulants in vasculotoxic envenomation	A2, WHO 2015	Adopted
Minimize the risk of renal damage from excreted myoglobin and/or haemoglobin	WHO 2015	Adopted
Pain and wound management	A2 and WHO 2015	Adopted
Snake venom Ophthalmia	A2 and WHO 2015	Adopted
<p>Criteria for fasciotomy in snake-bitten limbs (WHO)</p> <ul style="list-style-type: none"> <li>• Haemostatic abnormalities have been corrected (antivenom with or without clotting factors)</li> <li>• Clinical evidence of an intracompartmental syndrome</li> <li>• Intracompartmental pressure &gt;40 mmHg (in adults)</li> </ul> <p>Early treatment with antivenom remains the best way of preventing irreversible muscle damage.</p>	A2, WHO 2015	Adopted. There is little objective evidence that the intracompartmental pressure due to snakebite in India, ever reaches the prescribed limit for a fasciotomy. Very limited trial data has tended to confirm this. In a small case study in India, using a Stryker monitor, despite grossly swollen limbs, which matched the 6Ps, only one case from 12 achieved an intracompartmental pressure where fasciotomy would be considered. By the time coagulation was restored in the victim, the intracompartmental pressure had reduced to normal levels.
In any case, fasciotomy should not be contemplated until haemostatic abnormalities have been corrected, otherwise the patient may bleed to death.	WHO 2015	Adopted
Intra-compartmental pressure >40 mmHg of normal saline (in adults). This can be confirmed by vascular Doppler and rising CPK in thousands.	WHO 2015	Adopted. Bedside Compartment pressure measurement procedure given in case Insert a 16 no. needle in the suspected compartment at a depth of 1 cm and connect to a simple tubing irrigated with normal saline. Measure rise in the saline column in the tubing. A rise more than 40 cm of saline corresponds to 30mm Hg of lymphatic/ capillary pressure and is

		suggestive of compartment pressure. This necessitates fasciotomy procedure.
Management of snake bite patients at basic or Primary healthcare facilities	WHO 2015	Adapted – referral criteria added - referral to a higher centre depending on availability of ASV, ventilation facility, hemodialysis facility and infrastructure.
Equipping a Basic Hospital for Effective Snakebite Management	A2	Adopted

## 9. STAGES OF MANAGEMENT

The following steps or stages are often involved:

### Management of snakebite

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

## 10. FIRST AID TREATMENT GUIDELINES

### First aid: Bystanders/victim

Snakebite first aid remains a critical part of snakebite management to enable them to reach the nearest medical facility in the best possible condition and yet a lack of clarity and attention to the evidence has resulted in little positive progress (Simpson, 2008). Much of the first aid currently carried out is ineffective and dangerous (Simpson, 2006). Historical and newer methods continue to hold sway when evidence has either rejected them or shown they have little merit. Untrained personnel usually apply first aid in the immediate aftermath of snakebite. It is essential therefore that first aid advice is clear, simple to apply and provide the maximum benefit and least time delay

The following methods are recommended keeping in view the available evidence and concluded that other methods are not appropriate for the conditions in India.

## 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.

### Aims of first-aid

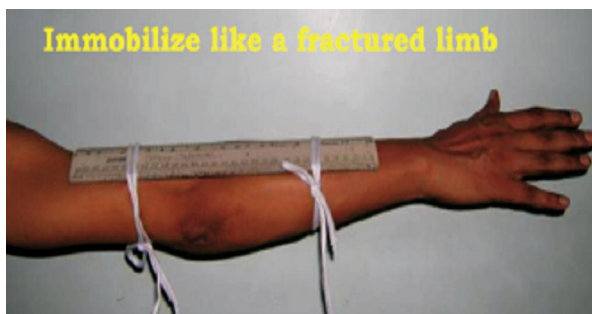
- Attempt to retard systemic absorption of venom.
- Preserve life and prevent complications before the patient can receive medical care
- Control distressing or dangerous early symptoms of envenoming.
- Arrange the transport of the patient to a place where they can receive medical care.

**ABOVE ALL, AIM TO DO NO HARM!**

Provide first-aid measures, supportive measures immediately. Observe for signs of envenomation. Administer ASV therapy as soon as there is evidence of envenomation.

### At the community or village level (Warrell 2010)

1. Check history of snakebite and look for obvious evidence of a bite (fang puncture marks, bleeding, swelling of the bitten part etc.). However, in krait bite no local marks may be seen. It can be noted by magnifying lens as a pin head bleeding spot with surrounding rash.
2. Reassure the patient as around 70% of all snakebites are from non-venomous species. Control anxiety as excitement will increase heart rate and lead to spread of venom.
3. Immobilize the limb in the same way as a fractured limb. Use bandages or cloth to hold the splints (Any rigid object may be used as a splint. e.g. spade, piece of wood or tree branch, rolled up newspapers, ruler etc.), **but do NOT block the blood supply or apply pressure**. Splint should extend the entire length of the limb, immobilizing all of the joints of the limb. Ideally the patient should lie in the recovery position (prone, on the left side) with his/her airway protected to minimize the risk of aspiration of vomitus.



4. Nil by mouth till victim reaches a medical health facility.

5. Traditional remedies have NO PROVEN benefit in treating snakebite.
6. Shift the victim to the nearest health facility (PHC or hospital) immediately.
7. If ASV available must be administered in appropriate dose before shifting victim to higher centers.
8. The patient must be quickly transported to a place where they can receive medical care (dispensary or hospital) as quickly, but as safely, passively 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. Ambulance with Transport ventilators are ideal, but very rarely available in Rural India, therefore, waiting for an ideal ambulance may DELAY transfer to a hospital. Motorbike is a practical alternative especially in rural areas for rapid transport but third person must sit behind the patient to support on bike.



Victim must not run or drive himself to reach a Health facility. Motorbike Ambulance may be a practical alternative for rural India where no other transport is available.

9. No time should be wasted in attempting to kill or capture the snake. This solely wastes time and can lead to other victims. However, if the snake has already been killed, it should be taken with the patient to the dispensary or hospital for identification by the doctor. However, **do not handle the snake with your bare hands as even a severed head can bite!** (WHO, A2)

#### At the PHC level

1. Secure IV line in PHC itself and use normal saline to keep iv access open. Start fluids if patient is in shock.
2. If possible PHC medical officer can accompany with patient to know the progress and management and treat shock and cardiopulmonary resuscitation (CPR) on the way.
3. Inform the doctor of any symptoms such as progress of swelling, ptosis or new symptoms

that manifest on the way to hospital.

4. Remove shoes, rings, watches, jewellery and tight clothing from the bitten area as they can act as a tourniquet when swelling occurs.
5. Leave the blisters undisturbed.

### Important don'ts

Do not attempt to kill or catch the snake as this may be dangerous. **As far as the snake is concerned - do not attempt to kill it as this may be dangerous. If possible to take a picture of the snake safely for identification by an expert.**



### **MOST TRADITIONAL FIRST AID METHODS SHOULD BE DISCOURAGED:**

- Discard traditional first aid methods (black stones, scarification) and alternative medical/herbal therapy as they have no role and do more harm than good by delaying treatment.
- Do not wash wound and interfere with the bite wound (incisions, suction, rubbing, tattooing, vigorous cleaning, massage, application of herbs or chemicals, cryotherapy, cautery) as this may introduce infection, increase absorption of the venom and increase local bleeding.
- Do NOT apply or inject antislake venom (ASV) locally.

### **Traditional methods to be discarded/ inappropriate methods**

Traditional methods should be discouraged as **THEY DO MORE HARM THAN GOOD!**

### Tight Tourniquets

Traditional tight (arterial) tourniquets made of rope, belt, string or cloth to be effective had to be applied around the upper part of the limb, so tightly that the peripheral pulse was occluded. Most of the debate about efficacy/practicability is explained by the fact that most tourniquets

are incorrectly tied around the lower part of the limb. Some authors have argued that this is because non-experts simply cannot apply a tourniquet effectively (Ismail, 1983). This method is 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.

Finally, psychologically, victims with ligatures tend to believe the venom flow has been inhibited. There is a further danger that this confidence in the power of the ligature will lead them to seek medical attention with less urgency. They have the following drawbacks and problems:

- Risk of Ischemia and loss of the limb (Warrell, 1999).
- Increased risk of necrosis with 4/5 of the medically significant snakes of India. (Fairly, 1929; Pugh et al, 1987; Warrell, 1995).
- Risk on release of tourniquet: Increased risk of massive neurotoxic blockade when tourniquet is released (Watt et al , 1988).
- Haemostatic Risks: Risk of embolism if used in viper bites. Pro-coagulant enzymes will cause clotting in distal blood. In addition, the effect of the venom in causing vasodilation presents the danger of massive hypotension when the tourniquet is released.
- They do not work! (Tun Pe,1987; Khin-Ohn Lwin, 1984). Venom was not slowed by the tourniquet in several experimental studies, as well as in field conditions. Often this is because they are tied on the lower limb or are incorrectly tied (Amaral, 1998; Nishioka, 2000).
- They give patients a false sense of security, which encourages them to delay their journey to hospital.
- Most tourniquets tied by lay people are ineffective as they are tied on the wrong portion of the limb and tied too loosely (Norris et al 2005).
- Tourniquets should not be applied if there is a danger of necrotic venom activity i.e. virtually all cobras and vipers (Sutherland et al, 1981).

**Tight (arterial) Tourniquets should NOT be used for snakebite first aid as it may cause gangrenous limbs.**

If victim is expected to reach the hospital in more than 30 minutes but less than 3 hours crepe bandage may be applied **by qualified medical personnel only** till the patient is shifted to the hospital. The bandage is wrapped over the bitten area as well as the entire limb with the limb placed in a splint. It should be capable of admitting a finger beneath it. If a trained personnel is not present do NOT try tourniquet) (Expert Group Consensus)

### Pressure –immobilization

The pressure-immobilization first aid technique was developed in the 1970's by Professor Struan Sutherland. Its purpose is to retard the movement of venom from the bite site into the circulation, thus "buying time" for the patient to reach medical care. Research with snake venom has shown that very little venom reaches the blood stream if firm pressure is applied over the bitten area and the limb is immobilised (Howarth et al, 1994). Bandage is applied upwards from the lower portion of the bitten or stung limb. Even though a little venom may be squeezed upwards. This is acceptable if pressure immobilisation is done on site of snake bite within minutes. Keeping Indian scenario in view, patient reaches medical facility after at least one hour to many hours, this technique then will be hazardous as it may lead to massive absorption of venom. Hence it is recommended to have immobilization from proximal to distal as shown in the photographs below

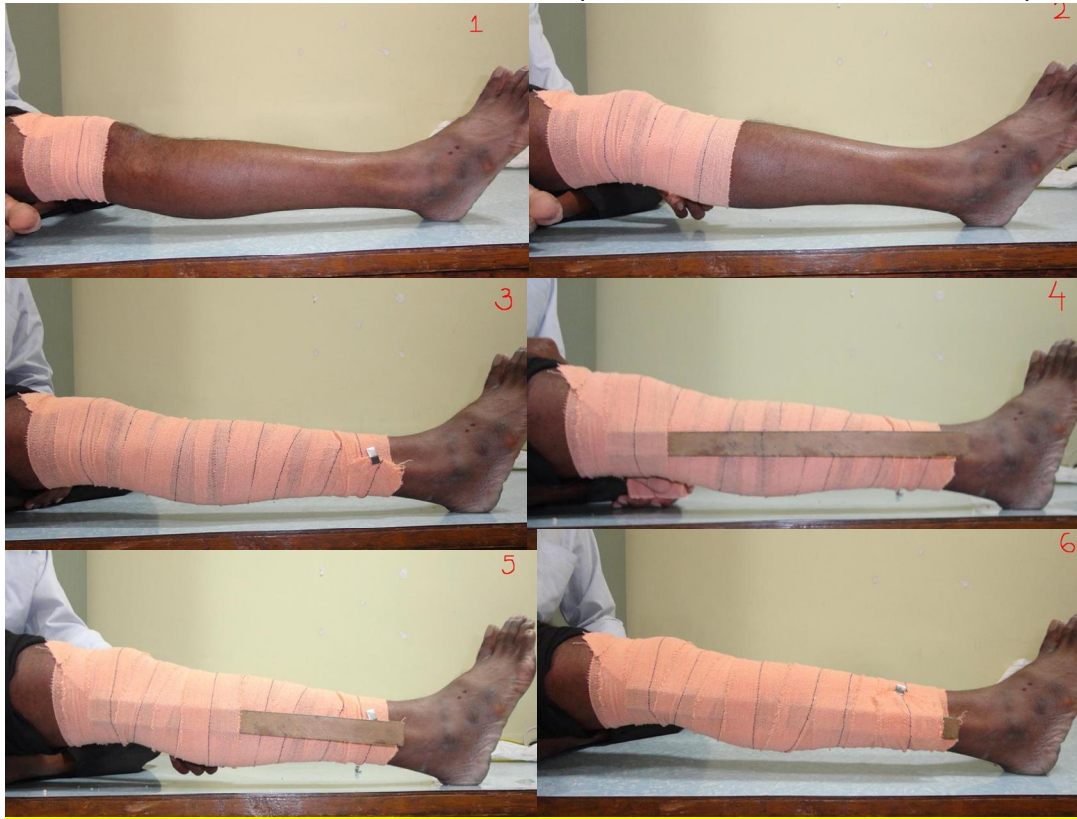


Figure 2:

Pressure immobilization (Sutherland method) From Sutherland et al 1979)

**In case of venomous envenomation, tourniquet/light band, bandages/ligatures should be removed only after patient has reached the hospital, medical staff and resuscitation facilities are available and antsnake venom has been started in the presence of the doctor by the bedside of the patient (Expert Consensus).**

If envenomation is confirmed on local examination and bite is non-venomous tourniquet, if any can be removed after establishing IV line. In case of multiple ligature, all the ligatures can be released in Emergency Room with doctor on the bed side of the patient EXCEPT the most proximal one; which should only be released after admission and all preparations for resuscitation facilities are available



and antivenom treatment has been started (Watt et al., 1988; Expert Consensus).

### Cutting and Suction

- Cutting the wound and the use of suction or suction devices remains controversial.
- However, the large number of viper bites globally, with the anti-haemostatic effect of the venom, makes cutting the wound highly hazardous as well as increasing the probability of infection.
- Cutting a victim with incoagulable blood increases the risk of severe bleeding as the clotting mechanism is no longer effective and increases the risk of infection. No venom is removed by this method.
- Suction devices increase the risk of tissue necrosis and also do not extract significant amount of venom from the wound. Hence suction devices are neither safe nor effective (Alberts et al, 2009; Hardy et al, 1992). Though suction devices are not usually used in India but lay people have strong belief on mouth suction, (as they are habituated to see in the cinemas) is strongly prohibited (Bush 2004).
- Washing the wound requires rubbing of the skin, which will inevitably involve massaging the tissue, thereby causing more venom to be absorbed. This should not be done as the action of washing increases the flow of venom into the system by stimulating the lymphatic system (Gray, 2003).

### Electrical Therapy and Cryotherapy

Electric shock therapy for snakebite received a significant amount of press in the 1980's. The theory behind it stated that applying an electric current to the wound denatures the venom (Guderian et al, 1986; Davis et al 1992). Much of the support for this method came from letters to journals and not scientific papers (Bucknall, 1991; Kroegal et al, 1986). Cryotherapy involving the application of ice to the bite was proposed in 1950s. However, subsequently showed increased necrotic effect of venom, thus practice of cryotherapy may do more harm (Glass 1991).

Do not wash wound and interfere with the bite wound (incisions, suction, rubbing, tattooing, vigorous cleaning, massage, application of herbs or chemicals, cryotherapy, cautery) as this may introduce infection, increase absorption of the venom and increase local bleeding

**Electrical therapy has no role in snakebite first aid and Cryotherapy may do more harm. (WHO 2015 and A2 2011).**

### Traditional Remedies

Traditional remedies are usually concerned with curing snakebite in its totality. Traditional healers and Ayurvedic medicine for example, offer a full treatment philosophy, which they believe 'cures' snakebite.



There is a key aspect to the mathematics of snakebite that must be understood to place traditional medicine in context. In the case of 100 snakebites, 70 are likely to result from a non-venomous species. The remaining 30 bites will result from a venomous species. However, approximately 50% of bites from venomous species result in a dry bite where no venom is injected. It is thus likely that in the case of 100 snakebites, 85 victims will have nothing wrong with them and not require any treatment.

This is the mathematics that shows how traditional treatments **APPEAR** to ‘cure’ snakebite.

Once the traditional healer realises that the victim has been truly envenomed then the victim is eventually sent to hospital. It is worth remembering that the traditional healer has the least interest in treating an envenomed victim as victims that die under traditional treatment reduce confidence in the healer. One or two specific traditional treatments need examination.

Sometimes prior ingestion and local application of these traditional remedial materials may complicate the clinical picture of a bite case. Vomiting induced or skin rashes with some swelling by these materials may mimic envenomation.

### Role of Snake Stones and Scarification

The use of Black Snake Stones to attempt to cure snakebite is common in some developing countries and might contribute to delay in sending the victim to the health facility. In Africa and other countries scarification is a common traditional treatment for snakebite. Cuts are administered to ‘help’ remove the venom from the envenomed victim. In common with generalised cutting this activity is dangerous, as it will encourage bleeding and is ineffective.

<b>No role of black stones and scarification</b>
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## 11. 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, passively 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 (WHO 2015). Any muscular contraction will increase the spread of venom from the site of the bite. A stretcher, bicycle, motorbike, cart, horse, motor vehicle, train or boat whichever mode of transport is available, or if nothing is available 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.

