# National Snakebite Management Protocol (India), 2008 (Shortened version)

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Snakebite Victims come mostly from poor rural communities and many are children. WHO figures show that 84,000 Indians are bitten and envenomated each year and of these 11,000 die. The number affected by permanent disability is also high. Many other medical conditions receive greater attention while snakebite remained a "forgotten medical condition". However there is now room for optimism as Government of India responded by developing and approving National Snakebite protocol in the year 2008.

Areas of known weaknesses in the Indian scenario were identified, and analyzed by an Expert and Scientific Committee in its brainstorming sessions in 2006 at a Conference in Kochi, under the auspices of WHO. From these deliberations, evidence based Protocol was developed in 2007 and approved by ICMR – MOHFW in 2008. The protocol contains some of the latest thinking about the treatment of anaphylaxis around mode of treatment and timing. Clinical teams in busy emergency departments tend to develop decision rules for effective patient care. With an approved National Protocol in place, personal rules will no longer be ethical or acceptable.

National Protocol for Snakebite management has followed a common pattern of statement of relevant question, review of relevant literature for gathering evidence, theoretical constructs behind clinical decision rules. With effective first aid measures applied, the victims are given the best chance of arriving at hospital in the best

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condition for the doctor to achieve a successful outcome (1) Making people aware of the correct first aid measures in the event of a bite and reducing the reliance on traditional methods, which have been proven to be ineffective and a waste of vital time, is very crucial.

Provision of adequate, consistent, safe and effective ASV to all Health Centers where Snakebite is experienced cannot be over emphasized. The priority is to neutralize the Circulating Venom at the earliest and at a health facility closest to the site of accident. "Disposing of the victim to a higher centre" for neutralizing the Venom is the greatest risk factor for lifethreatening complications in the Snakebite Victim.

Clinical rules for ASV dosage are clearly mentioned in the protocol and the West Bengal study in 2008 has validated the Protocol, including dramatically reducing wastage of ASV (2). The ability of the doctor to treat can be boosted only by providing him the appropriate information on National Protocol during his learning period in medical school and experience with this new protocol subsequently during his Internship. A PDF download in the official website of any hospital on the tier-specific medical support for snake envenomation will ensure greater dissemination of this life saving information.

There is a strong belief that snake venom often changes as you move to different regions. Research should establish whether such a regional variation exists and if so, how to combat it. The development of ELISA technology to enable the doctor to identify the type of snake responsible for the bite and the level of envenomation within a short time of arrival at hospital is another research priority. As we strive to improve on research previously carried out, Doctors have a responsibility not only in treatment by following the National protocol in a consistent manner but also to raise awareness in general population as to how to avoid activities which put children/people at risk for Snakebite.

1.Jacobsen IM. Making the difference – A community based approach to Snakebite First Aid. Ind Jl Emergency Pediatrics 2009;1:7-13.

2.Ghosh S, Maisnam I, Murmu BK, Mitra PK, Roy A, Simpson ID. A locally developed snakebite management protocol significantly reduces overall anti snake venom utilization in West Bengal, India. Wilderness Environ Med 2008; 19:267-74.

#### Introduction

India is estimated to have the highest snakebite mortality in the world, with WHO estimates placing the number at 11,000 per annum. There are about 236 species of snakes in India. Most of them are non-poisonous and their bites, apart from causing panic reaction and local injury, do not harm the patient. However, there are 15 varieties that are medically significant and among them, the cobras, the Russell's viper, the saw- scaled vipers and the kraits are the most common.

Many of these fatalities are preventable by use of the correct first aid, getting the victim to the hospital as soon as possible and the use of correct and up to date treatment methods.

The need for a protocol for managing snakebites in the Indian context could not be over emphasized. The national snakebite management protocol recognizes the need to bring in behavioural change among the community regarding occupational risks and its reduction. It also recognizes the fact that the earlier an envenomed patient is treated with ASV once signs of envenomation are established, the better the outcome. It clearly delineates the management principles and protocols at all levels. The implementation of the protocol in a limited way in the states of Tamil Nadu, West Bengal, Puducherry and Rajasthan, Madhya Pradesh and Kerala, has shown improved

outcomes in terms of lives saved and decrease in quantum of ASV used.

#### Poisonous Snakes in India

Substantial number of snakebites in India is due to non poisonous snakes. Even, many bites by poisonous snakes are dry bites implying that the snakes fail to inject the venom. However, the non-poisonous bites and the dry bites may cause panic reaction and local injury. There are 15 varieties that are highly venomous and four among them, namely cobra (Naja naja), the Russell's viper (Daboia russelii), the saw-scaled viper (Echis carinatus) and the krait (Bungarus caeruleus)cause are included in the ASV venom mix. Cobras and Kraits belong to Elapidae and the vipers belong to Viperidae family. These four 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 Pit Viper as a species capable of causing life threatening symptoms has demonstrated this.

Further research needs to be undertaken to establish a definitive list of medically significant snakes in India. Readers are requested to refer to Fig.1 in page 84.

#### **Clinical Features**

Snake venom contains proteins that are predominantly neuro toxic or haemotoxic. Cobras and Kraits have neuro toxins and present with neurological manifestations. Haemostatic abnormalities are prima facie evidence of a Viper bite. Russell's viper can occasionally also manifest neurotoxic symptoms in a wide area of India. Saw Scaled Vipers do not cause renal failure whereas Russell's viper and Hump-nosed Pit Viper do.

In bites by poisonous and non-poisonous snakebites, anxiety is a predominant manifestation. Non poisonous snakebites may also leave puncture marks and swelling at the site.

The table below summarizes the nature of toxin, the signs at the bite site and the systemic manifestations of envenomation.

Common Name of	Nature of Toxin	Local symptoms and signs at	Systemic symptoms and
the snake	Tractare of Toxili	bite site	signs
Russell's Viper	Haemotoxic	Pain at bite site (Not always)	Rise in CT/BT, Bleeding
(Daboia russelii)	Neurotoxic	Ecchymoses and swelling	from the gingival sulci,
(Dubbin russein)	Neurotoxic	Blister formation at the site	epistaxis, GI bleeding.
			1 0
		of bite and on the affected	haematuria, melaena.
			Hemorrhage results in
		Necrosis of the limb	anemia, renal failure
			coagulopathy, and
			hypotension. Can also
			cause initial neurotoxic
			symptoms i.e. ptosis etc.
Saw Scaled Viper	Haemotoxic	Local pain (not always)	Rise in CT/BT, Bleeding
		Ecchymoses and swelling	from the gingival sulci,
(Echis		Bleeding from the site	epistaxis, GI bleeding.
carinatus/sochureki)		Rapid discoloration at the	hematuria, melena,
		site	Hemorrhage results in
			anemia, coagulopathy,
			and hypotension
			· ·
Cobra	Neurotoxic	Local pain (not always)	Sluggish pupillary
(Naja	( post synaptic)	Swelling, ecchymoses	response, diplopia
naja/kaouthia/		and local necrosis	Ptosis, dilated pupils,
oxiana)			arrhythmia, difficulty in
			breathing, hypotension,
			unconscious state,
			cardiac arrest and
			respiratory arrest
Common Krait	Neurotoxic	Small puncture marks often	Sluggish pupillary
(Bungarus	(pre-synaptic)	not discernable	response, ptosis,
caeruleus/fasciatus/	(1)	Minimal or absent local	diplopia, difficulty in
sindanus Spp/niger)		symptoms	swallowing due to
		5) 11.P 10 11.15	glossopharyngeal
			dysfunction, Dilated
			pupils, difficulty in
			respiration, arrhythmia,
			Hypotension, loss of
			conciousness, coma,
			respiratory arrest, and
			sudden cardiac arrest
Llump Magad Dit	Unamataria	Local pain	
Hump Nosed Pit	Haemotoxic	Local pain	Rise in CT/BT, Bleeding
Viper		Ecchymoses and swelling	from the gingival sulci,
(Hypnale hypnale)		Bleeding from the site	epistaxis, GI bleeding.
			hematuria, melena.
			Hemorrhage results in
			anemia, renal failure
			coagulopathy, and
			hypotension

