INTRODUCTION

Snake bite is a well known occupational hazard among farmers, plantation workers and other outdoor workers and results in morbidity and mortality throughout the world. This occupational hazard is no more an issue restricted to a particular part of the world; it has become a global issue. Accurate statistics of the incidence of snake bite and its morbidity and mortality throughout the world does not exist, however it is certain to be higher than that is reported. This is because even today most of the victims initially approach traditional healers for treatment and even many are not registered in the hospital. Since this is a preventable cause of death, the patients of snake bite should be treated on emergency basis.

First Aid & Pre-hospital Care

First Aid treatment is carried out immediately after the bite, before patient reaches a dispensary or hospital.

Aims of First Aid

It is an attempt to retard systemic absorption of venom, preserve life and prevent complications before the patient can receive medical care, and control distressing or dangerous early symptoms of envenoming.

Recommended First Aid Methods

Reassure the victim who may be very anxious (70% of all snake bites are by non-venomous snakes and 50% of bites by venomous species are dry bites). Immobilization of the affected limb with a splint or sling is required. Place patient in the lateral recumbent position. If non-breathing, insert an oral airway or perform rescue breathing if necessary. Application of “constriction band” to delay the absorption and venom spread has been advocated to the affected limb (in case neurotoxic bites). A firm, but not tight, ligature may be applied just above the bite so that one finger can pass between the limb and the bandage and that will impede lymphatic drainage but not arterial or deep venous flow. It should preferably not be released until the administration of anti snake venom. Constriction band is completely contraindicated in Viper and Cobra bite (Asian species) because of local-necrotic effects.

The bite site should be inspected for retained fangs, which should be removed carefully and quickly. Skin surrounding the bite site should be irrigated with non-irritating fluid to prevent unabsorbed venom to absorb. Anti tetanus toxoid should always be given following snake bite. The patient must be transported to a place where they can receive medical care as quickly, but as safely and comfortably as possible.

Patient Assessment

Patient evaluation should begin with the assessment of the airway, breathing and circulatory status. Oxygen should be available to every envenomated patient and a large bore intravenous line with normal saline or ringer’s lactate established in the unbitten limb. Cardiac monitoring and pulse oximetry, if available should be kept ready. Attempts should be made to determine weather a venomous snake has actually bitten the patient, and the severity of
envenomation should be assessed (Table I)\(^2\).

**Clinical situations of urgent resuscitation**

1. Profound hypotension and shock resulting from direct cardiovascular effects of the venom or secondary effects such as hypovolemia or hemorrhagic shock.
2. Terminal respiratory failure from progressive neurotoxic envenoming that has led to paralysis of the respiratory muscles.
3. Sudden deterioration or rapid development of severe systemic envenoming following the release of a tight tourniquet or compression bandage.
4. Cardiac arrest precipitated by hyperkalemia resulting from skeletal muscle breakdown (rhabdomyolysis) after sea snake bite.
5. Late result of severe envenoming such as renal failure and septicemia complicating local necrosis\(^11\).

**DETAILED CLINICAL ASSESSMENT AND SPECIES DIAGNOSIS History**

A precise history of the circumstances of the bite and the progression of local and systemic symptoms and signs is very important.

Size, colour, shape and distinctive feature of the snake. In what part of body bite has occurred. When was bitten? Initial symptoms, type of first aid or traditional therapy received past medical history (e.g. asthma, cardiac disease, hemoglobinopathy), medication, if any, should be noted.

Prior history of antivenom administration, presence of priority symptoms (nausea, vomiting, blurred vision, dizziness, dyspnoea, syncope, weakness, chest pain, urinary retention, bleeding nose or gums, dark colored urine, melena hematochezia), Tetanus immunization status is to be recorded\(^1,3\).

**Early Clues that a patient has severe envenoming**\(^11\)

- Snake identified as a very dangerous one.
- Rapid early extension of local swelling from the site of the bite.
- Early tender enlargement of local lymph nodes, indicating spread of venom in the lymphatic system.
- Early systemic symptoms- Collapse (Hypotension, shock), nausea, vomiting, diarrhea, severe headache, ”heaviness” of the eyelids, drowsiness or early ptosis/ ophthalmoplegia.
- Early spontaneous systemic bleeding
- Passage of dark brown urine

**PHYSICAL EXAMINATION**

**Local Examination (Examination of the Bitten Part)**
The extent of swelling, tenderness. Lymphnodes draining the limb should be palpated and overlying ecchymosis and lymphangitis lines noted. Presence of fang mark, bleeding, discoloration should be noted. Presence of necrosis, compartmental syndrome, putrefaction, secondary infection, distal pulses should be mentioned\(^6\).