### Instructions while referring

- Inform the need for referral to the patient and/caregiver (family member or the accompanying attendant).
- Give prior intimation to the receiving centre using available communication facilities.
- Arrange for an ambulance. Call Emergency helpline 102/108 etc. Transport in an ambulance

equipped with transport ventilator. If ventilator is not available tight-fitting face mask connected to an anaesthetic (Ambu) bag should be available. However, do not waste time to get an ideal ambulance. Motorbike may be a practical alternative in rural areas for rapid transport but third person must sit behind the patient to support on bike.

- If ASV is not available at First contact centre transfer to the nearest health facility where ASV is available confirmed by telephone.
- Transfer to a higher health facility (Secondary Care Hospital or Tertiary Care Hospital) where mechanical ventilator and dialysis facilities are available for dialysis and ventilation, if required after completion of ASV infusion only.
- During transfer, continue life-supporting measures and provide airway support with the help of an accompanying staff, if required.
- Do not insert nasogastric tube routinely. It is indicated only if victim has obtunded mentation and or gag reflex is poor. If this is not possible give head up position to victim during transport to avoid aspiration of gastric content
- Send the referral note with details of treatment given clearly mentioning the clinical status at the time of referral.

## 12. RECOMMENDATIONS

### Clinical features of snakebite

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 hyperventilate so that they develop pins-and-needles sensation in the extremities, spasm of their hands and feet, and dizziness. Others may develop vasovagal shock after the bite or suspected bite, with faintness and collapse with profound slowing of the heart. Others may become highly agitated and irrational and may manifest a wide range of misleading symptoms (Ahmed et al, 2008).

The clinical presentation of a snakebite victim varies with the age and size of the patient, the species of snake, the number and location of the bites, and the quantity and toxicity of the venom.

### Treatment in the dispensary or hospital

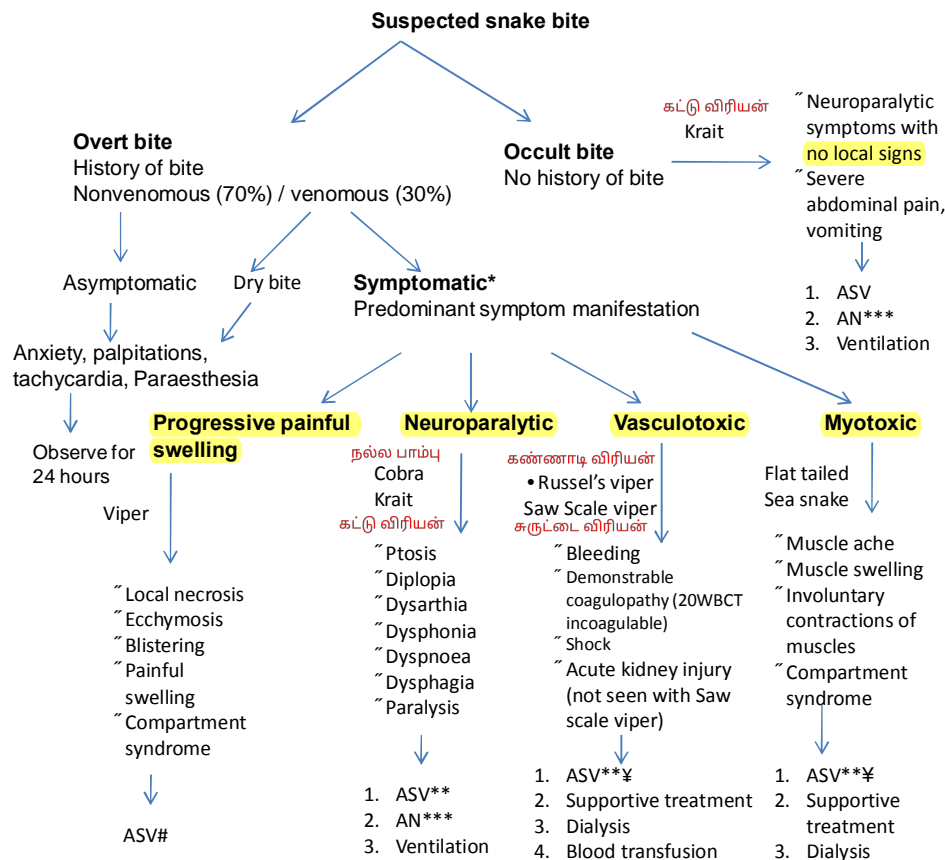
#### Signs and symptoms of snakebite

The signs and symptoms of snakebite follow the four main categories of envenoming i.e. progressive weakness, bleeding, myotoxic and painful progressive Swelling (Figure 1). The clinical presentation of a snakebite victim varies with the age and size of the patient, the species of snake, the number and location of the bites, and the quantity and toxicity of the venom. Victims of snakebite may suffer any or all of the following (WHO 2015):

1. No physical effects other than the fang/tooth puncture due to bites by non-venomous

snakes, animals other than snakes (lizards, fish, rodent, spiders), dry bite by venomous snake.

2. Local envenoming confined to the bitten part of the body. These effects may be transient, resolving in hours or a few days; may persist for few weeks or debilitating, some time permanently due to local necrotic effects of venom and complicating infections.
3. Systemic envenoming involving organs and tissues distant from the bitten part of the body. These effects may be transient, persistent, life threatening and debilitating, sometimes permanently.
4. Effects of anxiety prompted by frightening experience of being bitten (real or imagined) and by exaggerated beliefs about the potency and speed of action of snake venoms. The symptoms may mislead the treated personnel.
5. Effects of first-aid and other pre-hospital treatments that may cause misleading clinical features.



\* Even though present as predominant manifestation but there may be overlap of syndrome as well.

# ASV indicated in rapidly developing swelling only. Purely localized swelling with or without bite marks is not an indication of ASV.

\*\* For reaction to antivenom (ASV) Dose of Adrenaline 0.5 mg IM (in children 0.01 mg/kg)

¥ Specific ASV for sea snake and Pit viper bite is not available in India. However, available ASV may have some advantage by cross reaction.

\*\*\* 'AN' injection Atropine 0.6 mg followed by neostigmine (1.5mg) IV stat (In children Inj. Atropine 0.05 mg/kg followed by Inj. Neostigmine 0.04 mg/kg IV.) Repeat neostigmine 0.5 mg (in children 0.01mg/kg) with atropine every 30 minutes for 5 doses. Thereafter taper dose at 1 hour, 2 hour, 6 hours and 12 hour. Positive response is measured as 50% or more recovery of the ptosis in one hour. If no response after 3<sup>rd</sup> dose stop AN injection. **No AN injection in confirmed krait bite**

• The snake species shown above are indicative only. Russell's viper envenoming in Tamil Nadu and some other areas commonly causes paralysis – the venom of this species varies considerably across its range in India.

**Figure 1.** Four presenting clinical syndromes of snakebite i.e. progressive weakness (neuroparalytic/neurotoxic), bleeding (vasculotoxic/haemotoxic), myotoxic and painful progressive Swelling and its management.

## At a health care facility

### Diagnosis phase

#### History and Symptoms

Examine the bite site and look for fang marks, or any signs of local envenomation. **Fang mark or their patterns have no role to determine whether the biting species was venomous or non venomous or amount of venom injected, severity of systemic poisoning and nature of poisoning – Elapidae or viperidae venom etc.** Some species like Krait may leave no bite marks.

See figure 1 for presenting clinical syndromes of venomous snakebite.

### Asymptomatic (i.e., Non Venom Related Symptoms)

Many will appear to be asymptomatic as:

1. The bite is from a non venomous species (approximately 70% of snakebites are from non venomous species)
2. The bite is from a venomous species but has not injected enough venom to cause symptoms or has injected none at all (dry bites)
3. The venom is of a sufficiently high level to cause symptoms but is now progressing through the tissue without causing swelling to indicate its presence. The delayed appearance of symptoms and signs of snakebite is very common after krait envenoming. The victim may be envenomed but no visible signs or immediately detectable symptoms are visible (The victim may have incoagulable blood or bleeding or renal failure may be underway but not visible)

Patients many a times present with nonspecific symptoms related to anxiety. Common symptoms in these patients are:

- Palpitations, sweating, tremulousness, tachycardia, tachypnoea, elevated blood pressure, cold extremities and paraesthesia. These patients may have dilated pupils suggestive of sympathetic over activity.
- Differentiate from symptoms and signs of envenomation listed below.
- **Redness, increased temperature, persistent bleeding and tenderness locally.** However, local swelling can be present in these patients due to tight ligature

### Dry Bite

Bites by nonvenomous snakes are common and bites by venomous species are not always accompanied by the injection of venom (dry bites). The percentage of dry bites ranges from 10–80% for various venomous snakes. Some people who are bitten by snakes (or suspect or imagine that they have been bitten) or have doubts regarding bite may develop quite striking symptoms and signs, even when no venom has been injected due to understandable fear of the consequences of a real venomous bite. Even in case of dry bite, symptoms due to anxiety and sympathetic over-activity (as above) may be present. As symptoms associated with panic or stress sometimes mimic early envenoming symptoms, clinicians may have difficulties in determining whether envenoming occurred or not.

### Symptomatic Patients

#### Neuroparalytic (Progressive weakness; Elapid envenomation)

Neuroparalytic snakebite patients present with typical symptoms within 30 min– 6 hours in case of Cobra bite and 6 – 24 hours for Krait bite; however, ptosis in Krait bite have been recorded as late

as 36 hours after hospitalization.

These symptoms and signs can be remembered as 5 Ds and 2 Ps.

- 5 Ds – dyspnoea, dysphonia, dysarthria, diplopia, dysphagia
- 2 Ps – ptosis, paralysis
- In chronological order of appearance of symptoms – furrowing of forehead, **Ptosis (drooping of eyelids) occurs first** (Figure 3), followed by **Diplopia (double vision)**, then **Dysarthria (speech difficulty)**, then **Dysphonia** (pitch of voice becomes less) followed by **Dyspnoea** (breathlessness) and **Dysphagia** (Inability to swallow) occurs. All these symptoms are related to 3<sup>rd</sup>, 4<sup>th</sup>, 6<sup>th</sup> and lower cranial nerve paralysis. Finally, paralysis of intercostal and skeletal muscles occurs in descending manner.
- Other common signs are facial paralysis, inability to open mouth and protrude the tongue. **Patients who have no control over the neck (“broken neck sign.”) are at immediate risk and require urgent airway intervention..**
- Additional features like stridor, ataxia may also be seen.
- Associated hypertension and tachycardia may be present due to hypoxia.



Figure 3. Ptosis with neuroparalytic snakebite

To identify impending respiratory failure bedside lung function test in adults viz.

1. Single breath count – number of digits counted in one exhalation - >30 normal
2. Breath holding time – breath held in inspiration – normal > 45 sec
3. Ability to complete one sentence in one breath.

Cry in a child whether loud or husky can help in identifying impending respiratory failure.

***Bilateral dilated, poorly or a non-reacting pupil is not the sign of brain dead in elapid envenoming (Figure 3).***

**Refer patients presenting with neuroparalytic symptoms immediately to a higher facility for intensive monitoring after giving Atropine Neostigmine (AN) injection (schedule of AN injection described below).**

## Vasculotoxic (Haemotoxic or Bleeding)

### General signs and symptoms of Viperine envenomation)

Vasculotoxic bites are due to Viper species. They can have local manifestations as well as systemic manifestations.

**Local manifestations** – these are more prominent in Russell's viper bite followed by Saw scaled viper and least in Pit viper bite. Local manifestations are in form of:

- Local swelling, bleeding, blistering, and necrosis.
- Pain at bite site and severe swelling leading to compartment syndrome. Pain on passive movement. Absence of peripheral pulses and hypoesthesia over the fields of nerve passing through the compartment helps to diagnose compartment syndrome.
- Tender enlargement of local draining lymph node.

### Systemic manifestations –

- Visible systemic bleeding from the action of haemorrhagins (Figure 4) e.g. gingival bleeding, epistaxis, ecchymotic patches, hematemesis, hemoptysis, bleeding per rectum, subconjunctival hemorrhages, haematuria, continuous bleeding from the bite site, bleeding from pre-existing conditions e.g. haemorrhoids, bleeding from freshly healed wounds.
- Bleeding or ecchymosis at the injection site is a common finding in Viper bites.
- The skin and mucous membranes may show evidence of petechiae, purpura ecchymoses, blebs and gangrene.
- Swelling and local pain.
- Acute abdominal tenderness may suggest gastro-intestinal or retro peritoneal bleeding.
- Lateralizing neurological symptoms such as asymmetrical pupils may be indicative of intracranial bleeding.
- Consumption coagulopathy detectable by 20WBCT, develops as early as within 30 minutes from time of bite but may be delayed.



Figure 4. Local and systemic Vasculotoxic (haemotoxic or Bleeding) manifestations of Viperine envenomation.



### Locked-in syndrome (LIS)

Locked-in syndrome (LIS) is defined as quadriplegia and anarthria with preserved consciousness. Patients retain vertical eye movement, facilitating non-verbal communication. In complete locked in syndrome (LIS) patient cannot communicate in any form. Central LIS is seen commonly due to lesions in the ventral pons (Smith and Delargy, 2005; Prakash et al, 2008; Poovazhagi, 2013). Peripheral causes of LIS are severe acute polyneuropathies, neuromuscular junction blockade due to myasthenia gravis toxins and snakebite (Prakash et al, 2008). Knowing the peripheral causes are very important as one may make a wrong diagnosis of brain death and is treatable and complete recovery can be possible with timely intervention. Confirmatory tests like EEG, cerebral blood flow, nerve conduction velocities are recommended to avoid misdiagnosis of coma or brain death. Peripheral LIS usually occurs in Elapidae bites, especially Krait bite and hence increasing ones suspicion rate is important as they can be referred to a centre with ventilator support.

### Life threatening complications

- Acute Kidney Injury (AKI) e.g. declining or no urine output, deteriorating renal signs such as rising serum creatinine, urea or potassium. Some species e.g. Russell's viper (*Daboia* sp) frequently cause acute Kidney Injury. Patient presents with bilateral renal angle tenderness, hematuria, hemoglobinuria, myoglobinuria followed by oliguria and anuria with AKI.
- Hypotension due to hypovolaemia or direct vasodilatation or direct cardiotoxicity aggravates acute kidney injury.
- Parotid swelling, conjunctiva oedema, sub-conjunctival haemorrhage, renal failure, acute respiratory distress syndrome [leaking syndrome] and refractory shock.
- Long term sequelae e.g. pituitary insufficiency with Russell's viper (*Daboia* sp), Sheehan's syndrome (Tun-Pe et al, 1987) or amenorrhea in females.

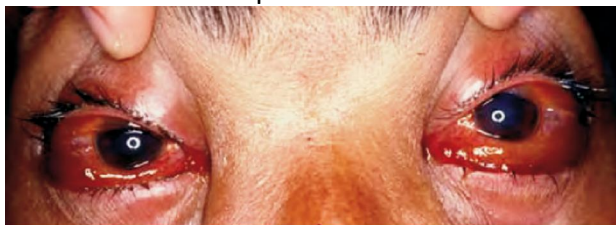
### Systemic capillary leak syndrome

Idiopathic systemic capillary leak syndrome (ISCLS) is a rare disorder characterized by episodes of severe hypotension, hypoalbuminemia, hemoconcentration without albuminuria. During "attacks" of ISCLS, profound derangement of the vascular endothelium results in leakage of plasma and proteins into the interstitial compartment. It is due to capillary hyper permeability with massive extravasation of plasma containing macro molecules smaller than 200KD.

Capillary leak syndrome is a sinister complication of *Daboia russelii* bite as it is beset with an excess of morbidity and mortality. It is seen in more commonly in males as compared to females. Manifestations like parotid swelling, conjunctival chemosis, myalgia, thirst & systemic hypotension



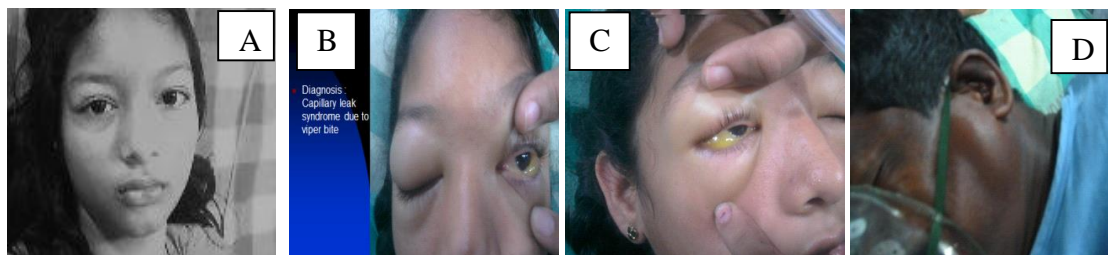
observed in patients of *Daboia russelii* bite indicate capillary leak syndrome.



**Bilateral conjunctival oedema (chemosis) after a bite by a Russell's viper**

Hemoconcentration, increased HCT, leukocytosis, pleural effusion are early laboratory and radiological markers of capillary leak syndrome and should alert the clinician to seek urgent interventions in *Daboia russelii* bite.

After the advent of capillary leak syndrome, meticulous monitoring of CPK and blood pressure control is necessary to avoid the inception of renal failure. Patients with capillary leak syndrome are likely to have severe renal failure and complications related to it. Patients with capillary leak syndrome required higher dose of ASV compared to those without it. Early recognition and effective treatment like infusion of fresh frozen plasma and reduction of hemoconcentration may play a key role to reduce its gruesome mortality (Menon et al, 2015; Atkinson et al, 1977).



