

India is estimated to have the highest snake bite mortality in the world with WHO estimates placing the number between 15,000 to 30,000 per annum. The oftquoted figure till recently was around 50,000. Conservative estimates put the deaths related to snakebite in between 35,000-50,000 per year in India alone. It is quite unfortunate that most of the deaths in our country are due to fright and wrong line of treatment.

The first thing to be verified is whether it is a snake bite at all. And if so whether it was a venomous snake bite. The victim may be shown a chart with photographs of venomous snakes in the area to help identification. Symptoms of pain out of proportion to the extent of injury are typical of envenomation. If the pain seems proportional to the injury seen, it may not be a snake bite at all and could be an injury from other causes.

The species identification does not really change the medically management at present, as the ASV we use is polyvalent i.e ASV which neutralizes the venom of all the "Big Four". The currently used polyvalent ASV would not cover king cobra bites, sea snake bites and would have nil or very minimal benefit in pit viper bite.

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.

DIAGNOSIS PHASE – SYMPTOMS

Hemostatic abnormalities are prima facie evidence of a viper bite. Cobras & Krait do not cause haemostatic disturbances. All the vipers can cause renal failure. Russell's Viper can also manifest neurotoxic symptoms in a wide area of India, especially southern India. This can sometimes cause confusion and further work is necessary to establish how wide this area might be. The neurotoxic symptoms of Russell's Viper are believed to be pre-synaptic or krait like in nature.

GENERAL SIGNS & SYMPTOMS OF VIPERIDAE ENVENOMATION

- Local pain & swelling and erythema over bitten part., Tender enlargement of local lymph nodes, Local necrosis and or blistering, Vomiting, abdominal pain
- The victim may bleed from any orifice or organ, hemoptysis, epistaxis, hematuria, hematemesis

and malena, chemosis, macular bleed, excessive menstrual bleed, bleeding from bite site or the canula, bleeding into muscles, bleeding from gingival sulci, epistaxis. Bleeding into skin & mucous membrane may show evidence of petichiae, purpura, epistaxis.

- Hypotension resulting from hypovolemia or direct vasodilatation.
- Low back pain, loin pain indicative of an early renal failure or retroperitoneal bleeding. The passing of reddish or dark brown urine or declining or no urine output.
- Lateralising neurological symptoms and asymmetrical pupils maybe indicative of intracranial bleeding

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 eye lids feel heavy.

Dysphagia, dysguesia involvement of sense of smell, diaphoresis. Circum oral pallor and paraesthesia, profound thirst, miosis, abdominal pain, vomiting, painful lymphadenopathy, palpitation, breathlessness, chest pain, Paralysis of jaw and tongue may lead to upper air way obstruction and aspiration of pooled secretions because of the patients inability to swallow.

Bulbar paralysis and respiratory failure. Paradoxical respiration, as a result of the intercostal muscles becoming paralysed is a frequent sign.

Hypoxia due to inadequate ventilation can cause cyanosis, altered sensorium and coma.

Stomach pain which may suggest submucosal haemorrhage in the stomach (Krait).

