Indian National Snakebite Protocol
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Indian National Snakebite Protocols 2007

First Aid and Snakebite Prevention
Snakebite Treatment
Support Concepts
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First Aid Treatment Protocol

Of primary importance is the need to recommend the most effective first aid for victims, to enable them to reach the nearest medical facility in the best possible condition. Much of the first aid currently carried out is ineffective and dangerous (Simpson, 2006). Indian research has agreed on the following recommended method having viewed and considered the available research and concluded that other methods are not appropriate for the conditions in India.

Recommended Method for India

The first aid being currently recommended is based around the mnemonic:

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

It consists of the following:

- **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 (Sharma et al, 2004), 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. This solely wastes time and can lead to other victims.
Traditional Methods to Be Discarded

Tourniquets
The use of tight tourniquets made of rope, belt, string or cloth have been traditionally used to stop venom flow into the body following snakebite. However, 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).
- Increased risk of massive neurotoxic blockade when tourniquet is released (Watt, 1988).
- 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 (Watt, 2003) (Amaral, 1998) (Nishioka, 2000).
- They give patients a false sense of security, which encourages them to delay their journey to hospital.

For the above reasons, Tourniquet use is contra-indicated for use in India.

Cutting and Suction
- 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 have been conclusively proven not to reduce the amount of circulating venom (Bush, 2000) (Bush, 2004). There has been some evidence that these devices increase envenomation as they inhibit natural oozing of venom from the wound (Alberts et al, 2004). In addition, they have been shown to increase the local effects of necrosis (Alberts et al, 2004).

Washing the Wound
Victims and bystanders often want to wash the wound to remove any venom on the surface. 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). Much of the support for this method came from letters to journals and not scientific papers (Bucknall, 1991) (Kroegal et al, 1986).

The research showed however that the venom is not denatured (Davis et al, 1992). In addition, it has been demonstrated that the electric shock has no beneficial effect (Dart et al, 1991) (Howe et al, 1988) (Russell, 1987) (Russell, 1987a) (Snyder et al, 1987) (Hardy, 1992). It has now been abandoned as a method of first aid.

Cryotherapy involving the application of ice to the bite was proposed in the 1950’s (Stanke 1951) (Glass, 1981). It was subsequently shown that this method had no benefit and merely increased the necrotic effect of the venom.

Newer Methods Considered Inapplicable in the Indian Context

Pressure Immobilisation Method (PIM)
Pressure Immobilisation has gained some supporters on television and in the herpetology literature. Some medical textbooks have referred to it. They have not however, reviewed the research, nor considered PIM’s applicability in the Indian context!

- PIM was developed in Australia in 1974 by Sutherland (Sutherland 1981). His research involved tying monkeys to wooden frames and injecting venom, then seeing if a pressure bandage would slow the absorption. He achieved some good results but there were mixed findings. He only used 13 monkeys which is not an adequate sample. He argued that a crepe bandage AND an integral splint be applied over the wound to a pressure of 55mm of Mercury. The version used in India of a bandage alone, Sutherland argued would be ineffective.
- Further work done by Howarth (Howarth 1994) demonstrated that the pressure, to be effective, was different in the lower and upper limbs. The upper limb pressure was 40-70mm of Mercury; the lower limb was 55-70mm of mercury.
- Howarth’s work also showed that full immobilisation was crucial. If the victim walked for 10 minutes after application the PIM would be ineffective (Currie, 1993). He also stated that pressures above the ranges specified would INCREASE the flow of venom. (Gray 2003) argued that pressures under the recommended range may also increase venom flow.
- Work carried out by (Norris 2005) showed that only 5% of lay people and 13% of doctors were able to correctly apply the technique!
- Further studies have demonstrated that improvised splints are ineffective (Davidson, 2001).
- In addition, pressure bandages should not be used where there is a risk of local necrosis, that is in 4/5 of the medically significant snakes of India (Bush, 2004).
Therefore, Indian rural workers would need:
1) To be in possession of crepe bandages and splints.
2) For the victim to immediately drop to the ground when bitten.
3) To have to be in pairs as the bystander must tie the bandage and splint, while the victim remains immobile.
4) To be able to tie the bandage to the correct level of pressure depending on whether an upper or lower limb was involved, when only 13% of emergency room doctors could achieve this.
5) And not to have to walk for more than 10 minutes.