**Figure** : A) 17 year old patient with viper bite at admission. B) & C) Same patient with periorbital swelling, Conjunctival chemosis and icterus 24 hours later. D) Another patient with viper bite developing parotid swelling 24 hours later.

### Painful Progressive Swelling (PPS)

Progressive painful swelling is indicative of local venom toxicity. It is prominent in Russell's viper bite, Saw scaled viper bite and Cobra bite. This is associated with

- Local necrosis which often has a rancid smell. Limb is swollen and the skin is taut and shiny. Blistering with reddish black fluid at and around the bite site. Skip lesions around main lesion are also seen. (Figure 5).
- Ecchymoses due to venom action destroying blood vessel wall.
- Significant painful swelling potentially involving the whole limb and extending onto the trunk.
- Compartment syndrome.
- Regional tender enlarged lymphadenitis.



**Envenomed foot**



Figure 5. Snakebite marks and local swelling and necrosis

### Myotoxic

This presentation is common in Sea snakebite. Patient presents with:

- Muscle aches, muscle swelling, involuntary contractions of muscles, trismus.
- Passage of dark brown urine.
- Compartment syndrome, cardiac arrhythmias due to hyperkalaemia, acute kidney injury due to myoglobinuria, and subtle neuromuscular signs.

### Occult Snakebite கட்டு விரியன்

- Krait bite victims often present in the early morning with paralysis with no local signs. Krait has nocturnal habitat and has small teeth. Hence bite marks usually cannot be identified even on close examination.
- Typical presenting history is that the patient was healthy at night, in the morning gets up with severe epigastric/umbilical pain with vomiting persisting for 3 – 4 hours and followed by typical neuromuscular symptoms within next 4- 6 hours. There is no history of snakebite. Vomiting, neurotoxicity and serum creatinine serve as useful signpost for clinical decision making, can help the clinician assess prognosis of their patients more accurately and predict mortality among inpatients with snake bite (Kalantri et al, 2005).
- Unexplained respiratory distress in children in the presence of ptosis or sudden onset of acute flaccid paralysis in a child (locked-in syndrome) are highly suspicious symptoms in endemic areas particularly of Krait bite envenomation. Sometimes patients may present with throat pain or chest pain also.

Early morning symptoms of acute pain abdomen with or without neuromuscular paralysis can be mistaken for a acute appendicitis, acute abdomen, stroke, GB syndrome, myasthenia gravis and hysteria (Bawaskar, 2002). Krait bite envenoming is diagnosed by developing descending neuromuscular paralysis while GB syndrome is by ascending paralysis. Strong clinical suspicion and careful examination can avoid not only costly and unnecessary investigations such as CT scan, MRI, nerve conduction studies, CSF studies and many others but also help in avoiding undue delay in initiation of a specific treatment with ASV. Atropine neostigmine (AN) test helps to rule out myasthenia gravis.

### Differential identification of type of snakebite based on the symptoms and signs

Though to a large extent the manifestation of snakebite depends upon the species of snake, unfortunately, in many cases the biting snake is not seen, and if it is, its description by the victim is often misleading (Harris et al, 2010). Therefore identification of the type of snake should not hold the treatment. At times the bite mark might not be visible (e.g., in the case of Krait). The clinical manifestations of the patient may not correlate with the species of snake brought as evidence. Examine carefully the snake, if brought, and identified if possible. *Discourage bringing the killed snake into the emergency department.* Identification of the species even if killed should be carried out carefully, since crotalids can envenomate even when dead. One smart phone photograph of the snake, dead or alive, if can be taken safely, for confirmation by an expert would also help in identifying the snake.

If snake is not available for identification in such a situation showing specimens of snakes preserved in formalin in glass jars or pictures of snakes would help the patient or the witness to recognize the offending snake which facilitates the judgment of the clinician (Figure 6).

Inspection of local site of bite can also help to identify snake's species. Local swelling, bleeding, blistering, necrosis suggests Cobra bite. Minimum local changes indicate Krait bite. Local bleeding suggests Nilgiri Russell's viper. Pain in abdomen and hyper peristalsis indicates Krait bite.

A more reliable method of identifying the offending snake is the detection of venom antigen through immunodiagnosis such as ELISA but this test is not available in India.



**Figure 6.** Snake identification by the patient

**ON PRESENTATION, PATIENTS CAN BE CRITICAL OR NON CRITICAL (FIGURE 1).**

Figure 1. Management of Snakebite

**Snakebite is a medical emergency, history, symptoms and signs must be obtained rapidly.**

#### **CRITICAL ARRIVAL**

##### **Rapid primary clinical assessment and resuscitation**

**SIGNS** and **SYMPTOMS** of an envenomation at some point in time, not necessarily current, which may be detected. They are NOT in themselves criteria for administering ASV (A2).

##### **Rapid primary clinical assessment and resuscitation:**

###### **CABDE approach**

Circulation (arterial pulse)

Airway

Breathing (respiratory movements)

Disability of the nervous system (level of consciousness)

Exposure and environmental control (protect from cold etc.)

Airway patency, respiratory movements, arterial pulse and level of consciousness must be checked immediately. Patients should be intubated if possible or provided with airway support and ventilated with a resuscitation bag. 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**).
- (e) Cardiac arrest precipitated by hyperkalaemia resulting from skeletal muscle breakdown (rhabdomyolysis) after bites by sea snakes, certain kraits and Russell's vipers. If the patient arrives late: Late results of severe envenoming such as renal failure and septicaemia complicating local necrosis.

If the victim underwent respiratory failure shortly before reaching the hospital, it is likely that a full recovery will be possible. This factor should be communicated to staff responsible for mechanical ventilation of the patient. Often a key decision is whether to continue with mechanical ventilation with a patient who is nonresponsive for several hours on the ventilator. **Patients with neurological envenomation may require many hours or days on a ventilator to achieve recovery** (Kularatne 2002), **particularly in the case of pre synaptic envenoming**. The reality is that in many developing countries ventilators are unavailable in most hospitals and even where present are in short supplies. There is thus a tendency to ventilate patients for a short period, achieve no response and then discontinue ventilation due to 'sepsis' or some other 'cause' of death. (A2)

In the case of pre synaptic envenoming this is disastrous! It is vital that the physician who initially receives the patient fully investigates the timeline of respiratory arrest and informs ventilation staff of the likely outcome. In reality, a patient that underwent respiratory arrest some distance from the hospital will not survive unless good airway support with a resuscitation bag and airway maintenance tools was provided in the interim period.

Vasculotoxic patients presenting with bleeding from multiple orifices with hypotension, reduced urine output, obtunded mentation (drowsy, confused), cold extremities need urgent attention, ASV and ICU care for volume replacement, pressor support, dialysis and infusion of blood and blood products (See following sections).

Neuroparalytic patients presenting with respiratory paralysis, tachypnoea or bradypnoea or paradoxical respiration (Breathing movements in which the chest wall moves in on inspiration and out on expiration, in reverse of the normal movements.), obtunded mentation, and peripheral skeletal muscle paralysis need urgent ventilator management with endotracheal intubation, ventilation bag or ventilator assistance along with ASV.

Other patients can be evaluated to decide severity of their illness.

**The clinician must detect the evidence of envenoming early as it governs the decision of administering antivenom therapy, which in turn has a direct impact on the prognosis.** These

observations and physical signs are based on local and systemic manifestations of envenoming. Since the manifestations of specific patterns of envenoming are snake specific, the identification of the offending snake would help the clinician to look for particular clinical signs and evidence. Properties of snake venom depend mainly on the species of the snake but geographical factors could further modify it. Thus it is prudent to look for features of envenoming as a whole with an open mind.

## **Patient assessment: Non critical arrival and Critical patients after stabilization**

### **Detailed clinical assessment and species diagnosis**

All patients will be kept under observation for a minimum of 24 hours.

#### **History**

- Ask questions as to what the victim was doing at the time of the bite. Some activities such as grass cutting or feeding stock animals in the evening can be suggestive of snakebite. A precise history of the circumstances of the bite and the progression of local and systemic symptoms and signs is very important. 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.
- Bite marks are of no use in identifying if a species is venomous or not though in some countries bite marks have limited use in determining species (Nishioka et al, 1995; Norris, 1995). Many non venomous species leave just two fang-like marks e.g. Wolf Snakes. Some species like the Krait may leave no bite mark at all. Many venomous species have more than two fangs, as they grow reserve fangs in case the main ones break off.
- Determine the exact time of the bite. This can give indications as to the progression of any symptoms. 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).
- 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.
- Where possible identify the snake responsible. Snake colouration is a very unreliable means of determining species. Have the victim carefully bring the snake to hospital if it has been killed. 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.



- Determine if any traditional medicines have been used. Traditional treatments can cause problems, in addition to the time taken to administer them. For example, the ingestion of herbal or other products can generate symptoms that confuse the diagnosis. In some areas the ingestion of clarified butter or 'ghee' is a common remedy use to induce vomiting. The rationale is that venom is thus vomited from the body. The victim's vomiting may be entirely unrelated to envenomation.
- Sometimes chilli is ingested to counteract the venom, which can result in abdominal pain in the victim. In areas where abdominal pain may be indicative of envenomation e.g. krait areas, this can mislead the doctor.
- Obtain a brief medical history (e.g., date of last tetanus immunization, use of any medication, presence of any systemic disease, and history of allergy)

#### Early clues that a patient has severe envenoming (WHO):

- Rapid early extension of local swelling from the site of the bite. In Cobra bite on finger, necrosis may start in few minutes.
- Early tender enlargement of local lymph nodes, indicating spread of venom in the lymphatic system
- Visible signs of neurological impairment such as ptosis, muscular weakness, respiratory distress or respiratory arrest.
- Early spontaneous systemic bleeding especially bleeding from the gums, bite site, haematuria, haemoptysis, epistaxis or ecchymoses.
- Unconsciousness either with or without respiratory arrest.
- Passage of dark brown urine
- Snake identified as a very venomous one i.e., Cobra, Russell's viper.

#### Handling Tourniquets

Care must be taken when removing tourniquets tied by the victim. Sudden removal can lead to a massive surge of venom leading to neurological paralysis, hypotension due to vasodilation etc.

Before removal of the tourniquet, test for the presence of a pulse distal to the tourniquet.

**In case of venomous envenomation, tourniquet should be removed only after starting of loading dose of ASV in the presence of the doctor (Expert Consensus).** Be prepared to handle the complications such as sudden respiratory distress or hypotension. If the tourniquet has occluded the distal pulse, then a blood pressure cuff can be applied to reduce the pressure slowly.

If envenomation is confirmed on local examination and bite is non-venomous, tourniquet, if any can be removed after establishing IV line in the presence of the doctor. In case of multiple ligature, all the ligatures can be released in Emergency Room EXCEPT the most proximal one; which should only be released after admission and all preparations (Expert consensus)

#### Physical examination

Careful assessment of the site of the bite and signs of local envenomation and examination of the patient should be carried out and recorded (Annexure 1). Monitor the patient closely and repeat all above, every 1-2 hourly.

Check for and monitor the following: Pulse rate, respiratory rate, blood pressure and 20 minutes Whole Blood clotting test (20 WBCT) every hour for first 3 hours and every 4 hours for remaining 24 hours.

Check distal pulses and monitor if there is presence of gross swelling. The presence of a pulse does not rule out compartment syndrome. Pain on passive movement, pallor, pulseless limb, hypoaesthesia over the sensory nerve passing through the compartment are suggestive of compartment syndrome. Measure compartment pressure directly if there is concern that a compartment syndrome is developing. The diagnosis is established if the compartment pressure, measured directly by inserting a 16 G IV cannula and connecting it with manometer, is raised above 40 cm water/saline. Direct measurement is necessary before resorting to fasciotomy since compartment syndrome is rare in snakebite victims and fasciotomy done without correction of hemostatic abnormality may cause the patient to bleed to death (Warrell 1999).

Physical examination 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 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) 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, ecchymoses and, in the conjunctivae, for haemorrhages and chemosis. Thoroughly examine the gingival sulci, using a torch and tongue depressor, as these may show the earliest evidence of spontaneous systemic bleeding. 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).



### ***Examination of pregnant women***

Potential complications of envenoming in pregnancy include antepartum and postpartum haemorrhage indicated by vaginal bleeding, premature labour, abortion/stillbirth and foetal distress. Monitor uterine contractions and foetal heart rate. Foetal bradycardia, tachycardia or later deceleration after each uterine contraction indicate foetal distress. In case of vaginal bleeding or the need for imminent surgery correct antihaemostatic abnormalities after antivenom treatment should be accelerated using blood products. Lactating women who have been bitten by snakes should be encouraged to continue breast feeding (WHO 2015).

## **Diagnosis Phase: Investigations**

### **20 Minute Whole Blood Clotting Test (20WBCT)**

It is considered as the most reliable test of coagulation and can be carried out, at the bedside without specialist training. It can also be carried out in the most basic settings.

A few ml of fresh venous blood is placed in a NEW, CLEAN AND DRY GLASS vessel/tube to avoid false positive tests (that Recycled glass vessels are not cleaned with detergents or other cleansing fluids) and left at ambient temperature for 20 minutes. The glass vessel should be left undisturbed for 20 minutes and then gently tilted, **not shaken**. **Caution:**

**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 XII – Hageman factor) and test will be invalid**

In case where the 20WBCT result is inconsistent with the patients' clinical condition, repeat the test in duplicate, including a "control" (blood from a healthy person such as a relative) (WHO 2015)

### ***Results Interpretation***

If the blood is solid i.e. has clotted the patient has passed the coagulation test and no **ASV is required at this stage**. 20 WBCT may remain negative (clotting) in patients with evolving venom – induced DIC, therefore, the patient is re-tested every hour for the first three hours and then 6 hourly for 24 hours until either test result is not clotted or clinical evidence of envenomation to ascertain if dose of ASV is indicated. Antivenom treatment should not be delayed if there is other evidence of spontaneous systemic bleeding distant from the bite site. In case test is non-clotting, repeat 6 hour after administration of loading dose of ASV. In case of neurotoxic envenomation repeat clotting test after 6 hours (Expert Consensus)

**Other investigations that may assist in the management of snake bite at various levels of healthcare**

### At Primary health centre

Peak flow meter in patients (adolescents and adults) presenting with neuromuscular syndrome. If Peak flow meter is not available in PHC then **assess respiratory function using bedside tests - single breath count, breath holding time and ability to complete one sentence** in one health as described earlier.

Urine examination for albumin and blood by dipstick.

### At District Hospital

In addition to the above

Prothrombin time

Platelet count,

Clot retraction time

Liver function test (LFT)

Renal Function test (RFT)

Serum Amylase

Blood sugar

ECG

Abdominal ultrasound

2D Echo (if available)

### At Tertiary Health Care Centre

In addition to the above

*In neuromuscular envenomation*

- Arterial blood gases. **Caution:** Arterial puncture is contraindicated in patients with haemostatic abnormalities.
- Pulmonary function tests
- *In Vasculotoxic venomation*
- For coagulopathy- BT, CT, PT, APTT, Platelet, Serum Fibrinogen, FDP D-Dimer assay, LDH, peripheral blood smear
- Hemolysis -Urine for myoglobin, Urine haemoglobin
- For renal failure- Urine microscopy for RBC, casts, RFT, urinary proteins, creatinine ratio
- Hepatic injury – LFTs including SGOT, SGPT, Alkaline phosphatase, serum proteins
- Cardiotoxicity- CK-MB, 2D Echo, BNP
- Myotoxic – CK, SGOT, Urine myoglobin, compartment pressure
- Infection- Serum procalcitonin, culture (blood, urine, wound) and sensitivity

Arterial blood gases and urine examination should be repeated at frequent intervals during the acute phase to assess progressive systemic toxicity).

### Rationale and interpretation of the tests:

- i. Hemogram: The hemogram may show transient elevation of hemoglobin level due to hemoconcentration (because of the increased capillary leak) or may show anemia (due to

hemolysis, especially in viper bites). Presence of neutrophilic leucocytosis signifies systemic absorption of venom (Warrell DA. 1999). Thrombocytopenia may be a feature of viper envenomation.

- ii. *Platelet count*: This may be decreased in victims of envenoming by vipers.

*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.

- iii. Serum creatinine: This is necessary to rule out acute kidney injury after viper and sea snakebite.
- iv. Serum creatine kinase (CK): Elevated levels of these markers suggests muscle damage (caution for renal damage) and raised amylase suggests pancreatic injury
- v. Prothrombin time (PT) and activated partial thromboplastin time (aPTT): Prolongation may be present in viper bite (to be repeated 6 hourly, if abnormal).
- vi. Fibrinogen and fibrin degradation products (FDPs): Low fibrinogen with elevated FDP is present when venom interferes with the clotting mechanism.
- vii. Urine examination for Proteinuria/ RBC/ Haemoglobinuria/ Myoglobinuria: 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.
- viii. Electrocardiogram (ECG): Nonspecific ECG changes such as bradycardia and atrioventricular block with ST-T changes may be seen (Nayak et al, 1990)
- ix. Electroencephalogram (EEG): Recently, EEG changes have been noted in up to 96% of patients bitten by snakes. These changes start within hours of the bite but are not associated with any features of encephalopathy. Sixty-two percent showed grade I changes, 31% cases manifested grade II changes (moderate to severe abnormality), and the remaining 4% showed severe abnormality (grade III). These abnormal EEG patterns were seen mainly in the temporal lobes (Ramachandran S et al, 1995). However, rarely needed for patient management.
- x. Pulse oximetry for oxygen in patients with respiratory failure or shock.
- xi. Electrolyte determinations: These tests are necessary for patients with respiratory paralysis and systemic symptoms.
- xii. Arterial blood gases and pH may show evidence of respiratory failure (neurotoxic envenoming) and acidaemia (respiratory or metabolic acidosis).
- xiii. X-Ray/ CT/ Ultrasound (The use of X-Ray and ultrasound are of unproven benefit, apart from identification of bleeding in Viperine bites).

