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A review on Snake Bite and Management in Nigeria- The Need for The Development of a Snake Bite StrategyBabangida, S.¹, Erhabor, O.¹, Erhabor, T.², Adias, T.C.³*Department of Haematology, Faculty of Medical Laboratory Science, Usmanu Danfodiyo University Sokoto, Nigeria¹, Medical Laboratory Science Council of Nigeria², Federal University Otuoke Bayelsa State³.**Author for Correspondence: samzstar45@gmail.com/+234-708-525-4127***Summary**

Snake-bites is a global public health and a well-known medical emergency in many parts of the world, especially in rural areas. The aim of this review is to look critically at the challenge of snake Bite in Nigeria and to advocate for the development of a Snake Bite Strategy in Nigeria. The prevention of mortality and morbidity depend upon availability of antivenom in the health facilities in these settings and their rational use. There is the urgent need for the development of a Snake Bite Strategy in Nigeria that takes into account the need for the development of prevention, improved community education, empowerment and effective first response. Mechanisms need to be developed to ensure universal access to antivenom by all needy patients. The Nigerian health system needs to respond to this challenge and logistics must be put in place to ensure timely availability of antivenom at the point of use to prevent preventable disability and death.

Keywords: Snake Bite, Snake Bite Strategy, Management, antivenom Nigeria.

Introduction

Snakebites account for significant morbidity and mortality worldwide, especially in South and Southeast Asia, sub-Saharan Africa, and Latin America. Venomous snakes are widely distributed around the world and clinical effects from envenomation can overlap to a great degree even among different families of snakes (Julian et al., 2019).

Snakebite envenoming comprises a major public health problem among communities of the savanna region of West Africa, notably in Benin, Burkina-Faso, Cameroon, Ghana, Nigeria and Togo. The precise incidence of snakebite is difficult to determine and is often grossly underestimated but a global reappraisal estimated the occurrence in the West African region of 10,001 to 100,000 snakebite envenoming with an incidence of 8.9-93.3/100,000 persons per year with an estimated 1001 to 10,000 deaths and a mortality rate of 0.5-5.9/100,000 persons per year (Kasturiratne *et al.*, 2008). A more recent study using a meta-analytic approach estimated that over 314,000 bites, 7,300 deaths and nearly 6,000 amputations occur from snakebites annually in Sub-Saharan Africa (Chippaux, 2011).

Epidemiology (Overview of Snakebite in Nigeria)

In parts of the Nigerian savanna snakebite victims may occupy over 10% of hospital beds. In the Benue valley of Nigeria, the estimated incidence is as high as 497 per 100,000 populations per year with 10 to 20% comprising untreated fatalities (Warrell, 1976). The saw-scaled or carpet viper (*Echis ocellatus*) has proved to be the most important cause of snakebite mortality and morbidity in the region. The African cobras (*Naja* spp.), puff adders (*Bitis arietans*) and mambas (*Dendroaspis* spp.) are frequently involved in attacks on humans while *Atractaspis* spp. and small vipers are only occasionally involved (Meyer, 1997). Snakebite affects farmers, nomads and rural dwellers of all ages. The main clinical features of *E. ocellatus*

envenoming are systemic haemorrhage, incoagulable blood, shock, local swelling, bleeding and occasionally necrosis. All body systems may be affected; cardiac and haemodynamic abnormalities may result while the strongest predictor of mortality is central-nervous-system involvement with intracranial haemorrhage. Neurotoxicity has been reported following Egyptian cobra (*Naja haje*) bites in certain parts of the country. Occasionally,

snakebite may lead to important complications such as amputation, blindness resulting from spitting cobra (*Naja nigricollis*) venom, ophthalmia, foetal loss, and wound infection, tetanus and scarring with potential for malignant transformation, and psychological consequences e.g., excessive anxiety, stress, hysteria and worry (Abdulrazaq, 2013). Figure 1 shows some types of snakes and their associated facts.