# Community Interventions: Occupational Risk and other ecological factors

The normal perception is that rural agricultural workers are most at risk and the bites occur first thing in the morning and last thing at night. However, this is of very little practical use to rural workers in preventing snakebite since it ignores the fact that

- 1. In rubber, coconut and areca nut plantations clearing the base of the tree to place manure causes significant numbers of bites.
- 2. Harvesting high growing crops like Millet which require attention focused away from the ground.
- 3. Rubber tapping in the early hours 03:00-06:00 AM.
- 4. Vegetable harvesting / fruit picking.
- 5. Tea and coffee plantation workers face the risk of arboreal and terrestrial vipers when picking or tending bushes.
- 6. Clearing weeds exposes workers to the same danger as their grass-cutting colleagues.
- 7. Walking at night without a torch barefooted or wearing sandals accounts for a significant number of bites.
- 8. Bathing in ponds, streams and rivers, in the evening. It should not be assumed that because the victim is bitten in water that the species is non-venomous. Cobras and other venomous species are good swimmers and may enter the water to hunt.
- 9. Walking along the edge of waterways.

#### **Preventative Measures**

- 1. Walk at night with sturdy footwear and use a torch! When walking, walk with a heavy step as snakes can detect vibration and will move away!
- 2. Carry a stick when grass cutting or picking fruit or vegetables or clearing the base of trees. Use the stick to move the grass or leaves first. Give the snake chance to move away. If collecting grass that has previously been cut and placed in a pile, disturb the grass with the stick before picking the grass up.
- 3. Keep checking the ground ahead when cutting crops like Millet, which are often

- harvested at head height and concentration is fixed away from the ground.
- 4. Pay close attention to the leaves and sticks on the ground when wood collecting.
- 5. Keep animal feed and rubbish away from your house. They attract rats and snakes will follow.
- 6. Try to avoid sleeping on the ground.
- 7. Keep plants away from your doors and windows. Snakes like cover and plants help them climb up and into windows.
- 8. During trekking etc through forests or mountains, stay on clearly marked tracks. Do not step or reach into an area where you cannot see the ground. Wear boots, long-sleeved shirts and long pants.

#### First Aid Treatment Protocol

The case management at the field level includes reassuring the victim, immobilising the bitten limb and transporting the victim to nearest treatment facility within the shortest possible time.

Do it R.I.G.H.T.

The first aid that's currently recommended to be administered by self or the community volunteer is based around the mnemonic:

#### "Do it R.I.G.H.T."

The letters in the mnemonic stands for:

R=Reassure the patient. 70% of all snakebites are from non-venomous species. Only 50% of bites by venomous species actually envenomate the patient

I=Immobilise in the same way as a fractured limb. Use bandages or cloth to hold the splints, not to block the blood supply or apply pressure. Do not apply any compression in the form of tight ligatures, they don't work and can be dangerous!

G.H.=Get to Hospital Immediately. Traditional remedies have NO PROVEN benefit in treating snakebite.

T=Tell the doctor of any systemic symptoms such as ptosis that manifest on the way to hospital.

This method will get the victim to the hospital quickly, without recourse to traditional medical

approaches, which can dangerously delay effective treatment and will supply the doctor with the best possible information on arrival.

The snake, if killed should be carefully taken to the hospital for identification by the doctor. No time should be wasted in attempting to kill or capture the snake. Further information on snakebite first aid can be availed from the previous issue of this journal (Jacobsen IM. IJEP 2009:1;7-13).

# Creating Awareness among the community about Do's and Don'ts

Awareness should be created among the community about the **Do's and Don't's** of the Snakebite.

### Do's

- 1. Reassure the victim that death is not imminent and that medical care is available. Reassure that most of the bites are non-venomous.
- 2. Remain calm; make the victim comfortable. Control anxiety. Excitement may increase heart rate and blood circulation. This will help spread the venom through your body much faster.
- 3. Lay down flat on the ground; Keep the bitten body part below heart level (do not lift the bitten part above the chest).
- 4. Remove shoes, rings, watches, jewelry and tight clothing from bitten area. They may act as a tourniquet in the event swelling occurs.
- 5. Immobilize the victim's bitten limb in the same way as for a fracture. Bandage it using a cotton bandage (or using any clean cloth material). Finally, apply a splint, and do not allow the limb or the muscles in the area of the bite to be moved much.
- 6. Be prepared to treat for shock and possibly administer CPR.
- 7. Get the victim to the nearest hospital as soon as possible using available transport.

#### Don't's

1. Do not apply a tourniquet or constriction band. You could cut off blood flow to the

- limb, causing more damage than the snakebite.
- 2. Do not wash the bite site with soap and water or any other solution to remove venom from the bite site. Action of washing increases the flow of venom into the system by stimulating the lymphatic system
- 10. Do not make cuts or incisions on or near the bitten area. Viper bites cause uncontrollable bleeding with incoagulable blood. You could also cut nerves, tendons or blood vessels and cause infection.
- 11. Do not use electrical shock.
- 12. Do not freeze or apply extreme cold to the area of the bite.
- 13. Do not apply any kind of potentially harmful herbal and folk remedies
- 14. Do not attempt to suck venom out with your mouth it is ineffective and does not remove venpom. You could have an ulcer or wound in your mouth, allowing venom to get into your bloodstream.
- 15. Do not give the victim drink, alcohol or other drugs. This can cause complications in the successful treatment of the bite.
- 16. Do not attempt to capture, handle or kill a venomous snake. More people are bitten during these activities than in any other situation.

Do not go to traditional healers or quacks as there are no proven traditional remedies. Traditional remedies only appear to work in non-venomous bites.

# Snake Bite Treatment Protocol: Diagnostic Phase

#### Patient Assessment Phase: On arrival

- 1. Deal with any life threatening symptoms on presentation. i.e. Airway, Breathing and Circulation.
- 2. If there is evidence of a bite, where the skin has been broken, give Tetanus Toxoid.
- 3. Routine use of anti-biotic is not necessary, although it should be considered if there is evidence of cellulitis or necrosis.

# Diagnosis Phase: General Principles

- 1. Where possible identify the snake responsible. Snake colouration is a very unreliable means of determining species as is most of the advice given concerning pupil shape and scalation. Have the victim carefully bring the snake to hospital if it has been killed.
- 2. Bite marks are of no use in identifying if a species is venomous or not. 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.
- 3. Determine if any traditional medicines have been used, they can sometimes cause confusing symptoms.
- 4. Determine the exact time of the bite. This can give indications as to the progression of any symptoms.
- 5. 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.

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

# Diagnosis Phase: Symptoms

#### General

Generic features have been dealt under section 3. The table below summarises the evidence based situation.