Feature	Cobras	Kraits	Russell's Viper	Saw Scaled Viper	Hump Nosed Viper
Local Pain/ Tissue Damage	YES	NO	YES	YES	YES
Ptosis/ Neurological Signs	YES	YES	YES!	NO	NO
Haemostatic abnormalities	NO	NO!	YES	YES	YES
Renal Complications	NO	NO	YES	NO	YES
Response to Neostigmine	YES	NO?	NO?	NO	NO
Response to ASV	YES	YES	YES	YES	NO

### Late-onset envenoming

The patient should be kept under close observation for at least 24 hours. Many species, particularly the Krait and the Hump-nosed pitviper are known for the length of time it can take for symptoms to manifest (Joseph et al 2003). Often this can take between 6 to 12 hours. Late onset envenoming is a well documented occurrence (Ho et al, 1986; Warrell et al, 1977; Reitz, 1989). In many cases of Common krait bites in West Bengal, bilateral ptosis appeared after 24- 36 h after admission for pain abdomen.

This is also particularly pertinent at the start of the rainy season when snakes generally give birth to their young. Juvenile snakes, 8-10 inches long, tend to bite the victim lower down on the foot in the hard tissue area, and thus any signs of envenomation can take much longer to appear.

### 13. ANTI SNAKE VENOM (ASV)

If ASV is indicated i.e. signs and symptoms of envenomation with or without evidence of laboratory tests, administer FULL dose as soon as indicated. In a patient with a history of bite; known or unknown, if there is spontaneous abnormal bleeding beyond 20 minutes from time of bite, start ASV, do NOT wait for 20 WBCT report.

There are no absolute contraindications to ASV. Do not routinely administer ASV to any patient claiming to have bitten by a snake without signs and symptoms of envenoming as ASV exposes such patients to the risks of ASV reactions unnecessarily; besides wastage of valuable and scarce stocks of ASV. However, at the same time do not delay or withhold ASV on the grounds of anaphylactic reaction to a deserving case. Do NOT give incomplete dose. Purely local swelling, even if accompanied by a bite mark from an apparently venomous snake, is not a ground for administering ASV. Swelling, a number of hours old is also not a ground for giving ASV. However, rapid development of swelling indicates bite with envenoming requiring ASV.

## **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.

**Routine use of ASV to any patient claiming to have bitten by a snake should be strongly discouraged as they expose patients who may not need treatment to the risks of antivenom reactions;** The patient may have reaction to any horse serum preparation like Antirabies immunoglobulin; they also waste valuable and scarce stocks of antivenom.

## **Monovalent vs. Polyvalent**

**Anti snake venom (ASV) in India is polyvalent i.e. it is effective against all the four common species; Russell's viper (*Daboia russelii*), Common Cobra (*Naja naja*), Common Krait (*Bungarus caeruleus*) and Saw Scaled viper (*Echis carinatus*). There are no currently available monovalent ASVs primarily because there are no objective means of identifying the snake species, in the absence of the dead snake. It would be impossible for the physician to determine which type of Monovalent ASV to employ in treating the patient.**

**The call for monovalent ASVs because “they are cheaper” is another example of intuition being emphasised over evidence. ASV production economics are complex and in many of the developing countries, which have a low cost of ASV, the use of monovalent ASVs may actually INCREASE the cost of the final product as batch, testing, distribution & storage costs for specific ASVs may be higher.**

It must be remembered that:

The majority of victims do not bring the dead snake for identification

Doctors are unreliable in making a correct identification even if the snake is brought

ELISA testing kits would need to be provided. India should make an attempt to establish this test will save maximum ASV and prevent ASV crisis

A number of monovalent ASVs would need to be provided to many physicians which has planning, logistical & cost implications

Producing a separate batch for each monovalent ASV may well increase the costs of production and testing versus polyvalent ASVs.

Very few countries have ELISA testing despite it being referred to for nearly 30 years; the main example is Australia where it is used to identify biting species NOT level of envenomation (World Health Organisation, 1981).

There are key problems with monovalent ASVs that are often overlooked:

The clinical symptoms to administer the ASV must be clear and mutually exclusive. If two species cause the same symptom, monovalent ASVs are not useful. A good example of this is the case of China where both the Chinese cobra (*Naja atra*) and the White-lipped pit viper (*Cryptelytrops albolabris*) produce significant local swelling. Local doctors have difficulty in determining whether to use SIBP *Naja atra* ASV or pit viper ASV.

If ELISA is to be developed:

It is costly to develop the base product

It must be rigorously tested to eliminate false positives and negatives

It must be based on local snakes; the kits cannot be imported. If your country does not have it now, then it will be many years before it is reliably available.

Enzyme Linked Immuno Sorbent Assay testing for snake species and level of envenomation ARE NOT YET AVAILABLE in India. There are known species such as the Hump-nosed pit viper (*Hypnale hypnale*) where polyvalent ASV is known to be ineffective. In addition, there are regionally specific species such as Sochurek's Saw Scaled Viper (*Echis carinatus sochureki*) in Rajasthan, where the effectiveness of polyvalent ASV may be questionable. Further work is being carried out with ASV producers to address this issue.

### ASV dosage forms

ASV comes in two forms lyophilised powdered and liquid. Lyophilised ASV is simply liquid ASV freeze-dried. There is **NO** evidence that clinically one form is better at neutralising venom than the other. They each have advantages or disadvantages that must be considered:

Lyophilised	Liquid
<b>Advantages</b>	<b>Advantages</b>
Long Shelf Life (3-5 Years)	Ready to use
Requires no cold chain	
<b>Disadvantages</b>	<b>Disadvantages</b>
Speed of reconstitution of 30-60 minutes	Short Shelf Life (2 years)
	Requires a cold chain

**Liquid ASV requires a reliable cold chain and refrigeration and has a 2 year shelf life. Lyophilised ASV, in powder form, requires only to be kept cool. This is a useful feature in remote areas where power supply is inconsistent.**

### ASV administration

ASV should be given only by the IV route, and should be given slowly, with the physician at the bedside during the initial period to intervene immediately at the first sign of any reaction. The rate of infusion can be increased gradually in the absence of a reaction until the full starting dose has been administered (over a period of ~1 hour).

**Epinephrine (adrenaline) should always be drawn up in readiness before ASV is administered.**

ASV must **NEVER** be given by the IM route because of poor bioavailability by this route. Also **do NOT** inject the ASV locally at the bite site since it is not effective, is extremely painful and may increase intra-compartmental pressure.

**Take all aseptic precautions before starting ASV to prevent any pyrogenic reactions to ASV.**

### ASV Dosage

In the absence of definitive data on the level of envenomation, such as provided by ELISA testing (Greenwood et al, 1974; Theakston et al, 1977; Ho et al, 1986), symptomology is not a useful guide to the level of envenomation. Any ASV regimen adopted is only a best estimate. What is important is that a single protocol is established and adhered to, in order to enable results to be reliably reviewed.

This suggests that the total required dose will be between 10 vials to 25 vials as each vial neutralises 6mg of Russell's Viper venom. Not all victims will require 10 vials as some may be injected with less than 63mg. Not all victims will require 25 vials. However, starting with 10 vials ensures that there is sufficient neutralising power to neutralise the average amount of venom injected and during the next 12 hours to neutralise any remaining free flowing venom. If the biting snake is identified to be a Saw Scaled Viper, 5 vials may be given as a starting dose. Otherwise in all cases, starting dose remains 10 vials.

Detect remaining free flowing Viper venom by 20WBCT at 6 hours from completion of first dose of 10 vials of ASV, additional 2<sup>nd</sup> dose can be given after six hours from the 1<sup>st</sup> dose.

There is no evidence that shows that low dose strategies (Paul et al, 2004; Srimannanarayana et al, 2004; Agrawal et al 2005) have any validity in India. These studies have serious methodological flaws: the randomization is not proper, the allocation sequence was not concealed, the evaluators were not blinded to the outcome; there was no a priori sample size estimation, and the studies were underpowered to detect the principle outcome.

The same problem relates to high dosage regimens (Wallace, 2004), often based on Harrison's textbook of medicine, which was written specifically for U.S. snakes and not intended for use in the developing world.

In an attempt to guide physicians, where possible, maximum dose levels have been provided. The amount of snake venom, injected by the snake is not infinite; it will have an upper range. There is a tendency amongst physicians to believe that more ASV is better, and to continue using ASV past the

point where the amount of ASV given is in excess of the maximum amount of venom possible (Bhat 1974). This is both wasteful of resources and expensive.

For neuroparalytic snakebite – ASV 10 vials stat as infusion over 30 minutes followed by 2<sup>nd</sup> dose of 10 vials after 1 hour if no improvement within 1<sup>st</sup> hour.

**For vasculotoxic snakebite** - Two regimens low dose infusion therapy and high dose intermittent bolus therapy can be used. Low dose infusion therapy is as effective as high dose intermittent bolus therapy and also saves scarce ASV doses (Adopted).

**Low Dose infusion therapy** – 10 vials for Russell’s viper or 6 vials for Saw scaled viper as stat as infusion over 30 minutes followed by 2 vials every 6 hours as infusion in 100 ml of normal saline till clotting time normalizes or for 3 days whichever is earlier.

**Or**

**High dose intermittent bolus therapy** - 10 vials of polyvalent ASV stat over 30 minutes as infusion, followed by 6 vials 6 hourly as bolus therapy till clotting time normalizes and/or local swelling subsides.

**No ASV for Sea snakebite, confirmed Green Pit snakebite even if with signs of envenomation as available ASV do not contain antibodies against them.**

The recommended dosage level has been based on published research that Russell’s Viper injects on average 63mg SD 7 mg of venom (Tun Pe, 1986). Logic suggests that initial dose should be calculated to neutralise the average dose of venom injected. This ensures that the majority of victims should be covered by the initial dose and keeps the cost of ASV to acceptable levels. The range of venom injected is 5mg – 147 mg by a Russell’s viper. The total required dose range between 10 and 30 vials as each vial neutralizes 6 mg of Russell’s Viper venom. Depending on the patient condition, additional vials can be considered.

### **ASV dosage in victims requiring life saving surgery**

#### **Initial Dosing Exceptions**

A major exception to the initial dosing guidelines is in the case of need for vital life saving surgery to resolve a serious complication of snakebite. For example, in the case of intracranial bleed, with a requirement for surgery to remove the clot, it is vital to restore coagulation. In such cases before surgery coagulation must be restored to avoid catastrophic bleeding and higher initial dose of ASV (up to 30 vials) can be administered (A2). The initial dose is high therefore significant care needs to be taken to observe any adverse reactions due to the volume of protein being administered.



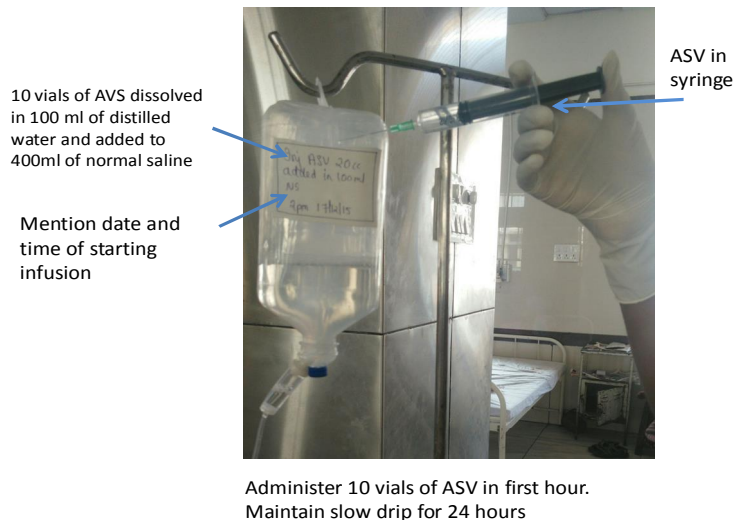


Figure 8. ASV infusion and dosage schedule Each vial of AVS be dissolved in 10 ml of distilled water and added to an infusion medium such as normal saline (i.e. 10 vials of AVS dissolved in 100 ml of distilled water and added to 400ml of normal saline). The volume of infusion is reduced according to the body size and the state of hydration of the patient. In oliguric patients restrict fluids and use infusion pump to give full dose of ASV over 30 minutes.

### What can ASV Do and more importantly what can it NOT Do?

It is vital to remember the capabilities and limitations of ASV if it is to be used effectively.

#### ASV Can

Bind to a venom molecule that it is effective against and neutralise that venom molecule rendering it unable to bind to the target cell but only whilst the venom molecule is circulating in the blood or lymph and is unbound.

ASV prevents the patient's condition from worsening by neutralising venom that otherwise could have bound and completed its damaging effect on the victim. It does not reverse anything nor does it make the patient better. The latter is the result of the body's normal functions, such as the liver replacing clotting factors, being able to return to normal by the elimination of the circulating venom.

#### ASV Cannot:

- 1) Reverse necrotic action of the venom on tissue
- 2) Reverse local swelling
- 3) Reverse renal failure
- 4) Reverse coagulopathy; the liver does this.
- 5) Reverse pre synaptic envenoming; the nerve damage is structural and large quantities of ASV are ineffective, the body must regenerate synaptic vesicles

- 6) Prevent local necrosis; the damage is done too quickly and the venom is in the tissue and therefore not reachable by the ASV (Gutierrez et al, 2007)
- 7) Prevent local swelling; the damage is done too quickly and the venom is in the tissue and therefore not reachable by the ASV (Gutierrez et al, 2007)

Some of these points should be obvious and yet they are frequently given as reasons for administering ASV.

### Swelling and ASV

The most controversial aspect of ASV use is in the case of swelling. The role of ASV in the case of swelling centres on whether:

1. Swelling can be controlled or reduced by ASV
2. Swelling is a useful criteria for administering ASV

### Swelling: Control or Reduction?

The proposed evidential support for ASV to be able to control swelling comes principally from the U.S.A. A number of studies purport to show that ASV has brought swelling under control (Heard et al, 1999; Thorson et al, 2003; Lavonas et al, 2004). These studies are not robust however, as they link the causal of administering ASV with the outcome of halted swelling: envenoming is a dynamic process and the halting of the swelling may be due to the fact that the oedema-causing portion of the venom is exhausted.

**Persistent swelling in Viper bites needs no more ASV after the clotting defect is cured. Surgical intervention may be needed to treat prolonged swelling.**

### Monitoring of Patients on ASV therapy

All patients should be watched carefully every 5 min for first 30 min, then at 15 min for 2 hours for manifestation of a reaction. At the earliest sign of an adverse reaction suspend temporarily. Maintain a strict intake output chart and note colour of urine to detect acute kidney injury early.

### 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).

Test doses have been shown to have no predictive value in detecting anaphylactoid or late serum reactions and should not be used (Warrell et al, 1999). These reactions are not IgE mediated but Complement activated. They may also pre-sensitise the patient and thereby create greater risk.

Skin or Conjunctival Test for ASV has been discarded in the WHO, 2010. A false negative Skin test may make the treating doctor reluctant to keep monitoring the patient for any adverse reaction to ASV.

### Victims who arrive late

Sometimes victims arrive late after the bite, often after several days, usually with acute kidney injury. Determine current venom activity such as bleeding in case of viperine envenomation. Perform 20WBCT and determine if any coagulopathy is present then administer ASV. If no coagulopathy is evident, treat kidney injury, if any.

In patients with neuromuscular envenomation (ptosis, respiratory failure etc.)

1. Continue respiratory support until recovery
2. Give 10 vials of ASV on arrival and if no improvement within one hour repeat 10 vials of ASV (No more than 20 vials of ASV).
3. No further ASV and Atropine Neostigmine (AN) infusion is required ONLY to reverse the Ptosis. Ptosis in Common Krait bite is due to presynaptic blockage, further ASV and Neostigmine dose beyond 3 doses cannot reverse it, since regeneration is a natural process and may take 4-5 days. Both ASV and AN injection should be stopped when the initial syndrome of pharyngeal muscle palsy is over.

### ASV and Pregnancy

There is little study data on snakebite during pregnancy, mainly due to the fact that much of the literature comes from developed countries where women working in rural areas whilst pregnant are rare. Snakebite during pregnancy is not common (Seneviratne et al, 2002; Sebe et al, 2005).

It is unclear if snake venom or components or ASV cross the placenta (Seneviratne et al, 2002).

The common expectation that snakebite invariably leads to spontaneous abortion of the foetus is not supported by available data. In one study in Sri Lanka, only 30% of victims aborted (Seneviratne et al, 2002). In the case of an envenomed victim, ASV is required to neutralise the unbound venom in the normal way. Where ASV is given there is good maternal outcome (Seneviratne et al, 2002).

The period of greatest risk appears to be during the first trimester and with cases of systemic envenoming, particularly with systemic bleeding and coagulopathy (Seneviratne et al, 2002).

This would indicate that wherever possible, patients in the first trimester, with systemic signs of envenomation particularly bleeding, should be referred to a gynaecologist for specialised review. In

cases of abortion this usually occurred within 7 days of the bite (Seneviratne et al, 2002).

### ***ASV dose in pregnancy***

Pregnant women are treated in exactly the same way as other victims. ASV should be given in the same dose and under the same criteria as standard victims. Refer the victim to a gynecologist for assessment of any impact on the foetus.

### **ASV in Paediatric victims**

There is often confusion as to the starting dose for children, which concentrates on their body size. It has been argued that children should receive less ASV due to their smaller body size or larger doses as their blood volume is less and therefore venom can spread faster.