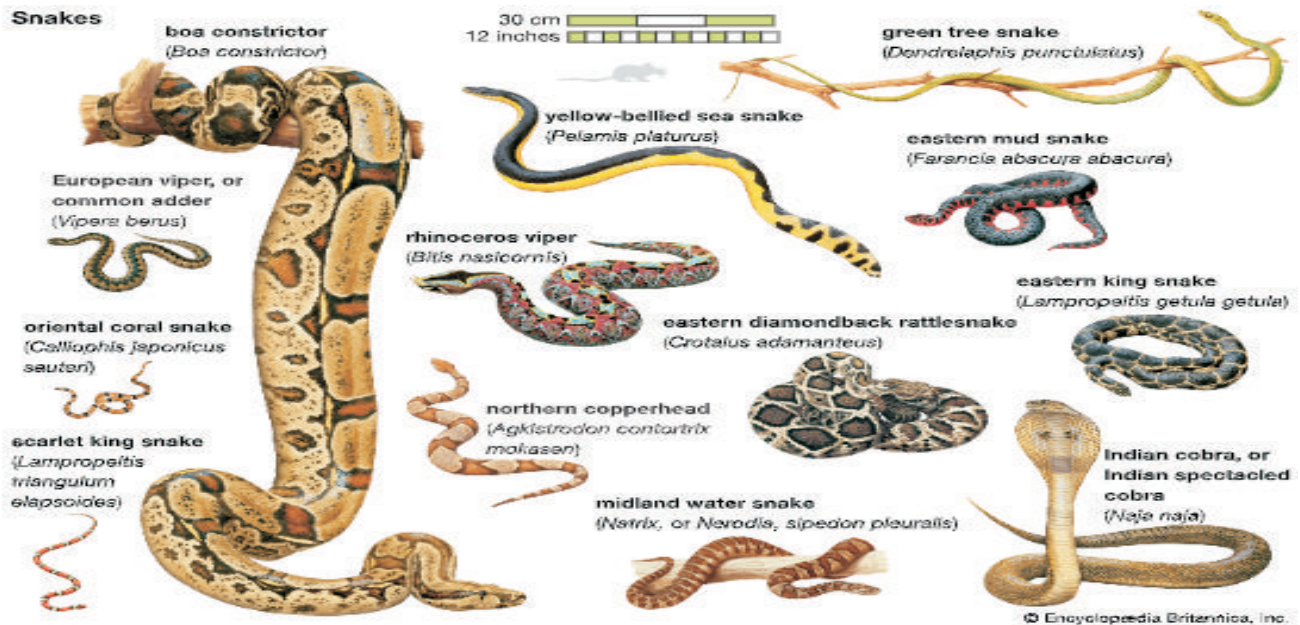


Figure 1: Snakes, Facts and Types (James and Peter, 2020)

Economic Impact of Snakebite

The burden of human suffering caused by snakebites has been greatly underestimated, ignored and neglected for far too long. Snakebites, a common phenomenon in rural areas of many tropical developing countries including Nigeria, mainly affect the youth or agricultural workers who lack a political voice that effectively represent their needs. From the foregoing, it is evident that several thousand Nigerians fall victims of snakebites annually. These are mostly farmers, herdsman and their rural-dwelling families. Each bite, whether or not accompanied by envenoming, leads to loss of work days. The high-risk groups are also the economically active population, so that their prolonged or short-term incapacitation at periods which coincide with the most intense farming activities can only lead to reduced agricultural production and low economic performance (Abdulrazaq, 2013). Apart from loss of work

days, the victims and their families have to bear the cost of treatment which can be quite high. It is not unusual for families to sell one or more cattle or a substantial portion of their harvest to pay for such treatment. In addition, a variable but unacceptably high percentage of victims die or are left with permanent mutilation each year. This constitutes a major liability to the families, since the victims are usually the breadwinners whose absence constitutes a permanent loss to the manpower resources available for the agricultural sector (Abdulrazaq, 2013).

Recently, snakebite-induced mortality was shown to be inversely correlated with the Human Development Index, the per capita government expenditure on health and gross domestic product per capita, and directly associated with the percentage of the labor force in agriculture. It was further shown that snake envenoming is negatively associated with governmental

expenditure on health, thus reaffirming its status as a disease of the poor (Harrison *et al.*, 2009). Clearly therefore, poverty predisposes to snakebite and it is not only a major health problem but it is also a major impediment to economic prosperity.

Snake Venoms and It's Effect

Snake venoms are mixtures of numerous proteinaceous components that exert diverse functional activities on a variety of physiological targets. Because the toxic constituents found in venom vary from species to species, snakebite victims can present with a variety of life-threatening pathologies related to the neurotoxic, cytotoxic and haemotoxic effects of venom (Julien *et al.*, 2017).

These snakes primarily use venom for facilitating prey capture, although when threatened or provoked they use venom defensively, as observed in cases of human snakebite. The snake venom system consists of a pair of venom secretory glands, found either side of the head on the upper jaw, that are connected to ducts which transmit venom from the gland to the base of modified teeth (fangs) used for injection (Kerkkamp *et al.*, 2015).