**General Examination**

*Include:* Blood pressure (sitting up and lying), heart rate and respiratory rate. Skin and mucous membrane for petechiae, purpura, ecchymoses and in the conjunctival chemosis. *Neurologic examination:* Cranial nerve examination, assess motor strength and symmetry, ptosis, bulbar palsy. *Respiratory examination:* Dyspnoea, dysphonia, use of accessory muscles of respiration, paradoxical respiration. *Abdomen:* Tenderness may suggest gastrointestinal or retroperitoneal bleeding and loin pain & tenderness suggests acute renal ischemia (Russell’s viper bite). *Coagulopathy:* Evaluate for retinal and gingival hemorrhage, bleeding from the nose or gastrointestinal tract and intracranial bleeding should be ruled out with neurologic examination. *Musculoskeletal Examination:* Evaluate for compartment syndrome, muscle tenderness. Urine examination for colour, casts, hematuria, hemoglobinuria, myoglobinuria. Assess

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**Table I. Assessment of Severity of Envenomation**

| No envenomation | Absence of local or systemic reactions, fang marks\(^+/-\) |
| Mild envenomation | Fang marks, moderate pain, minimal local edema (0-15 cms), erythema\(^+\), ecchymosis\(^+/-\), no systemic reactions. |
| Moderate envenomation | Fang marks\(^+\), severe pain, moderate local edema (15-30 cms), erythema\(^+\), ecchymosis\(^+\), systemic weakness, sweating, syncope, nausea, vomiting, or thrombocytopenia & anemia. |
| Severe Envenomation | Fang marks\(^+\), severe pain, severe local edema (>30cms), erythema\(^+\), ecchymosis\(^+\), hypotension, parasthesia, coma & respiratory failure. |
for Generalized rhabdomyolysis: - Especially of the neck, trunk and proximal limb muscle tenderness and painful on active or passive movements and later may become paralyzed. Myoglobinuria may be evident 3 hours after the bite (i.e. sea snakes and Russell's vipers in Sri Lanka and South India). Examination of Pregnant Women: - There will be concern about fetal distress (fetal bradycardia), vaginal bleeding and threatened abortion. Monitoring for uterine contraction and fetal heart rate is useful. Lactating women who have been bitten by snakes should be encouraged to continue breast feeding. Species diagnosis: - If the dead snake has been brought, it can be identified otherwise, the species responsible can be inferred indirectly from the patients description of the snake and clinical syndrome of the symptoms and signs

LABORATORY TESTS
(A) 20 minute whole blood clotting test (20 WBCT)
This very useful and informative bedside test requires very little skill and only one piece of apparatus- a new, clean, dry, glass vessel (tube or bottle). Place a few mls of freshly sampled venous blood in a small glass vessel. Leave undisturbed for 20 minutes at ambient temperature. Tip the vessel once. If the blood is still liquid (un-clotted) and runs out, the patient has hypofibrinogenemia (“in-coagulable blood”) as a result of venom induced consumption coagulopathy. In the South East Asian region, incoagulable blood is diagnostic of a viper bite and rules out an elapid bite. Warning ! if the vessel used for the test is not made of ordinary glass, or if it has been used before and cleaned with detergent, its wall may not stimulate clotting of the blood sample in the usual way and test will be invalid. If there is any doubt, repeat the test in duplicate, including a “control” (blood from a healthy person)

(B) ELISA (Enzyme Linked Immuno Sorbent Assay)
ELISA tests are now available to identify the species involved based on antigens in the venom. These tests are expensive and not freely available and limited value in diagnosis

(C) Laboratory Investigations
Although lab tests are of little value in the diagnosis of snake envenomation, nevertheless they are useful of monitoring the patient and deciding about specific interventions and prognosis.