The answer to this question lies in clearly understanding the role of ASV. Its function is to neutralise unbound venom, injected by the venomous snake. Snakes do not vary the amount of venom injected into children or adults and therefore the dose of ASV for children is **THE SAME** as that for adults.

**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.**

### ***ASV dose in children***

Children also are given exactly the same dose of ASV as adults as snakes inject the same amount of venom into children and adult.

Infusion: liquid or reconstituted ASV is diluted in 5-10 ml/kg body weight of normal saline. However, reduce amount of fluid in running bottle to 200 ml to avoid fluid over load.

### **ASV in Repeat bites**

It is rare for a patient to be bitten again, following a bite from a venomous species. Repeat bites, however, do carry a slight increased risk of adverse reaction to the ASV, as it has been administered previously. However, some professions like Herpetologists and snake charmers are prone to repeated venomous snakebite).

The dosage schedule for ASV in the event of a second bite is, however, unchanged. The same starting dose and repeat dose schedule as for a normal bite applies. If there is concern of an adverse

reaction due to a second administration of ASV, then a prophylactic regimen of adrenaline can be considered. Any reaction should be handled in the normal way.

## ASV REPEAT DOSE

### Repeat dose in vasculotoxic or haemotoxic envenomation

Repeat clotting test every 6 hours until coagulation is restored. Administer ASV every 6 h until coagulation is restored. Envenomation by the Hump-nosed Pit viper does not respond to normal Indian polyvalent ASV and coagulopathy may continue for up to 3 weeks. If 30 vials of ASV have been administered reconsider whether continued administration of ASV is serving any purpose, particularly in the absence of proven systemic bleeding. If large doses have been administered and the coagulation abnormality persists, give fresh frozen plasma (FFP) or cryoprecipitate (fibrinogen, factor VIII), fresh whole blood, if FFP or cryoprecipitate are not available.

### Repeat dose: neuromuscular or neurotoxic envenomation

ASV 10 vials stat as infusion over 30 minutes followed by 2<sup>nd</sup> dose of 10 vials if no improvement within 1<sup>st</sup> hour. Repeat 2<sup>nd</sup> dose may be required even after 2-3 hours if relapse of signs of neurotoxicity are noted (may be due to delayed absorption). Maximum dose is 20 vials of ASV for neurotoxically envenomed patients.

## Adverse Anti Snake Venom Reactions

The concept of adverse reactions to ASV has had a significant negative impact on snakebite treatment far in excess of the actual risk. Reported levels of ASV reactions have been very high, the risk of fatal anaphylactoid reactions stressed; with the result that doctors have been reluctant to treat victims (World Health Organisation, 1981; Warrell, 1993; Warrell, 1999; Ariaratnam et al, 2001; Warrell, 2003; Isbister et al, 2006; World Health Organisation, 2007; Simpson, 2008; Deshmukh et al, 2014; Deshpande et al 2013). These reactions however, if managed correctly can be easily treated in even the most basic medical facilities and moves for improvements in ASV quality need to be balanced with costs of so doing (Krifi et al, 1999).

**Early anaphylactic reactions** occurs within 10–180 min of start of therapy and is characterized by itching, urticaria, dry cough, nausea and vomiting, abdominal colic, diarrhoea, tachycardia, and fever. Minority of these patients may develop severe life-threatening anaphylaxis characterized by hypotension, bronchospasm, and angioedema (WHO 2015).

Any new sign or symptom after starting the ASV in drip should be suspected as a reaction to ASV such as vomiting, hot or cold feeling; sudden dry cough, new pain abdomen, dyspnoea; fall of BP and shock, swelling of face, conjunctiva and protrusion of the tongue due to angioedema.

**Pyrogenic reactions** usually develop 1–2 h after treatment. Symptoms include chills and rigors, fever, and hypotension. These reactions are caused by contamination of the ASV with pyrogens during the manufacturing process.

**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, immune complex nephritis and, rarely, encephalopathy. Patients who suffer early reactions that are treated with antihistamines and corticosteroids are less likely to develop late reactions. (WHO 2015)

### Mechanism of the Reaction

The specific mechanism responsible for generating adverse reactions is not clear.

1. Complement activation directly by the ASV proteins  
There is some evidence that ASV is able to activate complement in vitro (Sutherland, 1977; Leon et al, 2001; Leon et al, 2005)
2. Complement activation mediated by immune complexes

### Prediction of Adverse Reactions

A frequently used mechanism in response to ASV reactions is to try and predict them with the use of a ‘test dose’. An intra dermal test dose is administered to the victim, approximately 30 minutes is allowed to elapse and inspection is used to determine if any wheals are present indicating sensitivity.

Skin tests are widely used in testing for Type I hypersensitivity allergic reactions. They indicate high levels of IgE in the presence of a specific allergen. They are of no use in predicting ASV reactions for the following reasons:

1. They are non predictive – ASV reactions are complement activated and not mediated by IgG, they are also *de novo* reactions (Malasit et al, 1986; Gutierrez et al, 2007)
2. They waste time when the patient needs ASV
3. They may pre-sensitise the patient and make a severe reaction more likely when the major amount of ASV is administered.

**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.**

## Preventing Adverse Reactions

The use of prophylactic drugs to prevent adverse reactions to ASV is common. Despite the fact that developed country ASVs are often regarded as superior products, reaction rates of 25% or higher are reported when using these ASVs (Isbister et al, 2006; Isbister et al, 2008).

The prophylactic approach is based largely on two studies in Sri Lanka, which appeared to show that prophylactic doses of adrenaline or hydrocortisone and antihistamine prevented reactions (Premawardena et al, 1999; Gawarammana et al, 2004). No adverse reactions to the adrenaline were observed in this study. However, subsequent fatality (Dassanyake et al; 2002) raised concerns about intracranial bleeding (a known complication of systemic envenoming following bites by vipers, hypertension and arrhythmias, if adrenaline prophylaxis were to be used routinely especially in children, pregnant women and in patients with heart disease. Both these studies were statistically underpowered, with one stopping half way through the study as the results at that stage were regarded as good! Other poorly constructed retrospective studies also appear to support the use of premedication to prevent reactions (Williams et al, 2007). Other studies have shown no benefit to prophylactic regimens (Isbister et al, 2008)

Snake bite victims are anxious and have sympathetic overdrive in form of tachycardia hypertension excessive sweating, tachypnoea. Routine administration of adrenaline before ASV will lead to augmentation of this symptoms as well as hypertension. In patients with coagulation disorder this will lead to intracerebral bleed. In Indian scenario routine adrenaline is contraindicated in known hypertensive, cardiac disease patients, and if patient presents with blood pressure more than 140/90 in adult victim.

A study in Brazil indicated that antihistamine alone was not effective in preventing reaction (Wen-Fan et al, 1999). Systematic analysis by Habib 2011 reported a substantial beneficial effect of adrenaline pre-medication, but a marginal benefit with the combination of pre-medications used against early adverse reactions could not be excluded. Future studies are recommended and they should explore possible synergism of broader combinations of drugs and effects of mode of antivenom administration in large randomized controlled trials. Meanwhile, highly purified antivenoms with less risk of early anaphylaxis reaction should be made available in the rural tropics.

**Routine use of prophylactic adrenaline is recommended before ASV, except in known hypertensive, and if patient presents with blood pressure more than 140/90 in adult victims or if evidence of suspicion of underlying cardiovascular disease. The adult dose of adrenaline (epinephrine) is 0.25 mg of 0.1% solution by subcutaneous injection (Children 0.005 mg/kg body weight of 0.1% solution).**

**Use of histamine, anti-H1 and anti-H2 blockers, corticosteroids and the rate of intravenous infusion of antivenom between 10 and 120 minutes), do not affect the incidence or severity of early antivenom reactions. (WHO 2015; deSilva 2011; Habib 2011) 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]. WHO**

## **Treatment of Adverse Reactions**

ASV reactions are straightforward to manage if:

1. They are identified early
2. They are treated immediately
3. They are treated with the drug of choice
4. The correct mode of administration of the drug is used
5. Correct reassessment period is used

### **Step 1: Identified Early**

Many ASV reactions pass unnoticed as the doctor is not actively looking for them. Local experience with the ASV will almost certainly establish an average time to onset of the reaction. For example, with Indian ASVs the average onset time for reactions is 20 minutes (Kochar et al, 2007). This is a key period to examine the patient carefully, particularly across the trunk, as this is where reactions are first evident. A useful technique is to shine a torch across the trunk as this casts the urticaria in shadow.

### **Step 2: Treated Immediately**

At the first sign of a reaction, stop the ASV. The first signs include a single patch of urticaria or any itching. Often the patient will become restless just before these signs and symptoms manifest. Other symptoms are vomiting, hot or cold feeling; sudden dry cough, new pain abdomen, dyspnoea; fall of BP and shock, swelling of face, conjunctiva and protrusion of the tongue due to angio-oedema.

### **Step 3: Drug of Choice**

Administer Epinephrine (adrenaline) (1 in 1,000 solution, 0.5 mg (i.e. 0.5 ml) in adults **intramuscular over deltoid or over thigh**; In children 0.01 mg/kg body weight) for early anaphylactic and pyrogenic ASV reactions. Ideally 2 syringes should be drawn up ready if the ASV is known to cause frequent reactions.

Administer Chlorpheniramine maleate (adult dose 10 mg, in children 0.2 mg/kg) intravenously.

### **Step 4: Correct Mode of Administration**

The critical factor in managing ASV reactions is speed! The longer the reaction persists, the longer



will be the period the victim is without ASV and the more venom will be permitted to bind to the target cells. Therefore speed of effect of adrenaline is critical.

The mode of administration therefore is **intramuscular (IM)**. The deltoid muscle is the best site (American Association of Allergy, Asthma, and Immunology, 2003; McClean-Tooke et al, 2003; Simons et al, 2001).

The time for adrenaline to reach peak effect is 8 minutes via the IM route and 34 minutes via the subcutaneous route (Simpson, 2007). Despite a preponderance of doctors who would use the subcutaneous route, IM is the first option (Simons et al, 2001; Simpson, 2008).

In extremely rare, severe life threatening situations, 0.5mg of 1:10,000 adrenaline can be given IV. This carries a risk of cardiac arrhythmias however, and should only be used if IM adrenaline has been tried and the administration of IV adrenaline should be carried out in the presence of ventilatory equipment and ICU trained staff.

### **Step 5: Correct Reassessment Period**

Once the initial dose of adrenaline is given IM, the patient is closely monitored. Around 3 minutes, the patients pulse rate should begin to increase confirming the drug was correctly administered IM. At 8 minutes, the adrenaline will reach peak levels and at this stage 5-7 minutes are spent examining the patient for signs of improvement. If none are evident or the patient's condition has worsened, a second dose is administered IM. In very rare cases, a third dose may be necessary. (expert consensus).

The majority of patients will respond to a single dose, the remainder will respond to the second dose. Using the IM route it is possible to administer 2 doses of adrenaline in the same time, as it would take a single dose of subcutaneous adrenaline to reach peak effect.

After adrenaline, Promethazine HCl 25mg IM (children 0.5mg/kg/ day IV or Promethazine HCl can be used at 0.3-0.5mg/kg IM, or Chlorpheniramine maleate 10mg (children 0.2 mg/kg by IV injection over a few minutes and f hydrocortisone 100mg (children 2mg/kg) IV but is unlikely to act for several hours. Corticosteroids do not reduce the risk of recurrence (biphasic anaphylaxis). (WHO 2015)

**Once the patient has recovered the ASV can be restarted slowly for 10-15 minutes keeping the patient under close observation. Then the normal drip rate should be resumed. (WHO 2015)**

Late Serum sickness reactions can be easily treated with an oral steroid such as prednisolone, adults 5mg 6 hourly, paediatric dose 0.7mg/kg/day. Chlorpheniramine 2 mg 6 hourly orally (children 0.25 mg/kg/day in divided doses).

### **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.

These high risk patients may be pre-treated with subcutaneous epinephrine (adrenaline) 0.25 mg of 0.1% solution just before antivenom treatment is started followed by an intravenous antihistamines (both anti-H<sub>1</sub>, such as promethazine or chlorpheniramine; and anti-H<sub>2</sub>, such as cimetidine or ranitidine) and corticosteroid. In asthmatic patients, prophylactic use of an inhaled adrenergic  $\beta_2$  agonist such as salbutamol may prevent bronchospasm (de Silva et al, 2011).

### For high risk patients

In patients with history of hypersensitivity or exposure to animal serum such as equine ASV, tetanus-immune globulin or rabies-immune globulin in past, severe atopic conditions:

14. Give ASV only if they have signs of systemic envenoming.
15. Subcutaneous epinephrine (adrenaline) 0.25 mg of 0.1% solution to be given just before antivenom treatment is started
16. Give Inj. Hydrocortisone 200 mg and Chlorpheniramine maleate 22.75 mg prior to the administration of ASV.

### Treatment of Late (serum sickness–type) reactions

Inj. Chlorpheniramine 2 mg in adults (In children 0.25 mg/kg/day) 6 hourly for 5 days.

In patients who fail to respond within 24–48 h give a 5-day course of Prednisolone (5 mg 6 hourly in adults and 0.7 mg/kg/day in divided doses in children).

### Desensitization procedure only in case of severe anaphylaxis reaction to ASV

- Desensitization protocol is needed rarely in patients who develop severe anaphylaxis with shock and generalised anasarca after injection of very few ml of ASV usually less than 5 ml of diluted ASV. This protocol takes 3 - 4 hours and should be reserved for exclusively such patients.
- Change the batch of ASV.

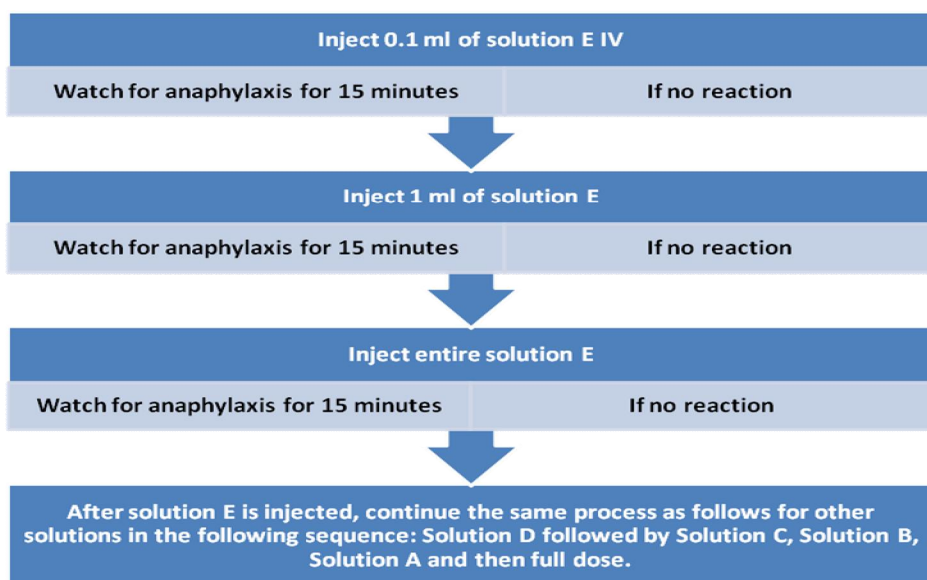
Pre-medication: Administer Inj. Hydrocortisone 100 mg I.V. and Inj. Adrenaline 0.5 ml subcutaneously/ intramuscularly ( $\pm$  Promethazine)

Table . Steps of dilution of ASV

Steps of dilution	Instructions	Total Volume	Solution	Dilution

1.	Dilute 1 ml of ASV in a vial with 10 ml of normal saline	10ml	A	
2.	1ml of solution A + 9 ml of saline	10 ml	B	1: 10
3.	1ml of solution B+ 9 ml of saline	10 ml	C	1: 100
4.	1ml of solution C + 9 ml of saline	10 ml	D	1: 1000
5.	1ml of solution D + 9 ml of saline	10 ml	E	1: 10,000

After dilution and preparation of Solution E,



### Observation of the response to ASV

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

*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.

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

*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.

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

*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.

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

Red colour urine may persist for several days in spite of adequate ASV treatment due to damage of Renal papillae, no further ASV can help).

### **ASV in 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:

- 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')<sub>2</sub> 80-100 hours; Fab 12-18 hours) (Ho et al., 1986; Ho et al., 1990)
- 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.

When coagulation has been restored no further ASV should be administered, unless a proven recurrence of a coagulation abnormality is established. There is no need to give prophylactic ASV to prevent recurrence (Srimannarayana et al, 2004). Recurrence has been a mainly US phenomenon, due to the short half-life of Crofab ASV. Indian ASV is a F(ab)<sub>2</sub> product and has a half-life of over 90 hours and therefore is not required in a prophylactic dose to prevent re-envenomation.

Evidence suggests that ‘reversibility’ of pre synaptic neurotoxic envenoming is only possible in the first few hours. After that the body recovers by using its own mechanisms. Large doses of ASV, over long periods, have no benefit in reversing envenomation.

Confusion has arisen due to some medical textbooks suggesting that ‘massive doses’ of ASV can be administered, and that there need not necessarily be a clear-cut upper limit to ASV’ (Pillay, 2005). These texts are talking about snakes which inject massive amounts of venom, such as the King Cobra or Australian Elapids. There is no justification for massive doses of 50+ vials in India (Agrawal et al, 2001), which usually result from the continued use of ASV whilst the victim is on a ventilator.