Feature	Cobras	Kraits	Russell's	Saw	Hump
			Viper	Scaled	Nosed
				Viper	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

Haemostatic abnormalities are prima facie evidence of a Viper bite. Cobras and Kraits do not cause haemostatic disturbances. Saw Scaled Vipers do not cause renal failure whereas Russells Viper and Hump-nosed Pitviper do.

Russells Viper can also manifest neurotoxic symptoms in a wide area of India. This can sometimes cause confusion and further work is necessary to establish how wide this area might be. The neurotoxic symptoms in Russell's Viper are believed to be pre synaptic or Krait like in nature. It is for this reason that a doubt is expressed over the response of both species to Neostigmine (See below for use of neostigmine).

# General signs and symptoms of Viperine envenomation

- 1. Swelling and local pain.
- 2. Tender enlargement of local lymph nodes as large molecular weight Viper venom molecules enter the system via the lymphatics.
- 3. Bleeding from the gingival sulci and other orifices such as epistaxis.
- 4. The skin and mucous membranes may show evidence of petechiae, purpura ecchymoses.
  - 5. Vomiting

- 6. Acute abdominal tendernesswhich may suggest gastro-intestinal or retro peritoneal bleeding.
- 7. Hypotension resulting from hypovolaemia or direct vasodilation.
- 8. Low back pain, indicative of an early renal failure or retroperitoneal bleeding, although this must be carefully investigated as many rural workers involved in picking activities complain of back pain generally.
- 10. The passing of reddish or dark-brown urine or declining or no urine output.
- 11. Lateralising neurological symptoms and asymmetrical pupils may be indicative of intracranial bleeding.
  - 12. Muscle pain indicating rhabdomyolysis.
- 13. Parotid swelling, conjunctival oedema, sub-conjunctival haemorrhage.

# General signs and symptoms of Elapid envenomation

- 1. Swelling and local pain (Cobra).
- 2. Local necrosis and/or blistering (Cobra).
- 3. Descending paralysis, initially of muscles innervated by the cranial nerves, commencing with ptosis, diplopia, or opthalmoplegia. The patient complains of difficulty in focusing and the eyelids feel heavy. There may be some involvement of the senses of taste and smell but these need further research.
- 4. Paralysis of jaw and tongue may lead to upper airway obstruction and aspiration of pooled secretions because of the patient's inability to swallow.
- 5. Numbness around the lips and mouth, progressing to pooling of secretions, bulbar paralysis and respiratory failure.
- 6. Hypoxia due to inadequate ventilation can cause cyanosis, altered sensorium and coma. This is a life threatening situation and needs urgent intervention.
- 7. Paradoxical respiration, as a result of the inter-costal muscles becoming paralysed is a frequent sign.
- 8. Stomach pain which may suggest submucosal haemorrhages in the stomach (Krait).

9. Krait bites often present in the early morning with paralysis that can be mistaken for a stroke.

### **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 pit viper are known for the length of time it can take for symptoms to manifest. Often this can take between 6 to 12 hours. Late onset envenoming is a well documented occurrence.

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.

### **Diagnosis Phase: Investigations**

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

Considered 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. It is significantly superior to the 'capillary tube' method of establishing clotting capability and is the preferred method of choice in snakebite.

A few milli litres of fresh venous blood is placed in a new, clean and dry glass vessel and left at ambient temperature for 20 minutes. The vessel ideally should be a small glass test tube. It is important that the tube is clean, glass and dry as the mechanism under review is the contact clotting mechanism. The use of plastic bottles, tubes or syringes will give false readings and should not be used.

The glass vessel should be left undisturbed for 20 minutes and then gently tilted, **not shaken**. If the blood is still liquid then the patient has incoagulable blood. The vessel must not have been washed with detergent as this will inhibit the contact element of the clotting mechanism.

The test should be carried out every 30 minutes from admission for three hours and then hourly after that to establish if envenomation is present. If incoagulable blood is discovered, the 6 hourly cycle will then be adopted to test for the

requirement for repeat doses of Anti Snake Venom.

# Other Useful Tests (depending on availability)

- 1. Haemoglobin/ PCV/ Platelet Count/ PT/ APTT/ FDP/ D-Dimer
  - 2. Peripheral Smear
- 3. Urine Tests for Proteinuria/ RBC/ Haemoglobinuria/ Myoglobinuria
- 4. Biochemistry for Serum Creatinine/ Urea/ Potassium
- 5. Oxygen Saturation/ PR/BP/ RR/ Postural Blood Pressure
- 6. ECG/ X-Ray/ CT/ Ultrasound (The use of X-Ray and ultrasound are of unproven benefit, apart from identification of bleeding in Viperine bites).
  - 7. ABG (if facilities available)

# **Immuno-diagnostics**

An Indian medical college is currently working to develop Enzyme Linked Immuno Sorbent Assay (ELISA) testing for snake species and level of envenomation. It will take years before a reliable and effective kit is available to doctors.

# **Snake Bite Treatment Protocol : Treatment Phase**

# Managing Pain

Snakebite can often cause severe pain at the bite site. This can be treated with painkillers such as 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 coagulation. 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.

### **Handling Tourniquets**

Though not recommended, the current practice being followed would see many snakebite victims reaching the emergency with tightly tied tourniquets. Care must be taken when removing tight tourniquets. Sudden removal can lead to a massive surge of venom leading to neurological paralysis, hypotension due to vasodilation etc.

- 1. Before removal of the tourniquet, check for the presence of pulse distal to the tourniquet. If the pulse is absent ensure a doctor is present before removal.
- 2. 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.

### Anti Snake Venom (ASV)

Anti snake venom (ASV) is the mainstay of treatment. The ASV available 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.

Lypholised ASV against known species in powder form has five year shelf life and requires only to be kept cool. This is a useful feature in remote areas where power supply is inconsistent. It is imperative that hospitals which cover areas where snakebite is a feature, maintain adequate stocks of ASV.

#### **ASV Administration Criteria**

ASV is a scarce, costly commodity and should only be administered when there are definite signs of envenomation. Unbound, free flowing venom, can only be neutralised when it is in the bloodstream or tissue fluid. In addition, Anti-Snake Venom carries risk of anaphylactic reactions and should not therefore be used

unnecessarily. The doctor should be prepared for such reactions.

If a patient has evidence to suggest systemic envenoming or severe current local envenoming then **only** ASV will be administered:

# **Evidence of systemic envenoming**

- **1. Evidence of coagulopathy**: Primarily detected by 20WBCT or visible spontaneous systemic bleeding from gums etc. Further laboratory tests for thrombocytopenia, Haemoglobin abnormalities, PCV, peripheral smear etc provide confirmation, but 20WBCT is paramount.
- **2.** Evidence of neurotoxicity: Ptosis, external ophthalmoplegia, muscle paralysis, inability to lift the head etc.

The above two methods of establishing systemic envenomation are the primary determinants. They are simple to carry out, involving bedside tests or identification of visible neurological signs and symptoms. In the Indian context and in the vast majority of cases, one of these two categories will be the main determinants of whether ASV is administered to a patient.

#### Other determinants are:

- i. Cardiovascular abnormalities: hypotension, shock, cardiac arrhythmia, abnormal ECG.
- ii. Persistent and severe vomiting or abdominal pain

#### 3. Severe Current Local envenoming

- i. Severe current, local swelling involving more than half of the bitten limb (in the absence of a tourniquet)
- ii. In case of (i) severe swelling after bites on the digits (toes and especially fingers) (ii) rapid extension of swelling (for example beyond the wrist or ankle within a few hours of bites on the hands or feet)
- iii. If a tourniquet or tourniquets have been applied these themselves can cause swelling, once they have been removed for 1 hour and the swelling continues, then it is unlikely to be as a result of the tourniquet and ASV may be applicable.