Laboratory test includes: - Complete blood counts, electrolytes, glucose, creatinine, serum amylase, creatinine phosphokinase (CPK), prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen and fibrin- degradation products (FDP's). Urine examination for haematuria, proteinuria, haemoglobinuria or myoglobinuria.

Arterial Blood Gases and PH for evidence of respiratory failure (neurotoxic envenoming) and acidaemia (respiratory or metabolic acidosis). Arterial blood gases and urine examination should be repeated at frequent intervals during the acute phase to assess progressive systemic toxicity

ANTIVENOM TREATMENT
What is Antivenom?
Anti Snake Venom (ASV) is an immunoglobulin (usually the enzyme refined F(ab)_2 fragment of IgG) purified from the serum or plasma of a horse or sheep that has been immunized with the venoms of one or more species of snakes.

Antivenoms may be species specific (monovalent) or effective against several species (polyvalent), usually the most important species, from a medical point of view, in a particular geographical area. For example, Haffkine Kasauli, Serum Institute of India and Bengal “Polyvalent Anti-snake Venom Serum” is raised in horses using the venoms of the four most important venomous species in India (Indian Cobra, Naja naja; Indian Krait, Bungarus caeruleus; Russell’s Viper, Daboia russelli; Saw-scaled Viper, Echis carinatus)

Indication of ASV
The correct use of antivenom is the most important component of the hospital care and not every bite, merits its use. Administration of anti-venom should be selective and based on severity of clinical symptoms. The main concern about the empirical use of antivenom is the risk of allergic reaction, its relative scarcity in some centres and the cost factor. It should therefore be used only in patients in whom the benefits of antivenom treatment are considered to exceed the risks (Table II)

DOSE & ADMINISTRATION OF ANTIVENOM
- Antisnake Venom (ASV) should be given within 4-6 hours of the bite and the dosage required varies with the degree of envenomation. Serum sensitivity should be tested by injecting 0.2ml of anti-venom subcutaneously. If a severe reaction occur within 15 minutes, anti-venom is contraindicated. Epinephrine (Adrenaline) should always be drawn up in readiness before anti-venom is administered. Freeze-dried (lyophilized) anti-venoms are reconstituted, usually with 10ml of sterile water for
Antivenom treatment is recommended if and when a patient with proven or suspected snake bite develops one or more of the following signs:

**Systemic Envenoming**
- **Haemostatic abnormalities:** Spontaneous systemic bleeding, Coagulopathy (20 WBCT) or thrombocytopenia (<100x10^9/litre).
- **Neurotoxic Signs:** Ptosis, external ophthalmoplegia, paralysis etc.
- **Cardiovascular abnormalities:** Hypotension, shock, cardiac arrhythmia, abnormal ECG.
- **Acute renal failure:** Oliguria/anuria, rising blood creatinine (> 2mEq/dl) / Urea.
- **Haemoglobin/Myoglobin-Uria:** Dark brown urine, urine dipsticks, other evidence of intravascular haemolysis or generalized rhabdomyolysis (muscle aches and pains, hyperkalemia (K>6mEq/dl).

**Local Envenoming**
- Local swelling involving more than half of the bitten limb (in the absence of a tourniquet) swelling after bites on the digits (toes and fingers).
- Rapid extension of swelling (beyond the wrist or ankle within a few hours of bites on the hands or feet).
- Development of an enlarged tender lymph node draining the bitten limb.

Two methods of administration are recommended:
- **Intravenous *Push* Injection:** Reconstituted freeze-dried anti-venom or neat liquid anti-venom is given by slow intravenous injection (not more than 2ml/minute). This method has advantage that the doctor/nurse/dispenser giving the anti-venom must remain with the patient during the time when some early reactions may develop. It is also economical saving the use of intravenous fluids, I.V. sets, cannulae etc.
- **Intravenous Infusion:** Reconstituted freeze-dried or neat liquid anti-venom is diluted in approximately 5-10ml of isotonic fluid per Kg body weight (i.e. 250-500ml of isotonic saline or 5% Dextrose) and is infused at a constant rate over a period of about one hour.

Local administration of anti-venom at the site of the bite is not recommended.