***No further doses of ASV are required; unless a proven recurrence of envenomation is established, additional vials to prevent recurrence is not necessary.***

#### **Facts to be remembered while administering ASV (Tamil Nadu)**

1. ASV is available in a polyvalent form and marketed in liquid or lyophilised preparations in 10ml vial / ampoule.
2. Remember to use and maintain cold chain system for liquid form. Users are informed to ascertain whether the cold chain is maintained.
3. There is no dose adjustment for ASV administration for children.
4. Before administering ASV, health staff should read and check the status of vial or ampoule containing ASV.
5. Elicit history of prior exposure to ASV. If a patient had received ASV earlier and comes back with features of snake envenomation again, he / she has to be considered as a fresh case and treated accordingly. However, care should be taken while administering ASV, since he / she has been sensitised.
6. ASV treatment should be initiated with readiness with adequate agents for managing anaphylaxis or anaphylactoid reaction.
7. Anaphylactic or late serum sickness cannot be determined or prevented by test dose. Therefore, do not administer ASV test dose.
8. ASV neutralises the unbound venom, hence give it early.
9. **ASV administration should not be delayed or denied on the grounds of anaphylactic reactions to a deserving case.**
10. ASV is required only in those who show definite signs and symptoms of envenomation.
11. ASV can be administered slowly as IV infusion or high dose intermittent bolus in normal saline. No local administration of ASV at the site of bite as it has been proven to be ineffective and painful, and raises the intra-compartmental pressure, particularly in the digits.
12. Give premedication with Epinephrine by SC route except in hypertensive and cardiovascular disease patients.

## **14. NEUROTOXIC ENVENOMATION**

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

Neostigmine is an anticholinesterase that prolongs the life of acetylcholine and can therefore reverse respiratory failure and neurotoxic symptoms. It is particularly effective for post synaptic neurotoxins such as those of the Cobra (Watt et al, 1986). There is some doubt over its usefulness against the pre-synaptic neurotoxin such as those of the Krait and the Russell's viper (Warrell et al, 1983; Theakston et al, 1990). However it is worth trying in these cases.

1. In all cases of neurotoxic envenomation the 'AN challenge Test' is administered, ***Do not give AN in case of confirmed krait bite.***

Atropine 0.6 mg followed by neostigmine (1.5mg) to be given IV stat and repeat dose of neostigmine 0.5 mg with atropine every 30 minutes for 5 doses (In children, Inj. Atropine 0.05 mg/kg followed by Inj. Neostigmine 0.04 mg/kg **Intravenous** and repeat dose 0.01 mg/kg every

30 minutes for 5 doses). A fixed dose combination of Neostigmine and glycopyrolate IV can also be used.

Thereafter to be given as tapering dose at 1 hour, 2 hour, 6 hours and 12 hour. Majority of patients improve within first 5 doses. Observe the patient closely observed for 1 hour to determine if the neostigmine is effective. After 30 minutes, any improvement should be visible by an improvement in ptosis. Positive response to “AN” trial is measured as 50% or more recovery of the ptosis in one hour.

Stop Atropine neostigmine (AN) dosage schedule if:

- a) Patient has complete recovery from neuromuscular paralysis. Rarely patient can have recurrence, carefully watch patients for recurrence.
- b) Patient shows side effects in the form of fasciculations or bradycardia.
- c) If there is no improvement after 3 doses.

Improvement by atropine neostigmine indicates Cobra bite. A few Nilgiri Russell’s viper bites victims also improve with this regimen.

Give one dose of “AN” injection before transferring to the higher centre. Rapid deterioration of Cobra bite neurotoxic syndrome may kill the patient on the way to transfer.

If there is no improvement after 3 doses of atropine neostigmine, this indicates probable Krait bite. Krait affects pre-synaptic fibres where calcium ion acts as neurotransmitter. Give Inj. Calcium gluconate 10ml IV (in children 1-2 ml/kg (1:1 dilution) slowly over 5-10 min every 6 hourly and continue till neuromuscular paralysis recovers which may last for 5-7 days.

**A trial of anticholinesterase (“AN 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.**

Some authors have suggested that it may be possible to treat patients with anticholinesterase drugs solely, in the case of elapid bites (Bomb et al, 1996). However this approach ignores the value of neutralising the free flowing venom before it can attach and require reversing. Anticholinesterase drugs being used, as a substitute for ASV should only be considered if no ASV is available (Bomb et al, 1996). The more venom that can be neutralised before it binds to target receptors reduces the severity of the envenomation (A2)

In case of Cobra bite, if the patient attends a small centre where indoor admission facility is not available; one dose of “AN” injection should be given before transferring to the next indoor centre. Rapid deterioration of Cobra bite neurotoxic syndrome may kill the patient on the way to transfer. This is applicable in emergency Ambulance service for Snakebite also.

## Airway Support Items

In the case of unconscious patients suffering from neurotoxic envenoming death may result from aspiration, airway obstruction or respiratory failure. In the vast majority of cases, if the patient's breathing is maintained, they will survive. The critical period is usually the journey from the initial contact with medical care to the more advanced hospital with mechanical ventilation. 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 (LMA) should be inserted. If this is impossible for any reason, a tracheostomy should be performed and a snugly-fitting or cuffed tracheostomy tube inserted.

All the Medical Officers posted in the Rural Health centres must have training (induction training after posting) on Endotracheal intubation. All the Ambulances and Rural Health Centres must have 2-3 LMA in stock).

*Training at Poison Control Centre at Madras Medical College could be a Model for each state.*

**Although artificial ventilation was first suggested for neurotoxic envenoming 140 years ago, patients continue to die of asphyxiation because some doctors believe that antivenom alone is sufficient treatment (WHO 2015).**

If treating the patient in a peripheral hospital with no access to mechanical ventilation, the patient's inability to perform a neck lift will trigger referral to a better-equipped hospital. The patient, either conscious or unconscious will require airway support on the journey, as that is where respiratory failure is likely to occur. A number of options are available.

In many primary care hospitals facilities are basic and airway support equipment is limited. Usually the equipment consists of a resuscitation bag alone, which can be used to maintain a victim's air supply in the short term. Family members or friends can be instructed in the use of this equipment should it become necessary on the journey. The important points to communicate are that the mask should be placed over both the nose and mouth in a rolling manner starting at the bridge of the nose. Preferably, bag-valve-mask ventilations are given using the "C-E" grips [thumb and index finger of each hand forming a "C" over top of the mask and long, ring and little fingers forming an "E" under the jaw – pressing the mask onto the face]. The bag should be squeezed at a specific cadence of "squeeze – release – release." This method ensures the victim receives a good quantity of air but also allows time for exhalation.

However, in cases of neurotoxic envenomation, if respiratory failure occurs it will be due to flaccid paralysis and there is a strong likelihood that the tongue will fall back and obstruct the airway. The effective functioning of a resuscitation bag in these circumstances will be highly limited. Nasopharyngeal airway (NPA) support is an excellent emergency measure in these situations (Bajaj et al, 2008). If available, NPAs should be inserted before transportation to the referral hospital, which will dramatically increase the probability of effective respiratory support during the journey.

It is possible however to improvise nasopharyngeal tubes (NT) from endotracheal tubes (ET), which are usually readily available or can be obtained easily. Two rubber or plastic size 6.5 ET tubes for females, size 7 for males or size 5 for either can be adapted to provide NT (Roberts et al, 2005). The tubes are cut to the distance between the nostril and the tragus, lubricated and inserted into the nostrils of a conscious or unconscious patient (Quraishi et al, 2008; Simpson and Jacobsen, 2009).

Cut to the correct length they will not trigger the gagging reflex and thus can be used when a patient is conscious (Simpson and Jacobsen, 2009). In the event that a patient cannot perform a neck lift and is to be transferred to a better-equipped hospital, the tubes can be inserted and the individuals accompanying the victim instructed to use the resuscitation bag if the victim stops breathing (Simpson and Jacobsen, 2009).

### **Bridging Devices**

An improved solution is the use of an airway-bridging device such as a laryngeal tube (LT) or laryngeal mask airway (LMA) (Simpson, 2007). These devices are not “definitive” airways (defined as a cuffed endotracheal tube positioned below the vocal cords), but provide excellent airway support. They are inserted blindly and give a very high percentage possibility of being inserted correctly (Bailey and Hett, 1994; Springer and Jahr, 1995; Pollack, 2001; Murphy, 2004; Murphy and Schneider, 2004; Wiese et al, 2008).

Use of such airways by accompanying laypersons has not been studied, but it is very possible that the lay provider can adequately ventilate the unconscious victim during transfer using a properly placed laryngeal tube. The creation of a better seal makes the use of an LT tube more preferable over rough journeys experienced when transporting snakebite victims in many developing countries (Ocker et al, 2002; Gaitini et al, 2008)

Use of the LMA requires greater skill in maintaining proper positioning, making it a less optimal choice for use by untrained individuals.

### **The Ideal Solution**

The ideal solution is the ability to endotracheally intubate the victim and provide a definitive airway defined as placing a cuffed tube below the vocal chords (Akram et al, 2004). However, in primary care centres in many developing countries, the equipment is unavailable and doctor confidence in performing intubation is not high (Simpson, 2007; Simpson and Jacobsen, 2009).

The endpoint therapy will be a mechanical ventilator to provide long-term respiratory support. In presynaptic envenoming, the period of ventilation may be extensive whilst the body restores synaptic vesicles.

However, in developing countries, where such facilities are limited, an improvised or bridging solution is necessary to ensure the victim survives the inevitable journey. Developed world derived protocols advising endotracheal intubation or tracheostomy, once loss of the gag reflex or pooling



of secretions occurs is simply impractical in most developing world facilities (Warrell, 1999; Simpson and Jacobsen, 2009).

## **15. HAEMOTOXIC ENVENOMATION, BLOOD PRODUCTS AND RENAL IMPAIRMENT**

The presence of systemic bleeding with or without hypotension is a common feature of snakebite, particularly in the case of viperine bites.

Hypotension, severe reductions in haemoglobin concentration, platelet reductions i.e. thrombocytopenia, or frank bleeding can increase the pressure to administer blood related products.

Hypotension due to action of the venom can have a number of causes in snakebite, ranging from loss of circulating volume due to haemorrhaging, vasodilation due to the action of the venom or direct venom effects on the heart.

Test for hypovolaemia by examining the blood pressure lying down and sitting up, to establish a postural drop.

In the majority of cases the timely use of ASV will stop systemic bleeding. However in some cases the bleeding may continue to a point where further treatment should be considered.

1. Strict bed rest to avoid even minor trauma.
2. Screen for hematuria, hemoglobinuria, myoglobinuria by Dipstick method. Dipstick test is positive in all three presentations listed above. Centrifuged urine showing pink colour indicates hemoglobinuria, clear supernatant (RBCs settle down as deposit) indicates myoglobinuria.
3. Closely monitor urine output and maintain 1 ml/kg/h urine output.
4. Volume Replacement in snake bite: 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 sterna angle (with the patient propped up at 45°). Observe the patient closely while this is being done. The fluid challenge must be stopped immediately if pulmonary oedema develops.

In cases where generalised capillary permeability has been established a vasoconstrictor such as dopamine can be used. Dosing is 2.5- 5µg/kg/minute.

Treatment is by means of plasma expanders and raising the foot of the bed. There is no conclusive trial evidence to support a preference for colloids or crystalloids. In addition fresh frozen plasma or factors present a possibility in order to boost volume and restore factors. In many areas, particularly in developing countries, the only available alternative will be fresh blood.

## Persistent or Severe bleeding

In the majority of cases the timely use of ASV will stop systemic bleeding. However in some cases the bleeding may continue to a point when further treatment should be considered. The major point to note is that clotting must have been re-established before additional measures are taken. Adding clotting factors, FFP, cryoprecipitate or whole blood in the presence of un-neutralised venom will increase the amount of degradation products with the accompanying risk to the renal function (White, 2005).

### Role of Anticoagulants

When there are signs of current bleeding such as bleeding from the gums, there is the intuitive thought that coagulants can play a role in inhibiting bleeding. For example, drugs such as Botropase, a coagulant, are sometimes used in response to visible bleeding. It is however, a compound derived from the venom of one of two South American pit vipers both of which cause coagulation by activating the clotting cascade. It uses the same means to achieve coagulation as the snake concerned in the envenomation and should not be used in viper bites as it simply prolongs the coagulation abnormality by causing consumption coagulopathy in the same way. Other drugs such as heparin have been intuitively thought to be beneficial in snakebite induced coagulation and DIC and apparently supported but by very weak research (Paul et al, 2003; Paul et al, 2008). However, like much of what is intuitively recommended in snakebite, heparin is contraindicated. Venom induced thrombin is resistant to Heparin, the effects of heparin on antithrombin III are negated due to the elimination of ATIII by the time heparin is administered and in itself heparin can cause bleeding. In the case of trial evidence, heparin has been shown to have no beneficial effect (Tin et al, 1992; White, 2005).

**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.

### 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.

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.

**Arterial puncture is contraindicated in such patients.**

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.

### **Longer Term Issues**

Russell's Viper bites are known to cause acute pituitary adrenal insufficiency (Tun Pe et al, 1987 ; Eapen et al 1976). This condition may contribute to shock. Follow-up checks on known Russell's Viper victims need to ensure that no long term pituitary sequelae are evident.

### **Renal Failure**

Renal failure is a common complication of species such as Russell's Viper. The contributory factors are intravascular haemolysis, DIC, direct nephrotoxicity and hypotension and rhabdomyolysis (Chugh et al, 1975; Shastry et al, 1977; Than-Than et al, 1989). The contributory factors are intravascular haemolysis, DIC, direct nephrotoxicity and hypotension (Chugh et al, 1975) and rhabdomyolysis.

Renal damage can develop very early in cases of Russell's viper bite and even when the patient arrives at hospital soon after the bite, the damage may already have been done. Studies have shown that even when ASV is administered within 1-2 hours after the bite, it was incapable of preventing ARF (Myint-Lwin et al, 1985).

Declining renal parameters require referral to a specialist nephrologist with access to dialysis equipment. Peritoneal dialysis could be performed in secondary care centres. Haemodialysis is preferable in cases of hypotension or hyperkalaemia.

### **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.

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 45°). 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 a recent case in CNMC&H

where Creatinine was 4mg/dl; this challenge test worked successfully to avoid Dialysis in a 45 y old female bitten by Russell's viper.

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, 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 45°). 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. If the patient has oliguria or dipstick positive for blood give a trial of forced alkaline diuresis (FAD) **within first 24 hours of the bite** to avoid pigment nephropathy leading to acute tubular necrosis (ATN). **Delayed FAD has no role.** Sequence of FAD in adults is as follows:
  - a) Inj. Frusemide 40 mg IV stat
  - b) Inj. Normal saline 500 ml + 20 ml of NaHCO<sub>3</sub> over 20 minutes
  - c) Inj. Ringer's lactate 500 ml + 20 ml of NaHCO<sub>3</sub> over 20 minutes
  - d) Inj. 5% dextrose 500 ml + 10 ml of Potassium Chloride over 90 minutes
  - e) Inj. Mannitol 150 ml over 20 min

Whole cycle completes in 2 h 30 min and urine output of 3 ml/min is expected. **If patient responds to first cycle continue for 3 cycles.** FAD converts oliguria into polyuria and avoid ATN and acute kidney injury needing dialysis in more than 75% patients.

**If there is no response to furosemide discontinue FAD** and refer patient immediately to a higher center for dialysis.

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
  - A. Give 10 ml of 10% calcium gluconate intravenously over 2 minutes (with ECG

- monitoring if possible) repeated up to three times
- B. Give 50 ml of 50% dextrose with 10 units of soluble insulin intravenously
  - C. Sodium bicarbonate (40 ml of 8.4%) by slow intravenous infusion
  - D. A  $\beta_2$  agonist aerosol by inhaler (e.g. salbutamol 5-10 mcg) 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 snakebite 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:** Indications for dialysis
- (a) Absolute value of Blood urea >130 mg/dl (27 mmol/L) (BUN 100 mg/dl), Sr. Creatinine > 4 mg/dl (500  $\mu$ mol/L) OR evidence of hypercatabolism in the form of daily rise in blood urea 30 mg/dL (BUN > 15), Sr. Creatinine > 1 mg/dL, Sr. Potassium > 1 mEq/L and fall in bicarbonate >2 mmol/L
  - Fluid overload leading to pulmonary oedema
  - Hyperkalaemia (>7 mmol/l (or hyperkalaemic ECG changes)
  - Unresponsive to conservative management.
  - Uremic complications – encephalopathy, pericarditis. nausea, vomiting, hiccups, fetor, drowsiness, confusion, coma, flapping tremor, muscle twitching, convulsions, pericardial friction rub, signs of fluid overload.

### Prevention of renal damage in patients with myoglobinuria or haemoglobinuria

#### To minimize the risk of renal damage from excreted myoglobin and/or haemoglobin (WHO 2015):

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)

### 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.

### 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.

### 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. PAIN, WOUND MANAGEMENT AND THE SURGICAL ASPECTS OF SNAKEBITE

### Pain and Wound Management

Snakebite is painful! The action of the spreading factor and tissue damaging toxins in the venom can cause significant pain at the bite site and in the bitten limb. Pain relief is a vital but often overlooked aspect of snakebite management.

The drug of choice is Paracetamol, Adult dose of 500-1000mg 4-6 hourly. Paediatric dose 10mg/kg every 4-6 hourly orally.

If available, mild opiates such as Tramadol, 50 mg can be used orally for relief of severe pain. In cases of severe pain at a tertiary centre, Tramadol can be given IV. **Aspirin should not be used** due to its adverse impact on haemostasis due to inhibition of platelet aggregation. Do not use non-steroidal anti-inflammatory drugs (NSAIDs) as they can cause bleeding. This can be particularly dangerous in a patient already having coagulopathy.