Purely local swelling, even if accompanied by a bite mark from an apparently venomous snake, is not grounds for administering ASV. Swelling a number of hours old is not grounds for giving ASV.

# Prevention of ASV Reactions - prophylactic Regimes

There is no statistical, trial evidence of sufficient statistical power to show that prophylactic regimes are effective in the prevention of ASV Reactions. Micro studies either show no benefit or modest benefit. These studies were underpowered to detect the true outcome effect. Well designed clinical trials are needed to conclude that the prophylactic treatment is beneficial.

### Two regimens are normally recommended:

1. 100 mg of hydrocortisone and H1 antihistamine (10mg chlorphenimarine maleate; 22.5mg IV phenimarine maleate IV or 25mg promethazine HCl IM) 5 minutes before ASV administration. The dose for children is 0.1-0.3mg/kg of antihistamine IV and 2mg/kg of Hydrocortisone IV. Antihistamine should be used with caution in pediatric patients.

# 2. 0.25-0.3mg adrenaline 1:1000 given subcutaneously

Since there is no evidence from good quality randomized clinical trials to support their routine use, decisions are grounded on criteria such as maximum safety policy, irrespective of the lack of definitive trial evidence. If the victim has a known sensitivity to ASV, pre-medication with adrenaline, hydrocortisone and antihistamine may be advisable, in order to prevent severe reactions.

#### Test Dose of ASV

Test doses have been shown to have no predictive value in detecting anaphylactoid or late serum reactions and should not be used. These reactions are not IgE mediated but Complement activated. They may also presensitise the patient and thereby create greater risk.

#### **ASV Administration: Dosage**

Symptoms and signs being not a useful guide for deciding the degree of envenomation and having no diagnostic methods to determine the level of venom in blood or tissue, any ASV regimen adopted could only be an estimate. There is no definite evidence to show the efficacy of low dose ASV regimens vs high dose and viceversa.

The recommended dosage level has been based on published research that Russell's Viper injects on average 63mg (Range 5mg – 147 mg; SD 7 mg) of venom.

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.

ASV is recommended to be administered in the above initial dose

# Neurotoxic/ Anti Haemostatic 8-10 Vials

### **Initial Dose**

ASV is recommended to be administered in the following initial dose:

**N.B.** Children receive the same ASV dosage as adults. The ASV is targeted at neutralising the venom. Snakes inject the same amount of venom into adults and children.

#### Mode of Administration

ASV can be administered in two ways:

- 1. Intravenous Injection: reconstituted or liquid ASV is administered by slow intravenous injection. (2ml/ minute). Each vial is 10ml of reconstituted ASV.
- 2. Infusion: liquid or reconstituted ASV is diluted in 5-10ml/kg body weight of isotonic saline or glucose.

All ASV to be administered over 1 hour at constant speed. The patient should be closely monitored for 2 hours.

**Local administration of ASV near or on to the bite site should not be done.** It has been proven to be ineffective, painful and raises the intra-compartmental pressure, particularly in the digits.

# ASV Dosage in Victims Requiring Life Saving Surgery

In very rare cases, symptoms may develop which indicate that life saving surgery is required in order to save the victim. An example would be a patient who presents with signs of an intracranial bleed.

Before surgery can take place, coagulation must be restored in the victim in order to avoid catastrophic bleeding. In such cases a higher initial dose of ASV is justified (up to 25 vials) solely on the basis on guaranteeing a restoration of coagulation after 6 hours.

# **Victims Who Arrive Late**

Look for signs of current venom activity. Venom can only be neutralised if it is unattached! Perform a 20WBCT and determine

if any coagulopathy is present. If coagulopathy is present, administer ASV. If no coagulopathy is evident treat renal failure by reference to a nephrologist and dialysis.

In the case of neurotoxic envenoming where the victim is evidencing symptoms such as ptosis, respiratory failure etc, it is probably wise to administer 1 dose of 8-10 vials of ASV to ensure that no unbound venom is present. However, at this stage it is likely that all the venom is bound and respiratory support or normal recovery will be the outcome.

#### **ASV Reactions**

Anaphylaxis with ASV may be lifethreatening. This is one of the factors contributing to reluctance on the part of PHC doctors in giving ASV. The patient should be monitored closely for urticaria, itching, fever, shaking chills, nausea, vomiting, diarrhoea, abdominal cramps, tachycardia, hypotension, bronchospasm and angio-oedema. If anaphylaxis is evident, then:

- 1. ASV will be discontinued.
- 2. 0.5mg of 1:1000 adrenaline will be given IM for adults. Children are given 0.01mg/kg body weight of adrenaline IM.
- 3. In addition, to provide long term protection against anaphylactoid reaction, 100mg of

hydrocortisone and an H1 antihistamine, such as Phenimarine maleate can be used at 22.5mg IV or Promethazine HCl can be used at 25mg IM, or 10mg chlorphenirmarine maleate if available, will be administered IV.

The dose for children is of Phenimarine maleate at 0.5mg/kg/ day IV or Promethazine HCl can be used at 0.3-0.5mg/kg IM or 0.2mg/kg of chlorphenimarine maleate IV and 2mg/kg of hydrocortisone IV.

# Antihistamine use in paediatric cases must be deployed with caution

If after 10 to 15 minutes the patient's condition has not improved or is worsening, a second dose of 0.5 mg of adrenalin 1:1000 IM is given. This can be repeated for a third and final occasion but in the vast majority of reactions, 2 doses of adrenaline will be sufficient. If there is hypotension or hemodynamic instability, IV fluids should be given.

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, it should only be used if IM adrenaline has been tried and the

administration of IV adrenaline is in the presence of ventilatory equipment and ICU trained staff.

The IM route for the administration of adrenaline is the option selected, due to the rapidity of development of life threatening situation in anaphylaxis. Studies have shown that adrenaline reaches necessary blood plasma levels in 8 minutes in the IM route, but up to 34 minutes in the subcutaneous route. The early use of adrenaline has been selected as a result of study evidence suggesting better patient outcome if adrenaline is used early.

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

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. Oral H1 Antihistamines provide additional symptomatic relief.

# **Neurotoxic Envenomation**

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. There is some doubt over its usefulness against the pre-synaptic neurotoxin such as those of the Krait and the Russells Viper. However it is worth trying in these cases.

#### **Neostigmine Test**

In the case of neurotoxic envenomation the 'Neostigmine Test' will be administered. This test involves administration of 1.5-2.0 mg of neostigmine IM, together with 0.6mg of atropine IV. The paediatric neostigmine dose is 0.04mg/kg IM and the dose of atropine in 0.05mg/kg.

The patient should be closely observed for 1 hour to determine if the neostigmine is effective. The following measures are useful objective methods to assess this:

- 1. Single breath count
- 2. Mm of Iris uncovered (Amount covered by the descending eyelid)

- 3. Inter incisor distance (Measured distance between the upper and lower incisors)
- 4. Length of time upward gaze can be maintained
  - 5. FEV 1 or FVC (If available)

For example, if single breath count or inter incisor distance is selected the breath count or distance between the upper and lower incisors are measured and recorded. Every 10 minutes the measurement is repeated. The average blood plasma time for neostigmine is 20 minutes, so by T+30 minutes any improvement should be visible by an improvement in the measure.

