

## ANTI SNAKE VENOM THERAPY- A REVIEW

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## ABSTRACT

India is estimated to have the highest snakebite mortality in the world. Snakebite victims come mostly from poor rural communities and many are children. Snake bites are life-threatening incidence that can require intensive care. The diagnosis and treatment of venomous snake bites is sometimes difficult for clinicians because sufficient information has not been provided in clinical practice including the administration of anti snake venom therapy. The most appropriate therapy for envenoming is timely administration of the species-appropriate anti snake venom. The rate of administration of anti snake venom should be based on the severity of the case and the patient's tolerance to the anti snake venom. The entire initial dose should be given as soon as possible and preferably within 4 hours of the bite. In severe envenoming, however, anti snake venom given up to 24 hours after the bite has been shown to reverse coagulation deficits. Before starting anti snake venom therapy, enquiry must be made as to any history of allergy or reaction. There are three types of anti snake venom reaction: early anaphylactic reaction, pyrogenic reaction and late serum sickness. If an immediate anaphylactic reaction occurs, administration of anti snake venom should be immediately discontinued and the patient given an antihistamine or adrenaline as appropriate. The key to management of venomous snakebite is the administration of specific anti snake venom or polyvalent anti snake venom.

**KEYWORDS:** Anti Snake Venom, Polyvalent, Antivenin, Anaphylaxis, Serum Sickness, Management etc.

## INTRODUCTION

Snake bite is a common life-threatening condition in many tropical countries; farmers, hunters and rice-pickers are at particular risk and prompt medical treatment is vital. The virtually global presence of venomous snakes explains the worldwide estimates of 3-5 million victims per year, with nearly 50000 deaths and a staggering 400000 amputations.<sup>[1]</sup> There are more than 2000 species of snakes in the world, and about 216 species in India, of which 52 are venomous. Every year about 2 lakh individuals are bitten, of whom an estimated 15000 subsequently die.<sup>[2]</sup> The most appropriate therapy for envenoming is timely administration of the species-appropriate anti snake venom. The entire initial dose should be given as soon as possible and preferably within 4 hours of the bite. The key to management of venomous snakebite is the administration of specific anti snake venom or polyvalent anti snake venom.<sup>[3]</sup>

Medically Important Poisonous Snakes of India<sup>[4]</sup>

**Saw scaled viper, Russell's viper, Common cobra [Indian cobra] and common krait** are traditionally referred to the "Big Four", because they are responsible for virtually all snakebites in India. The commonest snakes encountered in India include-

- Saw scaled viper (*Echic carinatus*).

- Russell's viper (*Vipera* or *Daboia russelli*).
- Common cobra (*Naja naja*).
- King cobra (*Ophiophagus hannah*).
- Common krait (*Bungarus caeruleus*).
- Banded krait (*Bungarus fasciatus*).
- Sea snakes.

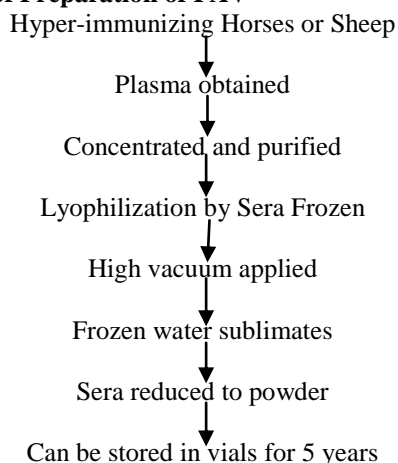
## Anti Snake Venom (ASV)

The anti snake venom serum may be monovalent (specific) i.e. effective against a specific snake (not available in India) or polyvalent which is effective against Cobra, Krait, Russell's viper and Saw scaled viper.<sup>[5]</sup> Monovalent anti snake venom is prepared by his prepared by hyperimmunising horses against the venom of a particular snake while polyvalent anti snake venom is prepared by hyperimmunising horses against the venoms of four common poisonous snakes, viz. (1) cobra, (2) common krait, (3) Russell's viper and (4) saw-scaled viper. The strength of the polyvalent anti snake venom is such that 1 ml will neutralize 0.6 mg of dried cobra venom, 0.45 mg of dried krait venom, 0.6 mg of dried Russell's viper venom and 0.45 mg of dried saw-scaled viper venom. The mortality from poisonous snake bite is nearly 40%. Anti snake venom treatment reduces it to less than 10%. It should be given as per instructions

accompanying the phial.<sup>[6]</sup> The serum is lyophilized by drying it from the frozen state under high vacuum. It is prepared in the Haffkine Institute Mumbai, King Institute Chennai, Serum Institute Pune and at Kasauli in India and is available in the form of lyophilized powder in an ampoule, which retains potency for about five years. It is useful when given within 4 hours of bite. It is of less value if delayed for 8 hours and is of doubtful value after 24 hours. Each vial of polyvalent ASV will neutralize about 6 to 8 mg of venom. Its half-life is about 90 hours.<sup>[7]</sup>