### Antibiotics and Tetanus

There are many factors that contribute to potential infection in snakebite, including poor or dangerous first aid, oral snake flora and environmental factors (Ehui et al, 2007; Habib, 2003). There has been considerable confusion concerning the role of antibiotics in snakebite management. Some texts have argued for routine prophylaxis with antibiotics, due to the bacterial content of the snakes mouth and saliva, others have argued against routine prophylaxis, reserving antibiotics for use only where local necrosis is present (Blaylock, 2001).

In cases where the victim has cut the wound or in cases of necrosis, antibiotic use is advised (Blaylock, 1999). Where wound infection is suspected give prophylactic broad-spectrum antimicrobial treatment for cellulitis after completion of first 10 vials of ASV) with following.

1. Inj. Amoxicillin+ clavulanic acid 1.2 g IV thrice daily for first 7 days then switch to oral therapy Tab. Amoxicillin+clavulanic acid 625 mg three times a day for further 3-7 days; In children, the dose is 100 mg/Kg/day in three divided doses intravenously; for oral therapy, the dose is 50 mg/kg/day in three divided doses.
2. Inj. Metronidazole 400 mg IV infusion thrice daily for 7 days; in children- 30 mg/kg/day in 3-4 divided doses.

Alternatively Inj Ceftriaxone 1 g IV twice daily (in children the dose is 100 mg/kg/day in two divided doses)for 7 days. Both Amoxicillin+ clavulanic acid and Ceftriaxone are mainly excreted through Kidney. Therefore, in case of acute kidney injury in Viper bites dose of both these antibiotics should be reduced and adjusted according to renal function.

Tetanus booster doses, if not immunized already should be given although these can be delayed until coagulation is restored in cases with incoagulable blood. In many areas tetanus inoculation will not be thorough and tetanus toxoid should thus be given.

## **17.SNAKE VENOM OPHTHALMIA**

Sometimes Naja Kouthia venom may spit into the eye of a careless snake handler while handling a Naja kouthia holding it close to the face. This venom is directed at the eyes and causes extreme pain and conjunctivitis.

### **Management of venom ophthalmia**

1. Urgent decontamination by copious irrigation with drinking water
2. Instill topical 0.5% adrenaline in the eye
3. Topical administration of local anaesthetics – Tetracaine or Proparacaine HCl. Exclude corneal abrasions by fluorescein staining with a slit-lamp examination and application of prophylactic topical antibiotics Moxifloxacin eye drops 6 times a day
4. Prevent posterior synechiae, ciliary spasm and discomfort with topical cycloplegics–
5. Antihistamines in case of allergic keratoconjunctivitis.

Topical or intravenous antivenom and topical corticosteroids are contraindicated. Corneal injury should be managed by an Ophthalmologist only.

### **Surgery and Snakebite**

Surgical interventions are a contributory factor in resolving snakebite but must be used with caution. In developing countries surgical procedures can be carried out unnecessarily based on reliance on developed world approaches. Some interventions are necessary and should be deployed

when required such as life saving procedures and removal of necrotic tissue. Others such as fasciotomy should be used sparingly and under much defined conditions.

Skin grafting and amputation of a necrotic digit may be required in some cases of snakebite. These cases should be referred to the surgeon after completion of antivenom treatment. Surgical interventions in these cases are in the general principles of surgery, not much related with Anti venom therapy.

### **Life Threatening Conditions Requiring Surgery**

A particularly serious consequence of snakebite is intra cranial bleeds. These frequently result in mortality and perhaps represent the worst of all complications. Key to survival is surgical intervention to remove the clot and thereby relieve pressure within the cranial cavity. Before surgery can take place coagulation must be restored rapidly and thus a very larger initial dose of ASV is given in excess of the normal dosage levels in order to ensure restoration of coagulation within a 6-hour period.

It is recognised that this large initial dose may be in excess of the required amount to achieve neutralisation of the venom. The critical point here is that coagulation must be definitively restored in the shortest period i.e. 6 hours, and thus the risk of exceeding the required amount is acceptable to ensure life saving surgery can take place.

### **Debridement of Necrotic Tissue**

Local and extensive necrosis resulting from venom action may necessitate debridement of necrotic tissue. The necrotic area should be kept clean and topical agents can be applied (Anindhya et al, 2004).

In most rural settings the victim will need referral to a facility that can perform surgery and is equipped with a surgeon.

It is worth waiting 5-7 days before commencing a debridement of necrotic tissue in order that the line of demarcation between viable and non-viable tissue can be specified (Blaylock, 2005)

## **18.COMPARTMENT SYNDROME**

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.

#### **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.

Compartment syndrome is a widely used concept in snakebite and is undoubtedly overused in many areas. The sight of the '6 Ps':

- Pain on passive stretching
- Pain out of proportion
- Pulselessness
- Pallor
- Parasthesia
- Paralysis

6 Ps with significant swelling in the limb, can lead to the conclusion that the intracompartmental pressure is above 40 mm of mercury and thus requires a fasciotomy. 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.

Avoid surgical intervention unless intracompartmental pressure is sufficiently high to cause blood vessels to collapse and lead to ischemia. Fasciotomy does not remove or reduce any envenomation.

#### **Criteria for fasciotomy in snake-bitten limbs (WHO)**

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

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

There is little objective evidence that the intracompartmental pressure due to snakebite in India, ever reaches the prescribed limit for a fasciotomy. Very limited trial data has tended to confirm this. In a small case study in India, using a Stryker monitor, despite grossly swollen limbs, which matched the 6Ps, only one case from 12 achieved an intracompartmental pressure where fasciotomy would be considered. By the time coagulation was restored in the victim, the intracompartmental pressure

had reduced to normal levels. (A2)

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]. (WHO)

The patient should be referred to a surgical specialist but it is worth the treating clinician ensuring that objective criteria are used to assess the actual intracompartmental pressure in the limb (A2).

The limb can be raised in the initial stages to see if swelling is reduced. However, this is controversial as there is no trial evidence to support its effectiveness.

Persistent moderate swelling of the limb after viper bite can be successfully managed by systemic broad spectrum antibiotics and repeated Magnesium Sulphate compress (in the layers of wet bandage, changed 2-3 times a day) for 5-7 days.

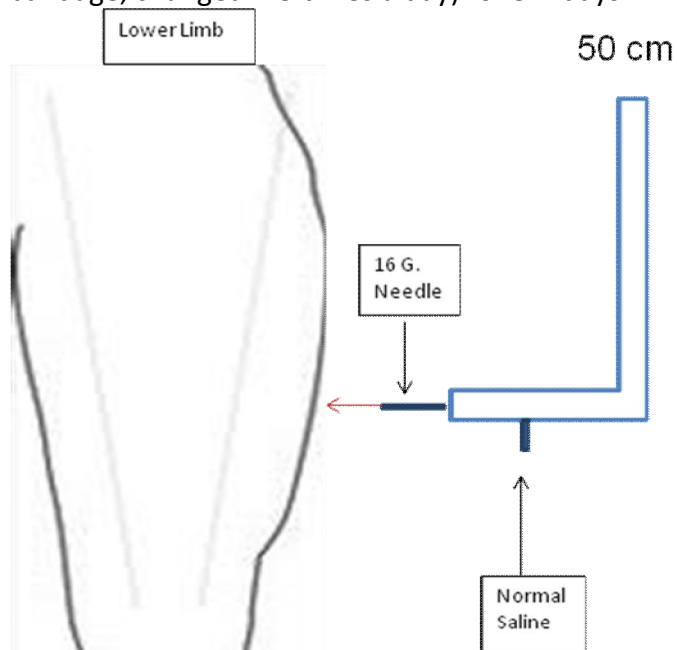


Figure 10. Compartment pressure measurement procedure.

## 19.DISCHARGE & FOLLOW-UP

### Discharge

If no symptoms and signs develop after 24 hours the patient can be discharged. Keep the patient under observation for 48 hours if ASV was infused.

### Follow-up

A snakebite victim discharged from the hospital should continue to be followed up. At the time of

discharge patient should be advised to return to the emergency, if there is worsening of symptoms or signs such as evidence of bleeding, worsening of pain and swelling at the site of bite, difficulty in breathing, altered sensorium etc. The patients should also be explained about the signs and symptoms of serum sickness. (fever, joint pain, joint swelling) which may manifest after 5-10 days.

## 20. REHABILITATION

1. In patients with severe local envenoming, maintain limb in a functional position. For example, in the leg, equinus deformity of the ankle should be prevented by application of a back slab.
2. Start simple exercises while the patient is still in hospital for restoration of normal function in the bitten part. Conventional physiotherapy after discharge from hospital may accelerate functional recovery of the bitten limb. Give a time table of rehabilitation activities.
3. Functional effects of local envenoming range from persistent stiffness and induration to severe deformity, tissue loss, especially dermonecrosis, requiring skin grafting and gangrene requiring debridement and amputation.

## 21. SNAKEBITE MANAGEMENT AT DIFFERENT LEVELS OF HEALTHCARE

### A. In basic or primary care facilities (PCF)

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.

**“FIRST HOUR is the Golden hour in Snakebite management”** should always be the Golden Rule in Snakebite Management. In whatever condition, after whatever hours of the actual bite a venomous bite patient arrives at a Health Facility, **FIRST DOSE of ASV MUST be given** at first contact health centre.

A key objective of this protocol is to enable doctors in Primary Care Facilities (PCF) or Basic Care Facilities (BCF) to treat snakebite with confidence. These facilities are the backbone of medical care in developing countries but are poorly equipped and with only one or a small number of doctors that staff them.

Evidence suggests that even when equipped with anti snake venom, PCF/BCF doctors lack the confidence to treat snakebite due to the absence of a protocol tailored to their needs and outlining how they should proceed within their context and setting. The following summarizes a sequence of activities to be carried out in these settings for optimal response.

### **At the community or village level (WHO)**

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. Victim must not run or drive himself to reach a Health facility. Motorbike Ambulance is a practical alternative for rural India but third person must support the patients

### **Referral Criteria**

#### **Referral Criteria: Vasculotoxic envenomation**

1. If no ASV is available, transfer to a hospital (where ASV availability is confirmed over the phone).
2. If 20 WBCT is “not clotted” after loading dose of 10 vials of ASV as in case of Viper bite.
3. If patient is continuing to bleed even after full dose of ASV transfer to a tertiary care medical college or higher level of health facility.
4. Progressive septicaemia
5. Signs of kidney injury or abnormal kidney function test transfer to a tertiary care medical college or higher level of health facility.

#### **Referral Criteria: Neurotoxic Envenomation**

1. Progressive neuromy paralysis - transfer with life support in ambulance for mechanical ventilation. Whilst it is entirely possible to maintain a neurotoxic victim by simply using a resuscitation bag, this should always be used as a last resort; the ideal means of support remains a mechanical ventilator (*Battery operated Transport Ventilator*) operated by qualified staff.
2. PHC and even many referral hospitals are not equipped with mechanical ventilators. The most important factor, therefore, is when to refer a patient to a hospital with a ventilator.
3. The key criteria to determine whether respiratory failure, requiring mechanical ventilation is likely, is the ‘neck lift’ to elicit broken neck sign. Neurotoxic patients should be frequently checked on their ability to perform a neck lift. If they are able to carry out the action then treatment should continue until recovery in the PHC. Neck lift test is also useful for children except very young children who may not be able to follow commands. Other tests which indicate descending paralysis are declining single breath count, pooling of saliva.
4. If the patient reaches the stage when patient cannot do neck lift immediately refer the patient to a hospital with a mechanical ventilator.
5. Maintain oxygen saturation using Pulse oximetry. Oxygen saturation <90% patient indicates requirement for ventilator support.



Figure 11. “Broken neck” sign observed in a 14-year-old girl bitten by a Russell’s viper in India. Envenoming by cobras, kraits and—in some areas—by Russell’s viper frequently leads to progressive descending paralysis. In this case, neuromuscular paralysis persisted for five days despite antivenom treatment, but without progression toward respiratory failure.(Alirol E et al , 2010)

#### Instructions while referring

- Inform the need for referral to the patient and/caregiver (family member or the accompanying attendant).
- Give prior intimation to the receiving centre using available communication facilities.
- Arrange for an ambulance. Call Emergency helpline 102/108 etc. Transport in an ambulance equipped with transport ventilator. If ventilator is not available tight-fitting face mask connected to an anaesthetic (Ambu) bag should be available. However, do not waste time to get an ideal ambulance. Motorbike is a practical alternative in rural areas for rapid transport but third person must sit behind the patient to support on bike.
- If ASV is not available at First contact centre transfer to the nearest health facility where ASV is available confirmed by telephone.
- Transfer to a higher health facility (Secondary Care Hospital or Tertiary Care Hospital) where mechanical ventilator and dialysis facilities are available for dialysis and ventilation, **if required after completion of ASV infusion only.**
- During transfer, continue life-supporting measures, and provide airway support with the help of an accompanying staff, if required.
- Insert nasogastric tube in case of severe neurotoxic envenomation
- Send the referral note with details of treatment given clearly mentioning the clinical status at the time of referral.

#### B. At a Primary health Care Center (PHC)

##### Patient Arrival & Assessment

1. Assess circulation, airway and breathing and deal with any life threatening symptoms on presentation.
2. Establish large bore intravenous access and start normal saline slow infusion.
3. Before removal of the tourniquet/ligatures, test for the presence of a pulse distal to the tourniquet. If the pulse is absent ensure a doctor is present before removal or ligatures.
4. **In case of clinically confirmed venomous bite, tourniquet should be removed only after starting of loading dose of ASV and keep Atropine Neostigmine injection ready.** In case of multiple ligatures, all the ligatures can be released in Emergency Room EXCEPT the most proximal one; which should only be released after admission and all preparations.
5. 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. The Glasgow Coma scale cannot be used to assess the level of consciousness of patients paralyzed by neurotoxic venoms.
6. The snake, if brought, should be carefully examined and identified, if possible. (One smart phone photograph of the snake, dead or alive, if available, should be taken for confirmation by an expert).
7. Clotting test '20WBCT' in clean, new, dry, glass test tubes should be carried out to diagnose vasculotoxic envenomation. Report should be given as Clotted or Not Clotted. Never write Positive/negative. If clotted continue every 1 hour for the 1<sup>st</sup> 3 hours from the time of hospitalization and then 6 hourly for 24 hours. If a neurotoxic snakebite is confirmed, clotting test can be repeated after 6 hours. If not clotted administer antivenom (ASV).
8. Give analgesia by mouth if required: Paracetamol (acetaminophen) (adult dose 500 mg to 1 g maximum 4 g in 24 hours; children 10-15 mg/kg/dose (maximum 100mg/kg/day). Do NOT give aspirin or non-steroidal anti-inflammatory drugs which can cause bleeding and renal dysfunction.
9. Assess the need and feasibility of transporting the patient to a higher level of the health service (see A above).
10. If the necessary skills, equipment, antivenom and other drugs are available, give intravenous fluid to correct hypovolaemic shock. These skills include ability to diagnose local and systemic envenoming, set up intravenous infusion or intravenous injection, identify the early signs of anaphylaxis.
11. If the patient fulfils criteria for antivenom treatment, give ASV. If no ASV is available, transfer to a health facility where ASV is available.
12. Adrenaline is made ready in two syringes of 0.5mg (1:1000) for IM administration if symptoms of any adverse reaction appear. If symptoms do appear, ASV is temporarily suspended while the reaction is dealt with and then recommenced (for details see treatment of early ASV reactions).
13. If the patient has evidence of respiratory paralysis, give oxygen by mask or laryngeal mask airway (LMA), and intubate the patient and make arrangements for transfer to a higher facility accompanied by a Medical Officer carrying an Ambu bag, additional endotracheal tubes, oxygen, facemasks and basic drugs for resuscitation. During the journey the endotracheal tube may slip into right bronchus leading to left lung collapse and right side pneumothorax may also occur. To prevent the tube being bitten, a mouth gag should be inserted. The tube may get obstructed due to secretions or kinking leading to cyanosis and resistance to Ambu-ventilation.

Then the tube should be pulled out immediately and Ambu- ventilation could be continued with a face mask.

Administer Atropine and Neostigmine before transferring to a hospital as recommended above.

**No AN** injection in confirmed Krait bite.

14. 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.
15. While admitted for observation, IV fluid with a slow plain drip of Normal saline should be started, and a Tetanus Toxoid given after ruling out or correction of coagulopathy.
16. Patient should be placed under observation for 24 hours (even if the victim gives a history of a nonvenomous snakebite. The bite victim becomes so frightened and confused immediately after a bite, many a time gives false identification history). If no symptoms develop after 24 hours the patient can be discharged.
17. Discourage the use of ineffective and potentially harmful drugs such as corticosteroids, antihistamines, and heparin.



### C. At the district hospital

Proceed as in B above in addition to the followings:

1. If ASV indicated and had not been given already start without any delay, do not wait for any test report.
2. Carry out a more detailed clinical and laboratory assessment including biochemical and haematological measurements, ECG or radiography, as indicated to get a baseline data.
3. If the patient is bleeding severely irrespective of full dose of ASV or is already seriously anaemic give transfusion of blood or fresh frozen plasma or transfer where facility is available.
4. Reassess analgesia (see B above) and, if required, consider giving Tramadol 50 mg orally. In case of severe pain administer Inj. Tramadol 50 mg IV. **Avoid pethidine or morphine in neurotoxic envenomation. A deeply sedated patient may create confusion regarding level of neuro-paralysis.**
5. Give tetanus toxoid booster (if not given already), to all snakebite victims provided coagulation is restored.
6. In case of cellulitis consider antibiotics, and consider surgical debridement of dead tissue.
7. If the patient has evidence of acute kidney injury (AKI), treat with dialysis. If this is not available, transfer to a specialized hospital. For details see Annexure.