If the victim responds to the neostigmine test then continue with 0.5mg of neostigmine IM half hourly plus 0.6mg of atropine IV over an 8 hour period by continuous infusion. If there is no improvement in symptoms after one hour, the neostigmine should be stopped.

Some authors have suggested that it may be possible to treat patients with anticholinesterase drugs solely, in the case of elapid bites. However this approach ignores the value of neutralising the free flowing venom before it can attach and carry out its task.

#### **Recovery Signs**

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

- 1. Spontaneous systemic bleeding such as gum bleeding usually stops within 15-30 minutes.
- 2. Blood coagulability is usually restored in 6 hours. Principal test is 20WBCT.
- 3. Post synaptic neurotoxic envenoming such as the Cobra may begin to improve as early as 30 minutes after antivenom, but can take several hours.
- 4. Presynaptic neurotoxic envenoming such as the Krait usually takes a considerable time to improve reflecting the need for the body to generate new acetylcholine emitters.
- 5. Active haemolysis and rhabdomyolysis may cease within a few hours and the urine returns to its normal colour.

6. In patients with Shock, blood pressure may increase after 30 minutes.

# Repeat Doses of ASV

#### Haemotoxic envenomation

In the case of haemotoxic envenomation, the ASV strategy will be based around a six hour time period. When the initial blood test reveals a coagulation abnormality, the initial ASV amount will be given over 1 hour.

No additional ASV will be given until the next Clotting Test is carried out. This is due to the inability of the liver to replace clotting factors in under 6 hrs.

After 6 hours a further coagulation test should be performed and a further dose should be administered in the event of continued coagulation disturbance. This dose should also be given over 1 hour. CT tests and repeat doses of ASV should continue on a 6 hourly pattern until coagulation is restored, unless a species is identified as one against which Polyvalent ASV is not effective.

The repeat dose should be 5-10 vials of ASV i.e. half to one full dose of the original amount. The most logical approach is to administer the same dose again, as was administered initially. Some Indian doctors however, argue that since the amount of unbound venom is declining, due to its continued binding to tissue, and due to the wish to conserve scarce supplies of ASV, there may be a case for administering a smaller second dose. In the absence of good trial evidence to determine the objective position, a range of vials in the second dose has been adopted.

#### Neurotoxic

The ASV regime relating to neurotoxic envenomation has caused considerable confusion. If the initial dose has been unsuccessful in reducing the symptoms or if the symptoms have worsened or if the patient has gone into respiratory failure then a further dose should be administered, after 1-2 hours. At this point the patient should be re-assessed. If the symptoms have worsened or have not improved, a second dose of ASV should be given.

This dose should be the same as the initial dose, i.e. if 10 vials were given initially then 10 vials

should be repeated for a second dose and then ASV is discontinued. 20 vials is the maximum dose of ASV that should be given to a neurotoxically envenomed patient.

Once the patient is in respiratory failure, has received 20 vials of ASV and is supported on a ventilator, ASV therapy should be stopped. This recommendation is due to the assumption that all circulating venom would have been neutralised by this point. Therefore further ASV serves no useful purpose.

Evidence suggests that 'reversibility' of post 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'. 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, 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.

#### **Recurrent Envenomation**

When coagulation has been restored no further ASV should be administered, unless a proven recurrence of a coagulation abnormality is established. **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.** 

### Anti Haemostatic Maximum ASV Dosage Guidance

The normal guidelines are to administer ASV every 6 hours until coagulation has been restored. However, what should the clinician do after say, 30 vials have been administered and the coagulation abnormality persists?

There are a number of questions that should be considered. Firstly, is the envenoming species one for which polyvalent ASV is effective?

The next point to consider is whether the coagulopathy is resulting from the action of the venom. Published evidence suggests that the maximum venom yield from say a Russells Viper is 147 mg, which will reduce the moment the venom enters the system and starts binding to tissues. If 30 vials of ASV have been administered that represents 180 mg of neutralising capacity. This should certainly be enough to neutralise free flowing venom. At this point the clinician should consider whether the continued administration of ASV is serving any purpose, particularly in the absence of proven systemic bleeding.

At this stage the use of Fresh Frozen Plasma (FFP) or factors can be considered, if available.

# Drugs not to be used in viper bites: Heparin and Botropase

Heparin has been proposed as a means of reducing fibrin deposits in DIC (Paul et al, 2003). However, heparin is contraindicated in Viper bites. 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 heparin can cause bleeding by its own action. Trial evidence has shown it has no beneficial effect.

Botropase is a coagulant compound derived from the venom of one of two South American pit vipers. It should not be used as a coagulant in viper bites as it simply prolongs the coagulation abnormality by causing consumption coagulopathy in the same way as the Indian viper venom currently affecting the victim.

### 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 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.

# Snake Bite Treatment Protocol: Treating complications

# Hypotension

Hypotension can have a number of causes, particularly loss of circulating volume due to haemorrhaging, vasodilation due to the action of the venom or direct effects on the heart. Test for hypovolaemia by examining the blood pressure lying down and sitting up, to establish a postural drop.

Treatment is by means of plasma expanders. There is no conclusive trial evidence to support a preference for colloids or crystalloids. In cases where generalised capillary permeability has been established a vasoconstrictor such as dopamine can be used. Dosing is 5- 10ì /kg/minute.

Russell's Viper bites are known to cause acute pituitary adrenal insufficiency. 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.

### **Surgical Intervention**

Whilst there is undoubtedly a place for a surgical debridement of necrotic tissue, the use of fasciotomy is highly questionable. The appearance of:

1. Pain on passive stretching, 2. Pain out of proportion, 3. Pulselessness, 4. Pallor, 5. Parasthesia, 6. Paralysis

AND 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. Fasciotomy is required if the intracompartmental pressure is sufficiently high to cause blood vessels to collapse and lead to ischemia. Fasciotomy does not remove or reduce any envenomation.

What is important is that the intracompartmental pressure should be measured objectively using saline manometers or newer specialised equipment such as the Stryker Intracompartmental Pressure Monitoring Equipment. Visual impression is a highly unreliable guide to estimating intra-compartmental pressure. 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 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.

#### Renal Failure

Renal failure is a common complication of Russell's Viper and Hump-nosed Pit viper bites. The contributory factors are intravascular haemolysis, DIC, direct nephrotoxicity and hypotension 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 Acute Renal Failure. A child in renal failure is evidence of the previous action of venom either directly on the kidney or by fibrin deposition. It is not evidence that child has currently has un-neutralised venom in the system and therefore requires ASV.

The following are indications of renal failure:

- 1. Declining or no urine output although not all cases of renal failure exhibits oliguria
  - 2. Blood Bio-Chemistry
- 3. Serum Creatinine > 5mg/dl or rise of > 1mg/day.
  - 4. Urea > 200 mg/dl
- 6. Potassium > 5.6 mmol/l Confirm hyperkalaemia with ECG.
  - 7. Evidence of Uraemia or metabolic acidosis.

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.

# Cardiac complications

Studies reveal rare manifestations of cardiac toxicity. Main manifestations are rhythm abnormalities which include, bradycardia, tachycardia, sinus arrhythmia, gallop rhythm and rarely pulmonary oedema and cardiomegaly. Apart from showing the rhythm abnormalities, ECG may also show tall T waves, pattern suggesting myocardial ischemia and atrio-ventricular block. A cardiologist needs to be consulted if the rhythm abnormalities or other ECG findings persist.