Krait bite 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

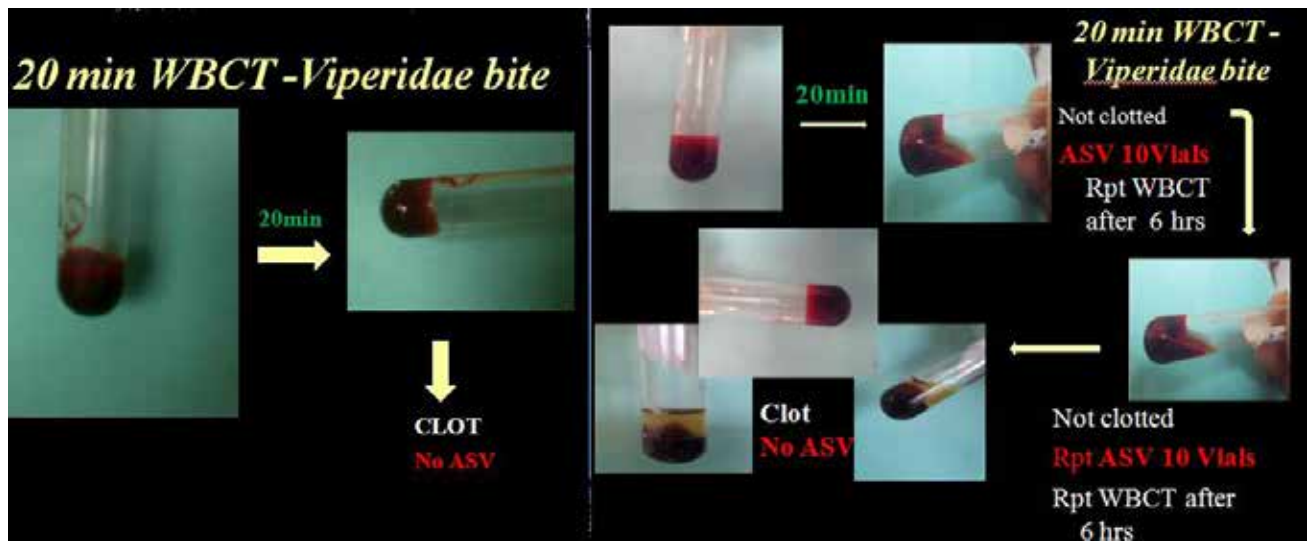


Fig. 1 : 20 min Whole blood clotting test (20 min WBCT)

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 to 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.

In the case of a cobra bite there is very little pain at the bite site immediately after bite. But if a lethal dose has been injected, slight local pain develops after about eight to 30 minutes. There may be very little swelling at the bite site.

BITE BY SEA SNAKE

The bite is usually painless and may go unnoticed. There is minimal or no local swelling and involvement of local lymph node is unusual. Generalised rhabdomyolysis is the dominant effect of envenoming by these snakes. Early symptoms include headache, a thick feeling of the tongue, thirst, sweating and vomiting, generalised aching, trismus, stiffness and tenderness of the muscles become noticeable between 30 minutes to 3½ hours after the bite. progressive flaccid paralysis with ptosis occur. The patient remains conscious until the respiratory muscles are sufficiently affected to cause respiratory failure.

Myoglobinemia and myoglobinuria develop 3 to 8 hours after the bite. Myoglobin and potassium released from damaged skeletal muscles may cause acute kidney injury.

INVESTIGATION

20 minute whole blood clotting test (20 WBCT) considered the most reliable test of coagulation in hematotoxic bite and can be carried out at the bedside without special training. It is significantly superior to the capillary tube method (Figure 1).

A few milliliters of fresh venous blood is placed in a new, clean, dry glass test tube and left at ambient temperature for 20 minutes. 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 test tube 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. If everything is normal, repeated at one hour interval till six hours after bite and twice more at 3 hour intervals the next 6 hours. If all reports are normal, no further triage would be needed. A normal 20 WBCT and clot lysis would exclude viperidae species. But it occasionally happens that the parameters become abnormal only 24 hours after the bite especially in pit viper bites.

- Simultaneously, a single breath counting test is done in suspected elapid bites and the same is repeated at 15 minutes interval over the first 2 hours.
- The onset of symptoms and sudden progression are more common with Elapidae bite rather than viperidae. Most sea snake, krait and cobra bite would show symptoms within the first 6 hours, the shortest time frame being for the sea snakes. Similarly, the mortality due to elapid bites are mostly in the first 24 hours. The likelihood of a "dry bite" from among the "big four" is most with a cobra.

OTHER USEFUL TESTS

Haematological: Hemoglobin, PCV, TLC, DLC, ESR, Peripheral smear (Figure 2). Platelet count- which is repeated 6 hourly the first 24 hours in viperidae bite.

Coagulation Work up: CT, BT, APTT >1.5 ULN, PT >1.5 ULN

DIC Work up: D. Dimer, FDP, Fibrinogen which are repeated on the third day.

Renal function: Blood urea, Serum creatinine

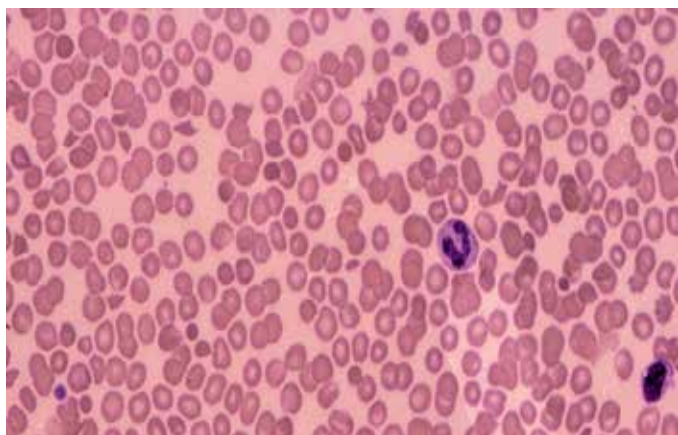


Fig. 2: Peripheral smear showing schistocytes and burr cells in a patient with hemotoxic snake bite

Liver function Tests

Muscle Enzymes: Creatinine phosphokinase (CPK)

Biochemistry: Na, K and Blood Sugar

Urine: Checked for myoglobin, Haemoglobin & Protein

Blood group : ABO, Rh (at the earliest as blood doesn't clot later)

Oxygen saturation/BP/Postural Blood Pressure/PR/RR

Arterial Blood gases.