8. If the patient has evidence of bulbar or respiratory paralysis, insert endotracheal tube with the help of the anesthesiologist if available or by a trained medical personnel or laryngeal mask airway (LMA). If there is evidence of respiratory failure, assist ventilation manually by anaesthetic bag or mechanical ventilator.
9. **Initial dose of ASV is administered over 1 hour. The first blood drawn from the patient should be typed and cross-matched, as the effects of both venom and ASV can interfere with later cross-matching.**
10. Atropine neostigmine "AN" challenge test is administered using 0.6mg of atropine IV first followed by 1.5 mg of neostigmine IV (Schedule described above). Rarely, if patient require more than 2<sup>nd</sup> dose of AN test. Stop after 3<sup>rd</sup> dose if there is no response. In Krait bite practice of continuing Neostigmine drip till ptosis persists beyond 24 h is not beneficial. Pre-synaptic blockage by Krait venom does not respond to AN injection.
11. If after 2 hours from the end of the first dose of ASV, the patient's symptoms have worsened i.e. paralysis has descended further, a second full dose of ASV is given over 1 hour.

#### D. At the tertiary care or medical college

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

1. In the ICU, the standard protocol should be followed during assisted ventilation and the patient should be monitored for all parameters including level of consciousness.  
Avoid drugs such as sedatives, morphine and neuromuscular blocking agents. Some patients go into a deep coma state but recover completely. Hence, diagnosis of brain death should not be considered.  
Recovery of respiratory muscles is reflected by improvement of neck flexors where flexing the neck against gravity indicates timing to wean off ventilation. Prophylactic antibiotics are unnecessary.
2. Multiple organ failure. Management is supportive, and prevention of organ damage in those at risk are therefore crucial. Aggressive early resuscitation, adequate antivenom therapy, excision of devitalized tissue and treatment of infection are important. Prompt recognition of organ dysfunction and immediate intervention may reverse organ impairment and improve the outcome.
3. If the patient has evidence of acute kidney injury peritoneal or haemodialysis or haemofiltration. Indications for dialysis as described above.
4. More advanced surgical management of local necrosis (e.g. split skin grafting).
5. More advanced investigations including bacterial cultures and imaging (CT scans) as indicated.
6. CNS complication and intracranial bleeding to be managed according to the standard practice. Neurosurgical opinion may be requested according to intracranial pathology. However, haemostatic abnormalities must be corrected.
7. **Coma, autonomic dysfunctions.** Patient in deep coma recovers fully provided there is no hypoxic brain damage. Autonomic dysfunctions are transient and don't need treatment. Sometimes treatment might be harmful e.g. treating with antihypertensive drugs to lower the increased blood pressure due to sympathetic hyperactivity.
8. **Uncommon complications such as** hepatic dysfunction, pancreatitis, endocrine insufficiency and deep venous thrombosis should be managed according to the standard practice.



9. Implement rehabilitation by physiotherapists.

## **22.CONDITIONS AND EQUIPMENT ACCOMPANYING NEUROTOXIC REFERRAL**

The primary consideration is to be equipped to provide respiration support to the victim if respiratory failure develops before or during the journey to the institution with mechanical ventilation.

The key priority is to transfer the patient with a facemask, resuscitation bag and a person, other than the driver of the vehicle, who is trained of how to use these devices. If respiration fails then the victim must be given artificial respiration until arrival at the institution.

Greater success can be achieved with two additional approaches, prior to despatch

In the conscious patient, two Nasopharyngeal Tubes (NP) should be inserted before referral. These will enable effective resuscitation with the resuscitation bag by not allowing the tongue to fall back and block the airway, without triggering the gagging reflex. Improvised Nasopharyngeal tubes can be made by cutting down size 5 endotracheal tubes to the required length i.e. from the tragus to the nostril. NP tubes should be prepared and kept with the snakebite kit in the Basic Medical Facility. This is preferable as the patient may well be unable to perform a neck lift but still remain conscious and breathing. The danger will be that respiratory failure will occur after the patient has left the BCF/PCF and before arriving at the eventual institution. In that case the patient will be pre-prepared for the use of a resuscitation bag by the use of NP tubes.

In the unconscious patient, a Laryngeal Mask Airway or preferably a Laryngeal Tube Airway should be inserted before referral, which will enable more effective ventilatory support to be provided with a resuscitation bag until the patient reaches an institution with the facility of mechanical ventilation.

## **23.EQUIPPING A BASIC HOSPITAL FOR EFFECTIVE SNAKEBITE MANAGEMENT**

### **Anti Snake Venom**

#### **Choice of ASV**

The type of ASV used will be determined by availability, cost and effectiveness of the cold chain. Lyophilised ASV, in powdered form has a shelf life of 5 years and requires merely to be kept out of direct sunlight. Liquid AV/ASV, which is easier to administer, has a shelf life of two years and requires refrigeration.

### **Assumptions**

The assumption in this section is that this is a basic setting i.e. without laboratory analysis capability, mechanical ventilator or renal dialysis capability. In such a situation the following basic principles

apply:

1. Victims with coagulopathy will require eventual transfer to a better-equipped hospital, due to the requirement to test for occult bleeding or renal failure.
2. Once the initial dose of ASV is given to a victim with coagulopathy, a six-hour window is available before ASV will require re-administration.
3. Neurotoxically envenomed patients can be treated entirely locally, if there is no evidence of respiratory failure and a need for long-term mechanical ventilation.
4. The trigger to indicate respiratory failure as being imminent is the failure of a patient to be able to perform a neck lift.
5. If the patient is unable to perform a neck lift, this will require transfer to a better-equipped hospital with a ventilator BUT will crucially require airway support for the journey as described in Section.

### **Holding Quantities of ASV/ Stocks of ASV**

It is imperative that hospitals which cover areas where snakebite is a feature, maintain adequate stocks of ASV. This should include locating institutions or vendors where ASV can be sourced quickly in the event of an upsurge in usage. Partly this problem can be eased by using the administration guidelines below. There remain a great number of occasions where ASV is used in non venomous bites because doctors have no clear guidelines and are not confident to wait for specific signs of envenomation. At the same time ASV stocks to be maintained well in advance of the peak seasons which has maximum demand.

Holding quantity can be established using the following equation:

**(xd X 1.2) t** where:

x = number of envenomings on average per month

d = the maximum number of vials likely to be applied at the medical facility to a single patient i.e. 2 doses to a Neurotoxically envenomed patient

t = length of time normally experienced for replenishment in months.

Suppose we are dealing with a basic facility with two envenomings per month then  $x=2$ : the maximum dose required per patient determines a key part of usage, so for example, if the maximum dose for a patient at a basic facility is 2 doses of 10 vials for a neurotoxic patient,  $d = 20$ . 1.2 represents the safety factor to ensure greater than minimal stock is available. The restocking time in months is represented by t. If the restocking period is 2 months for ASV to be replaced the equation would require  $2 \times 20 \times 1.2 \times 2 = 96$  vials would be the ASV base stock amount.

### **Other Support Drugs**

The following drugs should be held, stocking assumptions for each anticipated bite in a given period are as follows: -

#### **Adrenaline**

Adult dosage of 0.5mg of 1:1000 with a potential of three doses maximum per patient (i.e. stock of a minimum 10 vials)

### **Hydrocortisone and Antihistamine**

Adult dosage of antihistamine and hydrocortisone: only one application per patient is normally required before referral (i.e. stock of 10 vials)

### **Neostigmine and Atropine**

Adult dosage of 1.5mg for neostigmine and 0.6mg atropine for the test phase of treatment: ongoing support if test shows positive response is 0.5mg neostigmine every 30 minutes. Victims who are responsive usually recover quite rapidly so assume a dosage requirement of 12 hours i.e. 24 x 0.5mg ampoules. Further atropine may also be required @ 1 ampoule of 0.6mg atropine for every 5-6 ampoules of 0.5mg neostigmine.

Dose required per neurotoxic bite would be about 30 ampoules (0.5 mg) of neostigmine and five ampoules of atropine.

**Paracetamol:** 500mg tablets

**IV fluids:** Normal Saline

## **24.SNAKEBITE PREVENTION & OCCUPATIONAL RISK**

Snakebite prevention is an important activity and can make a contribution to reducing snakebite. It must be looked at with a degree of realism if it is to be successful.

## **25.PATIENT INFORMATION SHEET**

### **After snakebite occurs Do's and Don'ts**

#### **Do's**

- Seek medical help right away.
- Call ambulance and transfer patient to a medical health facility. Arrange transport of the patient to medical care as quickly, safely and passively as possible by vehicle ambulance (toll free no. 102/108/etc.), boat, bicycle, motorbike, stretcher etc.
- Keep the person calm. Reassure them that bites can be effectively treated in an emergency room. Restrict movement, and keep the affected area below heart level to reduce the flow of venom.
- Remove any rings or constricting items, because the affected area may swell.
- Create a loose splint (it should be capable of inserting one finger beneath) to help restrict movement of the area.
- Ideally the patient should lie in the recovery position (prone, on the left side) with his/her airway protected to minimize the risk of aspiration of vomitus.

- Monitor the person's vital signs -- temperature, pulse, rate of breathing, and blood pressure -- if possible. If there are signs of shock (such as paleness), lay the person flat, raise the feet about a foot, and cover the person with a blanket.

#### **Don'ts**

- Do **NOT** waste time in traditional first aid methods
- Do **NOT** allow the person to become over-exerted. If necessary, carry the person to safety.
- Do **NOT** apply a tourniquet. Do **NOT** block the blood supply or apply pressure.
- Do **NOT** apply cold compresses to snakebite.
- Do **NOT** cut into snakebite with a knife or razor.
- Do **NOT** try to suck out the venom by mouth or wash the wound.
- Do **NOT** give the person stimulants or pain medications unless a doctor tells you to do so.
- Do **NOT** give the person anything by mouth.
- Do **NOT** raise the site of the bite above the level of the person's heart.
- Do **NOT** attempt to kill or catch the snake as this may be dangerous. Bring in the dead snake only if this can be done safely. Do **NOT** waste time hunting for the snake, and do **NOT** risk another bite if it is not easy to kill the snake. Be careful of the head when transporting it - a snake can actually bite for several hours after it is dead (from a reflex).

#### **Prevention of snakebites**

- Snakebite is invariably an accident. As it is an accident, it can be avoided in many cases. Some judicious, timely precautions are extremely important to avoid the risk of snake – bites. People should be aware of such preventive measures.
- Education: Know your local snakes, know the sort of places where they like to live and hide, at what times of year, at what times of day/night or in what kinds of weather they are most likely to be active.

#### **Learn when and where snakes may be found:**

- Snakes rest in cool, shaded areas during hot weather.
- Snakes are predatory carnivores, but they are also preyed upon by other animals including snakes. For their preying habits and survival tactics, they tend to be secretive. Snakes avoid confronting larger animals and humans.
- Avoid snakes as far as possible, including snakes performing for snake charmers.
- Do **NOT** put your hands or fingers or feet into holes or nest or places you cannot see or any hidden place, where snakes may live.
- Most of the snakebites occur in the rainy season and after flood, because snakes are compelled to come out from their living and hiding places. Be especially vigilant about snakebites during the rainy season and after flood, and take adequate precautions while walking on the roads and fields.
- Mostly snakebite is encountered during ploughing, planting and harvesting.

#### **Leave snakes alone:**

- If you see a snake, do nothing; let it go and do **NOT** try to touch the snake. Keep a distance, it is better to run away. Snakes cannot attack when it is about 25 – 30 ft away.

- NEVER handle, threaten or attack a snake and never intentionally trap or corner a snake in an enclosed space. They do not attack man unless they are handled, threatened, trapped or cornered or their body parts are touched unintentionally (such as pressed down or crushed with the foot inadvertently).
- Do **NOT** pick up a dead snake or that appears to be dead. Even dead snakes can deliver venom through their fangs. Even an accidental scratching from the fang of a snake's severed head may inflict deadly venom.
- Rattlesnakes shake the ends of their tails to make a rattle sound that warns that it feels threatened. If you hear a rattlesnake, move away quickly.

#### **Learn what venomous snakes look like**

- People of a locality should know what sort of snakes (both venomous and non – venomous) are existing there, the habits of those snakes, their living and hiding places, at what time of year and at what time of day or night they are most likely to be out and active.
- Snake charmers and snake handlers carry greater risk of snakebite. Avoid free hand handling of venomous snakes; adequate equipment must be used for handling.
- Sea snakes may sometimes be caught in nets. Fishermen are advised not to touch those snakes.
- Venomous snakes are born fully equipped with venom and fangs. Young snakes are more pugnacious and ready to defend themselves, so do not discount a snake going by its size.

#### **Dress to protect yourself:**

- Wear shoes or boots and pants to protect your feet and legs.
- Always check footwear before wearing them.
- Identify major situational sources of bites; walk at night with sturdy footwear (preferably with high boots) and use a torch while walking outside the house.

#### **Outdoor**

- Avoid defecation in open field. If unavoidable carry torch or lamp.
- Light your path: Use a flashlight or lamp when you walk outside at night or visit the latrine (outdoor) at night.
- Do **NOT** walk in areas where you cannot see the ground.
- When walking, walk with a heavy step as snakes can detect vibration and will move away.
- Carry a stick when grass cutting or picking fruit or vegetables or clearing the base of trees or collecting wood. Use the stick to move the grass or leaves first. Give the snake a chance to move away. If collecting grass or leaves that have previously been cut and placed in a pile, disturb the grass with the stick before picking the grass up.
- Keep checking the ground ahead while cutting crops like millet, which are often harvested at head height and concentration is fixed away from the ground.
- Try to avoid sleeping on the ground. Use bamboo cot and scrupulous use of a mosquito net can prevent snakebites, scorpion stings, and mosquito bites alike. If you have to sleep on the ground use mosquito net that is well tucked in under the mattress or sleeping mat.



- During trekking, etc. through forests or mountains, stay on clearly marked tracks. Step on to rocks or logs rather than straight over them – snakes may be sunning themselves on the sides.

### **The Garden or Compound**

- Clear heaps of rubbish, building materials and termite mounds.
- Clear any bush or jungle.
- Keep grass short or cleared.
- Close rat holes, if any.

### **Indoor**

- In the house: Do not keep livestock, especially chickens, in the house, as snakes may come to hunt them.
- Regularly check houses for snakes and, if possible, avoid those types of house construction that will provide snakes with hiding.
- Store food in rat-proof containers.
- Also keep animal feed and rubbish away from your house. They attract rats and snakes follow.
- There is no chemical/onions which can effectively repel snakes. Bleaching powder or gammadane may be spread which may to some extent prevent the entry of snake in the house as they repel small creatures like rat and frog; snakes would not come following them.
- Seal any rat hole in and around the houses.
- Meticulously observe heaps of fire woods, cow dung cakes and similar materials at first and then handle.
- Keep plants away from doors and windows. Snakes like cover and plants help them climb up and into windows.
- Do **NOT** have tree branches touching the house. Keep grass short or clear the ground around the house and clear low bushes in the vicinity so that snakes cannot hide close to the house.
- Inspect mud made ovens or chulhas at first before cleaning.

### **During construction of new house**

- Indoor toilets should be made compulsory at the time of issuing permission for new housing construction.

## ANNEXURE 1. SNAKE BITE EXAMINATION PERFORMA

Name ..... Age ..... Sex M/F  
Address .....

Date .....time of bite .....Activity at time of bite .....

Sleeping on floor bed ... Yes/No .... Cot ..... Yes/No ..... Mosquito net Yes/No

Snake Seen Yes/No Killed Yes/No Specimen photo in mobile Yes/No

Identification of snake in photos specimen as .....

Confirmed specimen of snake .....

### Local site

Fangs marks .....Active bleeding from fangs Yes/No Blood clot Yes/No

Time of development of edema .....

Extension of edema .....

Regional lymphangitis .....

Pain in abdomen .....Vomiting .....

Blood pressure ..... Pulse rate .....

Active bleeding Gum/ from abrasions /any other site

<b>20WBCT on arrival</b>	Clotted /Not clotted	Time.....
Repeat 20WBCT	Clotted /Not clotted	Time.....
Repeat 20WBCT	Clotted /Not clotted	Time.....

**ASV administered** ..... **Dose given** .....vials **Time**.....

Repeat 20WBCT **after ASV** Clotted /Not clotted Time..... **Progress after ASV**

20WBCT at 1h .....2h.....3h.....6h.....12h.....18h.....24h...

Progress INR .....APTT .....

Blood urea .....Serum creatinine .....

Urine ..... Haematuria /hemoglobinurea

Haemogram .....Platelet count.....

Blood transfusion, if any .....

Fresh Frozen Plasma (FFP), if any .....

Dialysis, if any .....

**Compartment syndrome Present/Not present**

**Neuroparalytic symptoms**

Bilateral Ptosis ..... Ophthalmoplegia .....

Bulbar palsy .....

Respiratory rate ...../min      sPO<sub>2</sub> .....% One minute count .....

**Muscle power** on arrival

Upper limb .....lower limb ..... Progress .....

Pelvic girdle .....

Reflexes Planter on arrival .....Progress .....

Voice on arrival .....

Distance between Inter teeth margin .....On arrival ..... Progress .....

Protrude of tongue in relation to teeth margin .....On arrival .....progress

Pupil size ..... reacting to light..... On arrival.....

Progress after ASV total dose .....After Repeat dose .....

Intubation time .....Ambu bag ventilation/ Mechanical ventilator

**Follow up**

**Recovery time in days**..... **Total ASV dose given**.....

**Blood transfusion**      given/not given    **FFP** given/not given **Dialysis days**.....    Ventilations total

days .....    Disability.....

Hypoxic brain injury ..... Amputation of limb ..... Plastic surgery



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