For the above reasons, Pressure Immobilisation is not recommended for use in India.

Further First Aid Research
There has been some initial research that has suggested that a ‘Pressure Pad or Monash Technique’ may have some benefit in the first aid treatment of snakebite (Anker et al, 1982) (Tun Pe et al, 1995) (Tun Pe et al, 2000). In this method, a hard pad of rubber or cloth is applied directly to the wound in an attempt to reduce venom entering the system.

This method should be subjected to further research in India to assess its efficacy. It may have particular relevance to the Indian Armed Forces who carry Shell Dressings as part of their normal equipment, and would thus be ideally equipped to apply effective first aid in difficult geographic settings where the need is great.
Snakebite Prevention & Occupational Risk

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 often snakebites cluster around certain bio-mechanical activities, in certain geographic areas, at certain times of the day.

- Grass-cutting remains a major situational source of bites.
- In rubber, coconut and arecanut plantations clearing the base of the tree to place manure causes significant numbers of bites.
- Harvesting high growing crops like Millet which require attention focused away from the ground.
- Rubber tapping in the early hours 03:00-06:00.
- Vegetable harvesting/ fruit picking.
- Tea and coffee plantation workers face the risk of arboreal and terrestrial vipers when picking or tending bushes.
- Clearing weeds exposes workers to the same danger as their grass-cutting colleagues.
- Walking at night without a torch barefooted or wearing sandals accounts for a significant number of bites.
- 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.
- Walking along the edge of waterways.

Preventative Measures

☑ Walk at night with sturdy footwear and a torch and use the torch! 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. 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.
☑ 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.
☑ Pay close attention to the leaves and sticks on the ground when wood collecting.
☑ Keep animal feed and rubbish away from your house. They attract rats and snakes will follow.
☑ Try to avoid sleeping on the ground.
☑ Keep plants away from your doors and windows. Snakes like cover and plants help them climb up and into windows.
Snake Bite Treatment Protocol

Patient Assessment Phase: On arrival.
Deal with any life threatening symptoms on presentation. i.e. Airway, Breathing and Circulation.
If there is evidence of a bite, where the skin has been broken, give Tetanus Toxoid 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
- 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.
- All patients will be kept under observation for a minimum of 24 hours.
- In some countries bite marks have limited use in determining species (Nishioka et al, 1995) (Norris, 1995). However, in India 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.
- Determine if any traditional medicines have been used, they can sometimes cause confusing symptoms.
- Determine the exact time of the bite. This can give indications as to the progression of any symptoms.
- 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.

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. Pediatric dose 10mg/kg every 4-6 hourly orally.

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.

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.
Handling Tourniquets
Care must be taken when removing tight 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. If the pulse is absent ensure a doctor is present before removal.
- 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.

Diagnosis Phase: Investigations

20 Minute Whole Blood Clotting Test (20WBCT)

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 mls 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. If incoagulable blood is discovered, the 6 hourly cycle will then be adopted to test for the requirement for repeat doses of ASV.

Other Useful Tests depending on availability
- Haemoglobin/ PCV/ Platelet Count/ PT/ APTT/ FDP/ D-Dimer
- Peripheral Smear
- Urine Tests for Proteinuria/ RBC/ Haemoglobinuria/ Myoglobinuria
- Biochemistry for Serum Creatinine/ Urea/ Potassium
- Oxygen Saturation/ PR/BP/ RR/ Postural Blood Pressure
- ECG/ X-Ray/ CT/ Ultrasound (The use of X-Ray and ultrasound are of unproven benefit, apart from identification of bleeding in Viperine bites).
Diagnosis Phase: Symptoms

General
There are a great many myths surrounding snake symptoms. The table below summarises the evidence based situation. 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 Russells 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).