# Snakebite Management in Primary/ Community/Dispensary Health Care Centres

Objective of this protocol is to enable doctors in Primary Care Institutions to treat snakebite with confidence. Evidence suggests that even when equipped with anti snake venom, Primary Health Care 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.

#### Patient Arrival & Assessment

- 1. Patient should be placed under observation for 24 hours
- 2. The snake, if brought, should be carefully examined and compared to the snake identification material.
  - 3. Pain management should be considered.
- 4. 20WBCT in clean, new, dry, glass test tubes should be carried out every 30 minutes for the  $1^{\text{st}}$  3 hours and then hourly after that.
- 5. Attention should be paid for any visible neurological symptoms.
- 6. Severe, current, local swelling should be identified
- 7. If no symptoms develop after 24 hours the patient can be discharged with a T.T.

### Envenomation; Haemotoxic

If the patient has evidence of haemotoxic envenomation, determined by 20WBCT, then 8-10 vials of ASV are administered over 1 hour. 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.

#### Referral Criteria

Once the ASV administration is finished and the adverse reaction dealt with the patient should be automatically referred to a higher centre with facilities for blood analysis to determine any systemic bleeding or renal impairment.

The 6 hour rule ensures that a six hour window is now available in which to transport the patient.

#### **Envenomation**; Neurotoxic

If the patient shows signs of neurotoxic envenomation 8-10 vials are administered over 1 hour.

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.

A neostigmine test is administered using 1.5-2.0mg of neostigmine IM plus 0.6mg of atropine IV. An objective measure such as single breath count is used to assess the improvement or lack of improvement given by the neostigmine over 1 hour. If there is no improvement in the objective measure the neostigmine is stopped. If there is improvement 0.5mg neostigmine is given IM every 30 minutes with atropine until recovery. Usually this recovery is very rapid.

If after 1 hour 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. ASV is then completed for this patient.

If after 2 hours the patient has not shown worsening symptoms, but has not improved, a second dose of ASV is given over 1 hour. ASV administration is now complete for this patient.

#### Referral Criteria

The primary consideration, in the case of neurotoxic bites, is respiratory failure requiring long term mechanical ventilation. Whilst it is entirely possible to maintain a neurotoxic victim by simply using a resuscitation bag, and this should always be used in a last resort, the best means of support is a mechanical ventilator operated by qualified staff.

Primary Care and even most Secondary care hospitals are not equipped with mechanical ventilators. The most important factor therefore is when to refer a patient to a hospital with a ventilator and under what conditions.

The key criteria to determine whether respiratory failure, requiring mechanical ventilation is likely, is the 'neck lift'. 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 Primary care institution.

If the patient reaches the stage when a neck lift cannot be carried out then the patient should be immediately referred to a hospital with a mechanical ventilator.

# 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 face mask, 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 PHC. 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 PHC 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.

### Annexure-I

# Basic Minimal & Essential Drug and Equipment Profile for a Primary Health Centre

In order to be able to effectively respond to snakebite, the primary care centre needs a drug and equipment profile that supports snakebite treatment. Often the level of skill to design such a profile is not readily available. Good guidelines are therefore required for doctors and government procurement groups as to how to equip a primary centre for its role.

### Antivenom / Anti Snake Venom

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.

In this instance the 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 PHC to a single patient

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

Suppose we are dealing with a PHC with two envenomings per month then x=2 The maximum dose required per patient determines a key part of usage, so for example, in India the maximum dose for a patient at a PHC would be 2 doses of 10 vials for a neurotoxic patient, so 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 AV/ASV to be replaced the equation would require 2 X 20 X 1.2 X 2 = 96 vials would be the AV/ASV base stock amount.

### **Other Support Drugs**

#### Adrenaline

Adult dosage of 0.5mg of 1:1000 with a potential of three doses maximum per patient.

(Stock of Minimum 10 vials)

### Hydrocortisone and Antihistamine

Adult dosage of 10mg antihistamine and 100mg of hydrocortisone. Only one application per patient is normally required before referral (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 (as per generic indent of the PHC)

#### IV fluids

Normal Saline, Ringer Lactate and 5 % Dextrose (As per generic indent requirement of PHC)

#### **Support Equipment Routine**

- 1. Syringes and/or IV sets for AV/ASV usage and drug administration
- 2. Clean, New GLASS Test Tubes (plastic test tubes are useless in this setting)
  - 3. Blood Pressure Monitor
  - 4. Ambubag with mask

# Preferred Additional Equipment

# Oxygen Cylinder

Some primary centres already possess oxygen cylinders. For example, many of the Indian PHCs are equipped with a 40cft cylinder. This can be used not only for application of oxygen to a victim but newer equipment is becoming available that enables the cylinder to power a gas ventilator.

#### **Airway Support Equipment**

- 1. Laryngeal tube / LMA
- 2. Nasopharyngeal Airways (These can be improvised using size 5 Endotracheal Tubes cut to the required length
  - 3. Endo Tracheal tubes
  - 4. Laryngoscope
  - 5. Suction equipment

# Stryker Intra-compartmental Pressure Monitoring Equipment.

#### First Aid References

- 1. Alberts MB, Shalit M, Logalbo F, Suction for venomous snakebite: a study of "mock venom in a human model" Ann Emerg Med. 2004 Feb;43(2):181-6.
- 2. Amaral CF, Campolina D, Dias MB, Bueno CM, Rezende NA. Tourniquet ineffectiveness to reduce the severity of envenoming after Crotalus durissus snake bite in Belo Horizonte, Minas Gerais, Brazil. 1998 Toxicon. May;36(5):805-8.
- 3. Anker RL, Staffon WG, Loiselle DS, Anker KM, Retarding the uptake of mock venom in humans. Comparison of three first aid treatments Medical Journal of Australia 1982. I 212-214
- 4. Bucknall N, Electrical Treatment of venomous bites and stings: a mini review. Toxicon 1991; 29: 397-400

- 5. Bush SP, Snakebite suction devices don't remove venom: They just suck. Ann Emerg Med. 2004;43(2):181-186.
- 6. Bush SP Hegewald KG, Green SM, Cardwell MD, Hayes WK, Effects of a negative-pressure venom extraction device (Extractor) on local tissue injury after artificial rattlesnake envenomation in a porcine model. Wilderness Environ Medicine 2000; (11): 180-188
- 7. Bush SP, Green SM, Laack TA, Hayes WK, Cardwell MD, Tanen DA, Pressure Immobilisation delays mortality and increases intracompartmental pressure after artificial intramuscular rattlesnake envenomation in a porcine model Annals of Emergency Medicine 2004; 44(6):599-604
- 8. Currie B. Pressure-immobilization first aid for snakebite fact and fancy. 1993 XIII International Congress for Tropical Medicine and Malaria. Jomtien, Pattaya, Thailand 29 Nov-4 Dec. *Toxicon* 1992; 31 (8):931-932.(abstract).
- 9. Davidson TM, Sam splint for wrap and immobilisation of snakebite. Journal of Wilderness Medicine 2001; (12): 206-207
- 10. Davis D, Branch K, Egen NB, Russell FE, Gerrish K, Auerbach PS, The effect of an electrical current on snake venom toxicity. Journal of Wilderness Medicine 1992; (3): 48-53
- 11. Fairly NH, Criteria for determining the efficacy of ligatures in snakebite. Medical Journal of Australia 1929; I: 377-394
- 12. Gray S, Pressure Immobilisation of Snakebite Wilderness Environ Med 2003;14 (1): 73–73.
- 13. Glass TG, Cooling for first aid in snakebite. N Engl J Med 1981; 305: 1095.
- 14. Gray, S, Pressure Immobilization of Snakebite. Wilderness and Environmental Medicine 2003;14(1): 73–73.
- 15. Grenard S. Veno- and arterio-occlusive tourniquets are not only harmful, they are unnecessary. Toxicon. 2000;38(10):1305-6.
- 16. Guderian RH, Mackenzie CD, Williams JF. High voltage shock treatment for snakebite. Lancet 1986; 229.