Initial dose should depend upon an estimate of amount of envenomation (Table III)

### Table III. Dose of Anti-snake Venom (ASV)

<table>
<thead>
<tr>
<th>Envenomation</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>5 vials (50ml)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 10 vials (50 100 ml)</td>
</tr>
<tr>
<td>Severe</td>
<td>10 20 vials (100 200 ml) or more</td>
</tr>
</tbody>
</table>

- Criteria for Repeating the initial dose of Anti-venom:
  1. Persistence or Recurrence of Blood in-coagulability (20 WBCT) after 6 hours of initial dose of anti-venom.
  2. Deteriorating neurotoxic or Cardiovascular signs after 1-2 hours of ASV treatment.

### ANTI-VENOM REACTIONS AND THEIR TREATMENT

A proportion of patients, usually more than 20%, develop a reaction either early (within a few hours) or late (5 days or more) after being given anti-venom.

**Early Anaphylactic Reactions**

Usually with 10-180 minutes of starting anti-venom, the patient begins to itch (often over the scalp) and develop urticaria, dry cough, fever, nausea, vomiting, abdominal colic, diarrhea and tachycardia. A minority of patients may develop severe life-threatening anaphylaxis: hypotension, bronchospasm and angio-oedema.

In most cases, this reactions are more likely due to complement activation by IgG aggregate or residual Fc fragments or direct stimulation of mast cells or basophils by anti-venom proteins. It should be treated by adrenalin, antihistamine and corticosteroids.

**Pyogemic (endotoxin) Reactions**

Usually develop 1-2 hours after treatment. Symptoms include shaking chills (rigors), fever, vasodilatation and a fall in blood pressure. Febrile convulsions may be precipitated in children. These reactions are caused by pyrogen contamination during the manufacturing process. They are commonly reported. It should be treated with antipyretics.

**Late (Serum Sickness Type) Reaction**

Develop 1-12 (mean 7) days after treatment. Clinical features include fever, nausea, vomiting, diarrhoea, itching, recurrent urticaria, arthralgia, myalgia, lymphadenopathy,
periarticular swellings, mononeuritis multiplex, proteinuria with immune complex nephritis and rarely encephalopathy. Patients who suffer early reactions and are treated with antihistamines and corticosteroid are less likely to develop late reactions.

*Treatment of late (serum sickness) reactions:* Usually respond to a 5-day course of oral antihistamine. Patients who fail to respond in 24-48 hours should be given a 5-day course of prednisolone.

**ROLE OF ANTICHOLINESTERASE AGENTS**

Since Elapidae (Cobra) snakes result in primarily neurotoxic features as a result of selective d-tubocurarine like blockade, the post synaptic toxin of the venom leads to pathophysiological changes resembling those of myasthenia gravis. Anti Cholinesterase drugs have a variable, but potentially useful effect in patients with neurotoxic envenoming particularly postsynaptic neurotoxins of Indian cobra (N.naja). Acetyl-Choline Concentration at the neuromuscular junction can be increased either by stimulating increased release from pre-synaptic vesicles or by inhibiting the acetylcholinesterases. The goal of acetylcholinesterase inhibiter therapy is to increase the amount of neuro-transmitter available for voluntary muscle activities, forestalling the onset of respiratory paralysis. This should be treated with injection neostigmine 0.5mg I.V. and injection atropine sulphate 0.6mg I.V. given every 30 minutes for six doses, then every 6 hourly till the neurological signs subsides.

**HYPOTENSION & SHOCK:**

**Causes**

1. Anaphylaxis:
   - Vasodilation
   - Respiratory failure
2. Antivenom reaction:
   - Cardiotoxicity
   - Acute pituitary adrenal insufficiency
   - Hypovolemia
   - Septicemia.

This is usually the result of hypovolemia, venom induced vasodilation or direct myocardial effects with or without arrhythmias. Ideally, treatment with plasma expanders (colloids or crystalloids) should be controlled by observation of Central Venous Pressure. In patients with evidence of a generalised increase in capillary permeability, a selective vasoconstrictor such as dopamine may be given by intravenous infusion preferably to a Central Vein (Starting dose 2.5-5 µg/kg/minute). In victims of Russell’s Viper bites in Myanmar and South India, acute pituitary-adrenal insufficiency results from hemorrhagic infarction of the anterior pituitary may contribute to shock-Hydrocortisone is effective in thee cases.