The same may have to be repeated depending on the clinical course of the patient.

- The tests repeated on a daily basis are : Hb, PCV, CBC, urea, creatinine, platelets and urine protein.
- The coagulation work up usually normalizes within 24 to 48 hours of treatment. Exceptions are in cases of certain pit viper species, where it may take up to 2-3 weeks to normalize.

A peripheral smear is also sent for in which crenated RBC, schistocytes (fragmented red cells/ "helmet" cell) or burr cells are looked for. These suggest systemic envenomation and along with thrombocytopenia are markers for MAHA (microangiopathic haemolytic anaemia).

SNAKE BITE TREATMENT PROTOCOL – TREATMENT PHASE

1. Managing Pain

Snake bite can often cause severe pain at the bite etc. This can be treated with pain killers such as paracetamol. Mild opiates like Ketorolol 50 mg. can be used orally for relief of severe pain. In cases of severe pain, ketorolol can be given IV.

2. Handling tourniquets

Sudden removal can lead to a massive surge of venom leading to neurological paralysis, hypotension due to vasodilation, etc.

* Before removal of the tourniquet, check for the presence of pulse distal to the tourniquet.

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; Russells viper common cobra, common krait and saw scaled viper.

There are known species such as the Hump-nosed pit viper (*hypnale hypnale*) where polyvalent ASV is known to be ineffective. In addition there are regionally specific species such as sachureki' saw scaled viper (*Echis carinatus Sachureki*) in Rajasthan, where the effectiveness of polyvalent ASV may be questionable.

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 neutralized when it is in the blood stream or tissue fluid. In addition, Anti Snake Venom carries risks of anaphylactic reactions and should not therefore be used unnecessarily.

1. Evidence of Systemic Envenoming

Evidence of coagulopathy: Primarily detected by 20 minute WBCT[whole blood clotting test] PT &APPT or visible spontaneous systemic bleeding from gums etc.

Evidence of Neurotoxicity: Ptosis, external ophthalmoplegia, muscle paralysis, inability to lift head –broken neck sign.

OTHER DETERMINANTS ARE

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

PREVENTION OF ASV REACTIONS - PROPHYLACTIC REGIME

0.25 – 0.3 mg adrenaline 1 : 1000 given subcutaneously & (deep IM)

If the victim has a known sensitivity to ASV pre-medication with adrenaline, hydrocotisone and anti histamine may be advisable, in order to prevent severe reactions.

TEST DOSE OF ASV

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

ASV 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.

1 ml. of ASV neutralizes 0.6 mg. of Russel Viper venom, 0.6 mg. of Cobra venom, 0.45 mg. of krait venom, & 0.45 mg. of saw-scaled viper venom.

RUSSELL VIPER

- Russell's Viper injects on an average 63 mg. (5 to 147 mg. + 7) of venom.
- 1 ml. of ASV neutralizes 0.6 mg. of Russells Viper Venom.
- 1 vial i.e 10 ml. of ASV neutralises 6 mg. of Russells viper venom.
- The total required dose will be between 100 ml (10 Vial) to 250 ml. Starting with 10 vial ensures sufficient neutralizing power., Starting with 10 vials ensures that there is sufficient neutralizing power to neutralize the average amount of venom injected and during the next 12 hours to neutralize any remaining free flowing venom.
- Start IV Normal Saline with wide bore needle.
- Begin with 10 vials of ASV in 100 ml of Normal Saline and to start with 10-15 drops per minutes for 15 minutes and watch for reactions. If the patient is not having signs and symptoms of anaphylactic shock continue the ASV. All ASV are to be administered over 1 hour period at constant speed. Continue to monitor the vital signs at 5 minutes interval for first 30 minutes and then at 15 minutes interval for 2 hours.

REPEAT DOSE IN HAEMATOTOXIC ENVENOMATION

As already explained, initial blood test reveals coagulation abnormality 10 vials of ASV given. No additional ASV until next 6 hours (Liver unable to replace clotting factors in under 6 hours). After initial 6 hours, another 20 WBCT is done. If there is evidence of abnormality of 20 WBCT (continued coagulation disturbance) another 8-10 vials of ASV administered in one hour time. Repeat 20 WBCT and repeat ASV 6 hourly until coagulation is restored, unless a species is identified as one against which polyvalent ASV is not effective. (Usually in majority of cases 20 vial ASV is enough).