#### Method of Preparation of PAV<sup>[8]</sup>



#### Manufacturer of ASV in India<sup>[9]</sup>

S.N.	Manufacturer of Anti Snake Venom in India
01	Bharat Serum & Vaccines Ltd., Mumbai.
02	Central Research Institute, Kasauli.
03	Haffkine Biopharmaceutical Company Ltd. Mumbai.
04	King's Institute of Preventive Medicine, Chennai.
05	Serum Institute of India Ltd., Pune.
06	VINS Bioproducts Ltd., Hyderabad.

#### Efficacy of PAV<sup>[10]</sup>

S.N.	Venom	Each vial of PAV [10 ml] neutralizes following amount
01	Cobra	6 mg
02	Russell's Viper	6 mg
03	Common Krait	4.5 mg
04	Saw scaled Viper	4.5 mg

#### Indications<sup>[11]</sup>

- Cardiogenic shock.
- Spontaneous systemic bleeding.
- Incoagulable blood.
- Neurotoxicity.
- Haematuria.
- Other evidence of haemolysis/rhabdomyolysis.
- Rapidly progressive extensive local swelling.
- Bites on digits by snakes with known necrotic venoms.

desensitization is achieved by injecting multiple small doses under cover of adrenaline, antihistamines and corticosteroids.

#### Contraindication<sup>[12]</sup>

There is no absolute contra indication to anti snake venom therapy. If a person is sensitive to serum,

**Snakebite Envenomation Severity Scale (SESS)<sup>[13]</sup>**

Assessment of severity of envenomation-

S.N.	Category	Findings
01	No Envenomation	Absence of local or systemic reactions, fang marks +/-.
02	Mild Envenomation	Fang marks, moderate pain, minimal local edema (0-15 cm), erythema +, ecchymosis +/-, no systemic reactions.
03	Moderate Envenomation	Fang marks +, severe pain, moderate local edema (15-30 cm), erythema +, ecchymosis +, systemic weakness, sweating, syncope, nausea, vomiting, thrombocytopenia and anemia.
04	Severe Envenomation	Fang marks +, severe pain, severe local edema (>30 cm), erythema +, ecchymosis +, hypotension, parasthesia, coma and respiratory failure.

**Initial Dose of ASV<sup>[13]</sup>**

Antivenom should be given as soon as possible, 10 vials of polyvalent anti snake venom given at a rate of 5 ml/minute intravenously, or dilute in saline and infused over 30-60 minutes. For neuroparalytic snake bite, the dose of antivenom should be repeated if neurotoxic symptoms persist or fail to resolve when examined after 2 hours. For viperine bites, 10 vials of polyvalent anti snake venom should be given stat or if the whole blood clotting time is more than 20 minutes. A second dose of 10 vials may be needed if incoagulable blood [whole blood clotting time (WBCT) >20 min] persist for more than 6 hours after the first dose. A third dose can be given if WBCT >20 min persist after 12 hours of the bite. The dose of polyvalent anti snake venom should never exceed 20 vials (200 ml) for neuroparalytic snake bite and 30 vials (300 ml) for viperine/haemotoxic snake bites.<sup>[14]</sup> Children require the same dose as in adults.<sup>[15]</sup>

**Route of Administration<sup>[16]</sup>**

- Intravenous Bolus.
- Intravenous infusion.

**Golden Time of Administration<sup>[17]</sup>**

Within 4 hours. Less value after 8 hours and of doubtful value >24 hours.

**Hypersensitivity Testing<sup>[18]</sup>**

- (1) By s/c or intradermal injection or intracunjunctival instillation of diluted antivenom was once tried.
- (2) Not recommended now because-
  - Delay the start of antivenom treatment.
  - Risky, because may presensitize patient to PAV.
  - Poor predictors of early anaphylactoid reaction.
  - In serious envenomations, PAV therapy has to be administered anyway.