- 17. Hardy DL, A review of first aid measures for pit viper bite in North America with an appraisal of Extractor™ Suction and stun gun electroshock. 1992 In: Campbell JA, Brodie ED (eds). Biology of the Pit Vipers. Tyler, TX: Selva. 405-414.
- 18. Howarth DM, Southee AS, Whytw IM, Lymphatic flow rates and first aid in simulated peripheral snake or spider envenomation. Medical Journal of Australia 1994; 161: 695-700
- 19. Khin Ohn Lim, Aye-Aye-Myint, Tun-Pe, Theingie-New, Min-Naing, Russells Viper venom levels in serum of snake bite victims in Burma Trans. R Soc Trop Med Hyg. 1984; 78: 165-168
- 20. Kroegal C, Meyer Zum Buschfelde KH Biological Basis for High-Voltage-Shock Treatment for Snakebite Lancet 1986; 2: 1335
- 21. McPartland JM, Foster R, Stunguns and Snakebite Lancet 1988; 2:1141
- 22. Nishioka SA. Is tourniquet use ineffective in the pre-hospital management of South American rattlesnake bite? Toxicon 2000;38(2):151-2.
- 23. Norris RL, Ngo J, Nolan K, Hooker G, Physicians and lay people are unable to apply Pressure Immobilisation properly in a simulated snakebite scenario Wilderness and Environmental Medicine 2005;16:16-21
- 24. Pugh RN, Theakston RD. Fatality following use of a tourniquet after viper bite envenoming. Ann Trop Med Parasitol. 1987;81(1):77-8.
- 25. Russell FE, A letter on electroshock. Vet Hum Toxicol 1987; 29:320
- 26. Russell FE Another Warning about Electroshock for Snakebite Postgrad Med 1987a ;82 :32
- 27. Sharma SK, Chappuis F, Jha N, Bovier PA, Loutan L, Koirala S. Impact of snake bites and determinants of fatal outcomes in southeastern Nepal. Am J Trop Med Hyg. Aug;71(2):234-8.
- 28. Simpson ID Snakebite: Recent Advances 2006 in Medicine Update 2006 Ed Sahay BK The Association of Physicians of India 639-643

- 29. Snyder CC, Murdock RT, While GL, Kuitu JR Electric Shock Treatment for Snakebite Lancet 1989; 1:1022
- 30. Sutherland, Coulter AR, Harris RD, Rationalisation of first aid methods for elapid snakebite Lancet 1979; i :183-186
- 31. Sutherland SK, Harris RD, Coulter AR, Lovering KE, First aid for Cobra (Naja naja) bites. Indian Journal of Medical Research 1981;73: 266-268
- 32. Tun Pe, Tin-Nu-Swe, Myint-Lwin, Warrell DA, Than-Win, The efficacy of tourniquets as a first aid measure for Russells Viper bites in Burma Trans. R Soc Trop Med Hyg 1987; 81:403-405
- 33. Tun-Pe, Phillips RE, Warrell DA, Moore RA, Tin-Nu-Swe, Myint-Lwin, Burke CW. Acute and chronic pituitary failure resembling Sheehan's syndrome following bites by Russell's viper in Burma. Lancet 1987;(8562):763-7.
- 34. Tun Pe, Aye Aye Myint, Khin Ei Han et al, Local Compression pads as a first aid measure for victims of bites by Russells Viper (Daboia russelii siamensis) in Myanmar. Trans Royal Society of Trop Medicine 1995; 89:293-295
- 35. Tun Pe, Sann Mya, Aye Aye Myint, Nu Nu Aung, Khin Aye Kyu, Tin Oo, Field Trials of Efficacy of Local Compression Immobilisation First Aid Technique in Russells Viper (Daboia russelii siamensis) Bite Patients Southeast Asian J Trop Med Public Health 2000;31(2):346-348
- 36. Warrell DA, Clinical Toxicology of Snakebite in Asia 1995 in Handbook of Clinical Toxicology of Animal Venoms and Poisons Ed White J Meier J. CRC Press
- 37. Warrell, D.A. (Ed). 1999. WHO/SEARO Guidelines for The Clinical Management of Snakebite in the Southeast Asian Region. SE Asian J. Trop. Med. Pub. Hlth. 30, Suppl 1, 1-85.
- 38. Watt G, Padre L, Tuazon L, Theakston RDG, Laughlin L. Tourniquet Application after Cobra Bite: Delay in the Onset of Neurotoxicity and the Dangers of Sudden Release. Am J Trop Med Hyg 1988; 87: 618-622

#### References on Snakebite Treatment

- 1. Agrawal PN, Aqqarawal AN, Gupta D, Behera D, Prabhakar S, Jindal SK, Management of Respiratory Failure in Severe Neuroparalytic Snake Envenomation Neurol India. 2001; 49(1):25-28
- 2. Agarwal R, Aggarwal AN, Gupta D, Behera D, Jindal SK. Low dose of snake antivenom is as effective as high dose in patients with severe neurotoxic snake envenoming. Emerg Med J. 2005;22(6):397-9.
- 3. American Association of Allergy, Asthma, and Immunology. Media resources: position statement 26. The use of epinephrine in the treatment of anaphylaxis. www.aaaai.org/media/resources/advocacy\_statements/ps26.stm (accessed Apr 2003).
- 4. Anderson RJ, Linas ST, Berns AS, Henrich WL, Miller TR, Gabow PA, Schrer RW, Non-oliguric acute renal failure. New Eng Journal of Medicine. 1977; 296: 1134-1138
- 5. Bomb BS, Roy S, Kumawat DC, Bharjatya M, Do we need antisnake venom (ASV) for management of elapid ophitoxaemia? J Assoc Phys India 1996; 44: 31-33.
- 6. Chugh K, Aikat BK, Sharma BK, Dash SC, Mathew MT, Das KC, Acute Renal Failure Following Snakebite. The American Journal of Tropical medicine and Hyg. 1975;24(4): 692-697
- 7. Eapen CK, Chandy N, Kochuvarkey KL, Zacharia PK, Thomas PJ, Ipe TI. Unusual complications of snake bite: hypopituitarism after viper bites. In: Ohsaka A, Hayashi K, Sawai Y, eds. *Animal, plant and microbial toxins*. New York: Plenum ,467-473, 1976.
- 8. Gawarammana IB, Kularatne M, Abeysinga S, Dissarayake WP, Kumarasri RPV, Seranayake N, Ariyasena H, Parallel infusion of hydrocortisone ± chlorpheniramine bolus injection to prevent acute adverse reactions to antivenom for snakebites Med Journal of Australia. 2004;180(1):20-3.
- 9. Greenwood B, Warrell DA, Davidson NM, Ormerod LD, Reid HA, Immunodiagnosis of snakebite BMJ 1974; 4: 743-5
- 10. Ho M, Warrell MJ, Warrell DA, Bidwell D, Voller A, A critical reappraisal of the use of