NEUROTOXIC ENVENOMATION

Neostigmine is an anti cholinesterase 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 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 to 2 mg. of neostigmine IM together with 0.6 mg. of atropine IV. The paediatric neostigmine dose is 0.04 mg/kg IM and the dose of atropine is 0.05 mg/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.

- Single breath count, mm of Iris uncovered (amount covered by the descending eye lid), Inter incisor distance (measured distance between the upper & lower incisors), Length of time upward gaze can be maintained.
- FEV1 or FVC

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 30 minutes any improvement should be visible by an improvement in the measure.

ASV IN NEUROTOXIC ENVENOMATION:

Treat the patient with 10 vial of ASV initially as in the case of hematotoxic envenomation. If the Neostigmine test is positive, 0.5 mg of Neostigmine IM and 0.6 mg. Atropine IV at half hourly intervals for 5 injection, followed by repeating the same dose at increasing intervals of 2 to 12 hours. If there is no improvements in symptoms after 1 hour, Neostigmine should be stopped.

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.

REPEAT DOSE – NEUROTOXIC ENVENOMATION

Initial dose of 10 vials given and if symptoms persist or worsen or in respiratory failure repeat 10 more vials of ASV after 1-2 hours as a second dose and discontinue ASV. 20 vials is the maximum dose of ASV that should be given to a neurotoxically envenomed patient.

Once the patient 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 neutralized 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 mechanism. Large doses of ASV, over long period, have no benefit in reversing envenomation.

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

ASV IN CHILDREN

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

RECOVERY SIGNS

- Spontaneous systemic bleeding such as gum bleeding, bleeding from venepuncture sites etc. usually stops within 15 to 30 minutes. Blood coagulability is usually restored in 6 hours. Post-synaptic neurotoxic envenoming such as the Cobra may begin to improve as early as 30 minutes after ASV. Pre-synaptic neurotoxic envenoming such as the krait usually takes a considerable time to improve. Active hemolysis and Rhabdomyolysis may cease within few hours and urine return to its normal colour. In patient with shock, blood pressure may increase after 30 minutes.

RECURRENT ENVENOMATION

When coagulation has been restored no further ASV should be administered, unless proven recurrence of a coagulation abnormality is established. Indian ASV a F(ab)₂ product and has a half life of 90 hours and therefore is not required in a prophylactic dose to prevent re envenomation.

ANTI HEAMOSTATIC 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 abnormally 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 Pit Viper (*Hypnale Hypnale*) does not respond to normal ASV [Joseph et al 2007]. This may be a cause as, in the case of *Hypnale*, coagulopathy can continue upto 3 weeks

ASV IN SPECIAL SITUATION

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 (upto 25 vials) solely on the basis on guaranteeing a restoration of coagulation after 6 hours.

SNAKE BITE IN PREGNANCY

There is very little definitive data published on the effects of snake bite during pregnancy. Pregnant women are treated in exactly the same way as other victims.

VICTIMS WHO ARRIVE LATE

A frequent problem witnessed in our country is victims who arrive late after the bite, often after several days,

usually with acute renal failure. The key determining factor to decide on ASV treatment is to look for signs of current venom activity venom can only be neutralized if it is unattached. Perform a 20 WBCT and determine if any coagulopathy is present. If coagulopathy is present administer ASV. If no coagulopathy is evident treat renal failure.

In case of neurotoxic envenoming where the victim is evidencing symptoms such as ptosis, respiratory failure etc, it is probably wise to administer one dose of 8 to 10 vials of ASV to ensure that no unbound venom is present.

ASV REACTIONS

If anyaphylaxis is evident, then

- ASV will be discontinued temporarily. 0.5 mg of 1 :1000 adrenaline to be given IM in adults. Children are given 0.01 mg/kg adrenalin IM .
- There is better patient outcome if adrenaline is used early

POOR PROGNOSTIC INDICATORS IN VIPER BITE

- Low Platelets < 20,000/mm³, Polymorphonuclear leucocytosis with presence of band form, crenated RBC, Haemo concentration at presentation – indirectly denotes capillary leak, Raised D – Dimer, low fibrinogen, Low serum protein and albumin, haemoglobinuria, bilateral parotid swelling “Viper Head” appearance, Giddiness, syncope immediately following a snake bite, agitated behaviour – cerebral anoxia, profound thirst.

COMPLICATIONS

Capillary leak syndrome occurs in Viperidae bites due to heamorrhagins degrading the compact proteins of basement membranes, shifting fluid from intravascular to interstitial space.

Hypotension ARDS, acute kidney injury, pituitary insufficiency cardiac and neurological complications and, locked in syndrome in elapid bites are the important complications.

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