**Adverse Reactions of ASV**

There are three types of anti snake venom reaction: early anaphylactic reaction, pyrogenic reaction and late serum sickness type reaction.

**(1) Anaphylactic or type-i (immediate) reactions**

Early anaphylactic reaction commonly present with urticaria, itching, shivering, chills, cough, abdominal colic, diarrhea, nausea or vomiting, tachycardia, hypotension, bronchospasm and angio-oedema. It usually occurs in 10-180 min of starting anti snake venom.<sup>[13,19]</sup>

**(2) Pyrogenic reactions**

It usually develop 1-2 hrs after starting ASV therapy. Fever, rigor, chill, lower blood pressure are the features. They are due to pyrogenic contamination of ASV and diluting fluid.<sup>[19]</sup>

**(3) Serum sickness or type-iii (delayed) reactions**

Serum sickness clinical features include fever, chills, urticaria, myalgias, arthralgias, lymphadenopathy and possibly renal or neurologic dysfunction may develop 3 days to 3 weeks after anti snake venom administration. Serum sickness is dose related, as it occurs when >8 vials of polyvalent ASV are administered.<sup>[13,18]</sup>

**Treatment of Adverse Reactions****(1) Treatment of anaphylactic or type-i (immediate) reactions<sup>[13,19]</sup>**

- Stop PAV infusion.
- Administer 0.5 ml [1:1000] adrenaline i/m for adults and 0.01 ml/kg for children.
- Give hydrocortisone and antihistamines to provide longer term protection.
- If there is no improvement after 10-15 min give a second dose of adrenaline.
- Once the condition has improved start PAV infusion.

**(2) Treatment of pyrogenic reactions**

Give paracetamol but aspirin should not be given, as it may make the patient bleed.<sup>[19]</sup>

**(3) Treatment of serum sickness or type-iii (delayed) reactions**

Treat with systemic glucocorticoids e.g., oral prednisolone 1-2 mg/kg daily until all findings resolve; the dose is then tapered over 1-2 weeks. Also oral antihistamines and analgesics.<sup>[18]</sup>

**Prophylaxis Against Allergic Reaction to ASV**

Worldwide, the quality of antivenoms is highly variable. Rates of acute non-allergic anaphylactic reactions to some of these products exceed 50%. For this reason, some authorities have recommended pretreatment with IV antihistamines (e.g., diphenhydramine 1 mg/kg to a maximum of 100 mg and cimetidine 5-10 mg/kg to a maximum of 300 mg) or even a prophylactic subcutaneous or intramuscular dose of epinephrine (0.01 mg/kg, up to 0.3 mg). Further research is necessary,

however to determine whether any pretreatment measures are truly beneficial.<sup>[20]</sup>

#### Timing and Dose Repeation of PAV<sup>[14]</sup>

- A second dose of 10 vials may be needed if incoagulable blood [WBCT >20 min] persist for more than 6 hours after the first dose.
- A third dose can be given if WBCT >20 min persist after 12 hours of the bite.
- The dose of polyvalent anti snake venom should never exceed 20 vials (200 ml) for neuromparalytic snake bite and 30 vials (300 ml) for viperine/haemotoxic snake bites.

#### Recurrence of Systemic Envenoming<sup>[21]</sup>

Recurrence systemic envenomation has been observed within 24 to 48 hours of initial recovery. It is due to continuing absorption of venom from the deposit at the site of bite, perhaps after improvement in blood supply following correction of shock and hypovolemia and disappearance of ASV from circulations. It is seen less in India in view of prolonged half-life of polyvalent ASV produced in India (80-100 hours). The recurrence may also be due to redistribution of snake venom from tissue into vascular space as a result of anti snake venom therapy. Hence cases of snake bite should be observed for 48 hrs after recovery.

#### CONCLUSION

India is estimated to have the highest snakebite mortality in the world. The mortality from poisonous snake bite is nearly 40%. Anti snake venom treatment reduces it to less than 10%. Snake bites are life-threatening incidence that can require intensive care but due to lack of research work the diagnosis and treatment of venomous snake bites is sometimes difficult for clinicians because sufficient information has not been provided in clinical practice including the administration of anti snake venom therapy. The development of evidence based anti snake venom therapy in venomous snake bites is essential step to rationalize the anti snake venom therapy.

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