- enzyme-linked immunosorbent assays in the study of snakebite. Toxicon 1986; 24: 211-221.
- 11. Joseph S, Orthopedics in Trauma, in: Vasnaik M, Shashiraj E, Palatty B.U., Essentials of Emergency Medicine, New Delhi, Jaypee Brothers Medical Publishers (P) Ld, 2003: 175-183
- 12. Kalantri S, Singh A, Joshi R, Malamba S, Ho C, Ezoua J, Morgan M. Clinical Predictors of in-hospital mortality in patients with snakebite: a retrospective study from a rural hospital in central India Tropical medicine and International health. 2005; 11(1): 22-30.
- 13. Kularatne SA. Common krait (Bungarus caeruleus) bite in Anuradhapura, Sri Lanka: a prospective clinical study, 1996-98. Postgrad Med J. 2002;78(919):276-80.
- 14. Kumar V., Maheshwari R., Verma H. K. Toxicity and symptomatic identification of species involved in snakebites in the Indian Subcontinent J. Venom. Anim. Toxins Incl. Trop. Dis, 2006, V.12, N.1, P.3-18,
- 15. McLean-Tooke A P C, Bethune C A, Fay A C, Spickett G P, Adrenaline in the treatment of anaphylaxis: what is the evidence? BMJ. 2003; 327: 1332-1335
- 16. Myint-Lwin, Phillips RE, Tun-Pe, Warrell DA, Tin-Nu-Swe, Maung Maung Lay, Bites by Russells Viper (Vipera russelli siamensis) in Burma: Haemostatic vascular and renal disturbances and response to treatment. Lancet. 1985; 8467: 1259-1264
- 17. Nishioka SA, Silviera PVP, Bauab FA, Bite Marks are useful for the differential diagnosis of snakebite in Brazil. Journal of Wilderness Medicine 1995; (6): 183-188
- 18. Norris RL, Bite marks and the diagnosis of venomous snakebite. Journal of Wilderness Medicine 1995; (6): 159-161
- 19. Paul V, Pratibha S, Prahlad KA, Earali J, Francis S, Lewis F, High-Dose Anti-Snake Venom versus low dose anti-snake venom in the treatment of poisonous snakebites A critical study Journal of the Associations of Physicians of India 2004;52: 14-17
- 20. Paul V, Prahlad KA, Earali J, Francis S, Lewis F. Trial of heparin in viper bites. J Assoc Physicians India. 2003;51:163-6.

- 21. Peshin SS, Lall SB, Kaleekal T, Snake Envenomations In Ed Lall SB Management of Common Indian Snake & Insect Bites 1997 National Poisons Information Centre AIIMS Delhi.
- 22. Pillay VV, Modern medical Toxicology 2005 Editors Jaypee Brothers New Delhi.
- 23. Premawardenha A, de Silva CE, Fonseka MMD, Gunatilakee SB, de Silva HJ, Low dose subcutaneous adrenaline to prevent acute adverse reactions to antivenom serum in people bitten by snakes: randomised, placebo controlled trial BMJ. 1999; 318: 1041-1043
- 24. Reitz, C.J.. Boomslang bite time of onset of clinical envenomation. S. Afr. Med. J. 1989;76: 39-40.
- 25. Sampson HA, Mendelson L, Rosen JP. Fatal and near-fatal anaphylactic reactions to food in children and adolescents. N Engl J Med 1992;327:380-4.
- 26. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. J Allergy Clin Immunol 2001;108:871-3.
- 27. Simpson ID. Snakebite Management in India, The First Few Hours: A Guide for Primary Care Physicians. J Indian Med Assoc 2007;105:324-335
- 28. Srimannanarayana J, Dutta TK, Sahai A, Badrinath S, Rational Use of Anti-snake venom (ASV): Trial of various Regimens in Hemotoxic Snake Envenomation JAPI. 2004;52: 788-793
- 29. Theakston RD, Lloyd-Jones MJ, Reid HA, 'Mico-Elisa for detecting and Assaying Snake Venom and Antibody' Lancet 1977; (2):639-41
- 30. Theakston RD, Phillips RE, Warrell DA, Galagedera Y, Abeysekera, DT, Dissanayaka P, de Silva A, Aloysius DJ, Envenoming by the Common Krait (Bungarus caeruleus) and Sri Lankan Cobra (Naja naja) efficacy and complications of therapy with Halfkein antivenom. Transactions of the Royal Society of Tropical Medicine and Hygiene. 1990; (84): 301-308.
- 31. Tin Na Swe, Myint Lwin, Myint-Aye-Mu, Than Than, Thein Than, Tun Pe, Heparin Therapy in Russells Viper bite victims with

- disseminated intravascular coagulation: a controlled trial. Southeast Asian J Trop Med Public Health. 1992; 23(2):282-287
- 32. Tin-Na-Swe, Thin Tun, Myint Lwin, Thein Than, Tun Pe, Robertson JIS, Leckie BJ, Phillips RE, Warrell DA, Renal ischemia, transient glomerular leak and acute renal tubular damage in patients envenomed by Russells Vipers (Daboia russelii siamensis) in Myanmar. Trans Roy Soc Trop Med Hyg. 1993; (87): 678-681
- 33. Tun P, Khin Aung Cho. Amount of venom injected by Russells Viper (Vipera russelli) Toxicon 1986; 24(7): 730-733
- 34. Wallace JF, Disorders caused by venoms, bites, and stings. In: Kasper DL, Braunwald E, Longo DL, Hauser S, Fauci AS, Jameson JL (eds). Harrison's Principles of Internal Medicine. Vol II. 16<sup>th</sup> edn, 2004. McGraw-Hill Inc, New York. 2593-2595.
- 35. Warrell, D.A., Davidson, N. McD., Greenwood, B.M., Ormerod, L.D., Pope, H.M., Watkins, B. J., Prentice, C.R.M.. Poisoning by bites of the saw-scaled or carpet viper (Echis carinatus) in Nigeria. Quart. J. Med. 1977;46: 33-62.
- 36. Warrell DA, Looareesuwan S, White NJ, Theakston RD, Warrell MJ, Kosakarn W, Reid HA, Severe neurotoxin envenoming by the Malayan Krait Bungarus candidus (Linnaeus): response to anticholinesterase. BMJ. 1983; 286: 670-680
- 37. Watt G, Theakston RD, Hayes CG, Yambao ML, Sangalang R, Ranao CP, Alquizalas E, Warrell DA, Positive response to edrophonium in patients with neurotoxic envenoming by cobras (Naja naja Philippinensis) The New England Journal of Medicine 1986; 23: 1444-1448
- 38. Wen Fan H, Marcopito LF, Cardoso JLC, Franca FOS, Malaque CMS, Ferrari RA, Theakston RD, Warrell DA, Sequential randomised and double blind trial of Promethazine prophylaxis against early anaphylactic reactions to antivenom for Bothrops snake bites. BMJ. 1999; (318):1451-1453.

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Fig 1. Medically Significant Snakes of India

Top Row L-R Spectacled cobra (Naja naja), Common krait (Bungarus caeruleus), Banded krait (Bungarus fasciatus). Middle Row L-R Hood Patterns Spectacled cobra, Monocled cobra, King cobra and the hump-nosed viper (Hypnale hypnale). Bottom Row L-R Russells viper (Daboia russelii), Saw scaled viper (Echis carinatus), Northern saw scaled viper (Echis sochureki)

Note: Northern saw scaled viper limited to Rajasthan and Jammu