<table>
<thead>
<tr>
<th>Feature</th>
<th>Cobras</th>
<th>Kraits</th>
<th>Russells Viper</th>
<th>Saw Scaled Viper</th>
<th>Hump Nosed Viper</th>
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<tr>
<td>Local Pain/ Tissue Damage</td>
<td>YES</td>
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<td>YES</td>
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<tr>
<td>Ptosis/ Neurological Signs</td>
<td>YES</td>
<td>YES</td>
<td>YES!</td>
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<td>NO?</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Response to ASV</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>YES</td>
<td>NO</td>
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General signs and symptoms of Viperine envenomation
- Swelling and local pain.
- Tender enlargement of local lymph nodes as large molecular weight Viper venom molecules enter the system via the lymphatics.
- Bleeding from the gingival sulci and other orifices.
- Epistaxis.
- Vomiting (Kalantri SP et al. 2006).
- Acute abdominal tenderness which may suggest gastro-intestinal or retro peritoneal bleeding.
- Hypotension resulting from hypovolaemia or direct vasodilation.
- Low back pain, indicative of a 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.
- The skin and mucous membranes may show evidence of petechiae, purpura ecchymoses.
• The passing of reddish or dark-brown urine or declining or no urine output.
• Lateralising neurological symptoms and asymmetrical pupils may be indicative of intra-cranial bleeding.
• Muscle pain indicating rhabdomyolysis.
• Parotid swelling, conjunctival oedema, sub-conjunctival haemorrhage.

General signs and symptoms of Elapid envenomation
• Swelling and local pain (Cobra).
• Local necrosis and/or blistering (Cobra).
• Descending paralysis, initially of muscles innervated by the cranial nerves, commencing with ptosis, diplopia, or ophthalmoplegia. 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.
• Paralysis of jaw and tongue may lead to upper airway obstruction and aspiration of pooled secretions because of the patient’s inability to swallow.
• Numbness around the lips and mouth, progressing to pooling of secretions, bulbar paralysis and respiratory failure.
• Hypoxia due to inadequate ventilation can cause cyanosis, altered sensorium and coma. This is a life threatening situation and needs urgent intervention.
• Paradoxical respiration, as a result of the intercostal muscles becoming paralysed is a frequent sign.
• Stomach pain which may suggest submucosal haemorrhages in the stomach (Kularatne 2002) (Krait).
• 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 pitviper (Joseph et al, 2006) 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 (Ho et al, 1986) (Warrell et al, 1977) (Reitz, 1989).

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.

Anti Snake Venom (ASV)
Anti snake venom (ASV) in India is polyvalent i.e. it is effective against all the four common species; Russells 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.

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

There are known species such as the Hump-nosed pitviper (*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 is produced in both liquid and lyophilised forms. There is no evidence to suggest which form is more effective and many doctors prefer one or the other based purely on personal choice. 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.

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.

**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 risks of anaphylactic reactions and should not therefore be used unnecessarily. The doctor should be prepared for such reactions.

**ONLY** if a Patient develops one or more of the following signs/symptoms will ASV be administered:

**Systemic envenoming**

- Evidence of coagulopathy: Primarily detected by 20WBCT or visible spontaneous systemic bleeding, gums etc.
  
  Further laboratory tests for thrombocytopenia, Hb abnormalities, PCV, peripheral smear etc provide confirmation, but 20WBCT is paramount.

- 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 sole determinant of whether ASV is administered to a patient.

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

Severe Current Local envenoming
- Severe current, local swelling involving more than half of the bitten limb (in the absence of a tourniquet). In the case of severe swelling after bites on the digits (toes and especially fingers) after a bite from a known necrotic species.
- Rapid extension of swelling (for example beyond the wrist or ankle within a few hours of bites on the hands or feet). **Swelling a number of hours old is not grounds for giving ASV.**

Purely local swelling, even if accompanied by a bite mark from an apparently venomous snake, is not grounds for administering ASV.

N.B.
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.

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.

Of the three published studies on the efficacy of prophylactic regimens for prevention of reactions to ASV, one (Wen Fan et al) showed no benefit and the other two (Premawardenha et al, 1999) (Gawarammana et al, 2003) showed modest benefit. However, because these studies were underpowered to detect the true outcome effect, larger clinical trials are needed to conclude that the prophylactic treatment is beneficial.