**Oliguria and renal failure**

- Detection of renal failure: No urine output, Rising blood urea/creatinine, Clinical “uremic syndrome” - nausea, vomiting, hiccups, fetor, drowsiness, confusion, coma, flapping tremor, muscle twitching, convulsions, pericardial friction rub, signs of fluid overload.
- Oliguric phase of renal failure: Oliguria-defined as urine output of less than 400ml/day or less then 20ml/hour.
- Treatment of renal failure includes intravenous diuretics and if no improvement hemodialysis.
- Prevention of renal damage in patients with myoglobinuria or haemoglobinuria include - correct hypovolemia and maintain saline diuresis (if possible), correct severe acidosis with bicarbonate. In diuretic phase - water and electrolytes (k+) must be carefully monitored and replaced. In persisting renal dysfunction as observed in Russell’s viper bite victims, those develop patchy/diffuse cortical necrosis, may require regular maintenance dialysis and eventual renal transplantation.

**HAEMOSTATIC DISTURBANCES**

Bleeding and clotting disturbances usually respond satisfactorily to treatment with specific antivenom, but the dose may need to be repeated several times, at six hourly intervals, before blood coagulability (assessed by the 20 WBCT) is finally and permanently restored.In exceptional circumstances, such as severe bleeding, once specific antivenom has been given to neutralize venom, procongulants and other antihaemostatic toxins, restoration of coagulability and platelet function can be accelerated by giving fresh frozen plasma(FFP), cryoprecipitate (fibrinogen, factor VIII), fresh whole blood or platelet concentrates. As per the WHO recommandation, heparin should not be given but a recent study of effect of LMWH in treatment of vasculotoxic snake bite was conducted from March 2008 to November 2009 at SCB Medical College & Hospital, Cuttack in the Department of Medicine.120 patients admitted to the hospital with history of vasculotoxic snake bite and in coagulable blood were subjected to the study. 60 patients (Control group) were given only ASV & supportive therapy. 60 patients (test group) were given LMWH (dose 40mg S.C. O.D.) for 5 day with ASV and supportive therapy. The study showed that there is not much difference in the duration of hospital state and average number of ASV vials...
required both in test and control group. But number of persons requiring hemodialysis for ARF were much less in test group than the control group. Mortality was only 01 in test group (1.66%) where as 4 in control group (6.66%). So LMWH seems to have a beneficial role in the treatment of vasculotoxic snake bite both in reducing the mortality and morbidity\(^9\). This is in contradiction to WHO recommendation.

**TREATMENT OF THE BITTEN PART**

The bitten limb, which may be painful and swollen, should be nursed in the most comfortable position, preferably slightly elevated. Broad spectrum antibiotics and local dressing to be done.

Features of compartmental syndrome include - Severe pain, weakness of intracompartamental muscles, Pain on Passive stretching of muscles, hypoaesthesia of skin, immobile, tensely swollen, cold and apparently pulseless snake bitten limb, Intra compartmental pressure exceeding 40 mm Hg may carry a risk of ischemic necrosis (e.g. Volkmann's ischemia/anterior compartment syndrome). Treatment is fasciotomy\(^1\).

**Role of N Acetyl Cysteine in Renal Failure following Vasculotoxic Snake Bite**

The study was conducted in the Department of Medicine, S.C.B. Medical College, Cuttack. 63 cases of snake bite were taken, 33 cases were given N- Acetyl Cysteine 600 mg 12 hrly for 3 days and 30 cases were not along with ASV and other supportive measures. The clinical and laboratory parameters (serum urea, serum creatinine, G.F.R., lipid peroxidation value) were compared in both groups on day 1 and day 7 of admission.

In 33 patients of snake bite, who received N- Acetyl Cysteine, 16 patients develop renal failure and only 6 patients required dialysis. The blood urea, serum creatinine and lipid peroxidation value decreased significantly and GFR is increased significantly after 7 days of treatment.

In 30 patients who did not received N- Acetyl Cysteine, renal failure developed in 24 cases and out of them 16 cases require dialysis. The blood urea, serum creatinine and lipid peroxidation value increased significantly and GFR decreased significantly after 7 days of treatment.

Thus it conclude that vasculotoxic snake bite with renal failure had more severe oxidant damage and N-Acetyl cysteine have a significant role in preventing oxidant injury in renal failure and reduce morbidity and mortality\(^10\).

**REFERENCES**

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