Two regimens are normally recommended:

- 100mg of hydrocortisone and H1antihistamine (10mg chlorphenimarine maleate; 22.5mg IV phenimarine maleate IV or 25mg promethazine HC1 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.
0.25-0.3mg adrenaline 1:1000 given subcutaneously.

The conclusion in respect of prophylactic regimens to prevent anaphylactic reactions, is that there is no evidence from good quality randomized clinical trials to support their routine use. If they are used then the decision must rest on other grounds, such as political policy in the case of Government Hospitals, which may opt for a 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 anti-histamine may be advisable, in order to prevent severe reactions.

**ASV Administration: 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.

The recommended dosage level has been based on published research that Russells Viper injects on average 63mg SD 7 mg of venom (Tun Pe, 1986). Logic suggests that our 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.

This suggests that the total required dose will be between 10 vials to 25 vials as each vial neutralises 6mg of Russells 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.

There is no evidence that shows that low dose strategies (Paul et al, 2004) (Srimannanarayana et al, 2004) (Agraval 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.
NO ASV TEST DOSE MUST BE ADMINISTERED!
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.

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

**Neurotoxic/ Anti Haemostatic** 8-10 Vials

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.

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 the bite site, has been proven to be ineffective, painful and raises the intracompartmental pressure, particularly in the digits. It should not be used.

**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.

**Snakebite in Pregnancy**
There is very little definitive data published on the effects of snakebite during pregnancy. There have been cases reported when spontaneous abortion of the foetus has been reported although this is not the outcome in the majority of cases. It is not clear if venom can pass the placental barrier.

Pregnant women are treated in exactly the same way as other victims. The same dosage of ASV is given.
The victim should be referred to a gynaecologist for assessment of any impact on the foetus.

**Victims Who Arrive Late**

A frequent problem is victims who arrive late after the bite, often after several days, usually with acute renal failure. Should the clinician administer ASV? The key determining factor is, are there any 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 any 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 is life-threatening, but despite the reluctance in giving ASV due to reactions (Kalantri et al, 2005), if the correct protocol is followed, it can be effectively treated and dealt with. Anaphylaxis can be rapid onset and can deteriorate into a life-threatening emergency very rapidly. Adrenaline should always be immediately available.

The patient should be monitored closely (Peshin et al, 1997) and at the first sign of any of the following:

- Urticaria, itching, fever, shaking chills, nausea, vomiting, diarrhoea, abdominal cramps, tachycardia, hypotension, bronchospasm and angio-oedema

1. ASV will be discontinued
2. 0.5mg of 1:1000 adrenaline will be given IM,

Children are given 0.01mg/kg body weight of adrenaline IM.

In addition, to provide longer 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 chlorphenimarine 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 pediatric cases must be deployed with caution.
Indian National Snakebite Protocols

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.

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.

The IM route for the administration of adrenaline is the option selected, due to the rapidity of development 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 (American Association, 2003) (Simons, 1998). The early use of adrenaline has been selected as a result of study evidence suggesting better patient outcome if adrenaline is used early (Sampson et al, 1992).

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

It is widely believed that anaphylactoid reactions are under reported (McLean-Tooke et al, 2003)

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 (Watt et al, 1986). There is some doubt over its usefulness against the pre-synaptic neurotoxin such as those of the Krait and the Russells Viper (Warrell et al, 1983) (Theakston et al, 1990). However it is worth trying in these cases.

In the case of neurotoxic envenomation the 'Neostigmine Test' will be administered, 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:
Indian National Snakebite Protocols

a) Single breath count
b) Mm of Iris uncovered (Amount covered by the descending eyelid)
c) Inter incisor distance (Measured distance between the upper and lower incisors)
d) Length of time upward gaze can be maintained
e) 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 (Bomb et al, 1996). However this approach ignores the value of neutralising the free flowing venom before it can attach and carry out its task.

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

a) Spontaneous systemic bleeding such as gum bleeding usually stops within 15-30 minutes.
b) Blood coagulability is usually restored in 6 hours. Principal test is 20WBCT
c) Post synaptic neurotoxic envenoming such as the Cobra may begin to improve as early as 30 minutes after antivenom, but can take several hours.
d) 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.
e) Active haemolysis and rhabdomyolysis may cease within a few hours and the urine returns to its normal colour.
f) In shocked patients, blood pressure may increase after 30 minutes.

**Repeat Doses: Anti Haemostatic**
In the case of anti haemostatic 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.

**Recurrent Envenomation**
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 U.S. phenomenon, due to the short half-life of Crofab ASV.

*Indian ASV* is a F(ab)\(_2\) 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? For example, it has been established that envenomation by the Hump-nosed Pitviper (*Hypnale hypnale*) does not respond to normal ASV. This may be a cause as, in the case of Hypnale, coagulopathy can continue for up to 3 weeks!

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.
Repeat Doses: 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’ (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.

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 5-10μg/kg/minute.

Russells 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 Russells 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 (Joseph, 2003):

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

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. 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.

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.

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 intracompartmental 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 and ASV

Renal failure is a common complication of Russells Viper and Hump-nosed Pitviper bites (Tin-Nu-Swe et al, 1993) Joseph et al, 2006). 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 Russells 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).

The following are indications of renal failure:

1. Declining or no urine output although not all cases of renal failure exhibits oliguria (Anderson et al, 1977).
2. Blood Testing
   - Serum Creatinine > 5mg/dl or rise of > 1mg / day.
   - Urea > 200mg/dl
   - Potassium > 5.6 mmol/l Confirm hyperkalaemia with EKG.
3. 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.

Use of Heparin and Botropase in Viper Bites

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 (Tin Na Swe, 1992)

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

A key 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 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 (Simpson, 2007).

Patient Arrival & Assessment
Patient should be placed under observation for 24 hours
The snake, if brought, should be carefully examined and compared to the snake identification material.
Pain management should be considered.
20WBCT in clean, new, dry, glass test tubes should be carried out every 30 minutes for the 1st 3 hours and then hourly after that.
Attention should be paid for any visible neurological symptoms.
Severe, current, local swelling should be identified
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 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. Again ASV is now completed 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.

**Basic Minimal & Essential Drug and Equipment Profile for a Primary 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 AV/ASV used will be determined by availability, cost and effectiveness of the cold chain. Lyophilised AV/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:

\[
(x \times d \times 1.2) \times t
\]

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 \(2 \times 20 \times 1.2 \times 2 = 96\) 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.

Hydrocortisone and Antihistamine
Adult dosage of 10mg antihistamine and 100mg of hydrocortisone. Only one application per patient is normally required before referral.

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.

Pain
Paracetamol: 500mg tablets

Support Equipment

Routine
Syringes and/or IV sets for AV/ASV usage and drug administration
Clean, New GLASS Test Tubes (plastic test tubes are useless in this setting)
Blood Pressure Monitor
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 40cfi 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
- Laryngeal tube / LMA
- Nasopharyngeal Airways (These can be improvised using size 5 Endotracheal Tubes cut to the required length
Indian National Snakebite Protocols

The Future of Snakebite Management in India
It is recognised that this protocol represents the best available information and guidelines for dealing with snakebite in India. It will be constantly updated to reflect the best evidence based research that emerges during its use.
Appendix 1
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Appendix 2

Support Factors to Enhance Snakebite Protocols

Snakes of Medical Significance

Indian venomous snakes of medical significance have usually been regarded as only four species: Russells 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. The W.H.O. Model, produced in 1981, has been adopted as the Indian preferred method for categorising snakes of medical importance. The model is shown below:

Snakes of Medical Significance based on (W.H.O. 1981)

- **Class I:** Commonly cause death or serious disability
  RUSSELLS VIPER/COBRA/SAW SCALED VIPER
- **Class II:** Uncommonly cause bites but are recorded to cause serious effects (death or local necrosis)
  KRAIT/HUMP-NOSED PIT VIPER/KING COBRA/MOUNTAIN PIT VIPER
- **Class III:** Commonly cause bites but serious effects are very uncommon.

Further research is being undertaken to establish a definitive list of medically significant snakes in India.