Venoms consist of complex mixtures of proteinaceous components (circa 50–200), which are commonly referred to as toxins. These toxins have evolved from a number of nont-oxic housekeeping genes by a variety of processes, most commonly gene duplication followed by neo functionalization under the action of positive selection, but also via alternative splicing, recombination and simple modification of expression (Vonk *et al.*, 2013). Venomous snakes in Africa are basically grouped into five (5) categories according (WHO 2010) and they include:

Category 1: Snakes that bite frequently, and are associated with serious or life-threatening envenoming. Most commonly found in Nigeria includes;

- a. White bellied carpet viper *Echis Leucogater* found in Sokoto
- b. West African or Ocellated carpet viper *Echis Ocellatus* found in Kaltungo in Bauchi State.
- c. Puffer adder *bitis arietain* found in Garki, Abuja.

- d. Zebra spitting cobra found in Abuja.
- e. Egyptian Cobra *Naja haje* in Zaria, Kaduna State.
- f. Black or Black–mouth Mamba in Benue State,

Category 2: Snakes that bite frequently, but rarely causes serious or life-threatening envenoming. Most commonly found in Nigeria include;

- a. Slender burrowing asp *Atractaspis*
- b. Western rhombic night adder *causus maculatus* found in Zaria
- c. Saharan sand viper *cerastes vipera*

Category 3: Snakes that bite rarely, but are capable of causing severe or life-threatening envenoming:

- a. Boomslang
- b. Vine, Bird, Twig or tree snakes
- c. Neurotoxic cobras
- d. Desert black snakes

Category 4: Snakes that bite rarely and have not caused significant envenoming

- a. Minor adders (*Bitis Caudalis*)
- b. African garter snakes

Category 5: Other potentially venous snake which have not caused documented bites.

- a. Ethiopian Mountain adders
- b. Bush vipers
- c. Burrowing asps.

The primary function of snake venom is to help the snake immobilize and eventually digest its prey. Snake venoms are complex mixtures of numerous toxic and non-toxic components. Because of the diversity of toxic components found in the venom of any one snake, the pathological consequences of envenoming can be diverse and multifactorial. Moreover, variables such as the location of the bite site and the amount of venom injected can be highly variable can contribute to the severity of clinical signs observed in snakebite victims (Alirol *et al.*, 2015).

The amount of venom injected during a bite depends on various factors; species and size of the snake, mechanical efficiency of the snake bite, whether one or more fangs penetrated the skin and whether there are repeated bites. Within

the same species larger snakes tend to inject more venoms than smaller ones, but the effect of the latter may be richer in some very dangerous components (Julien *et al.*, 2017).

Snake Venom Composition

The most important venom components that cause serious clinical effects are procoagulant enzymes, cytolytic or necrotic toxins, haemolytic and myolytic phospholipases, pre- and post-synaptic neurotoxin and haemorrhagin (WHO, 2010).

Procoagulant Enzymes

These are found mainly in vipers. They activate different steps of the blood clotting cascade. Ultimately, this leads to the formation of fibrin in the blood. Most of the fibrin is broken down by the body's fibrinolytic system. This process depletes the body's own levels of clotting factors and eventually the blood does not clot. This is called consumption coagulopathy (WHO, 2010).

Cytolytic Or Necrotic Toxin

These are digestive hydrolases (proteolytic enzymes and phospholipases) and polypeptides that may destroy cell membrane and tissue and

therefore increase the permeability of the vascular endothelium. This leads to local swelling, blistering and oedema (WHO, 2010).

Pre-Synaptic Neurotoxins

These are mainly found in elapid venoms and in some vipers. They are phospholipases A2 that damage nerve ending, initially releasing acetylcholine followed by interfering with its release (WHO, 2010).

Post-Synaptic Neurotoxins

These are mainly found in elapid venoms. They are polypeptide that compete with acetylcholine for binding at neuromuscular junction receptors and lead to curare-like paralysis (WHO, 2011).

Haemorrhagins

Spontaneous systemic bleeding attributable to haemorrhagins which damage vascular endothelium. These are zinc metalloendopeptidase. Some of which have disintegrin-like, cysteine-rich and lectin domains. The combination of incoagulable blood, thrombocytopenia and vessel wall damage result in massive bleeding (WHO, 2010).

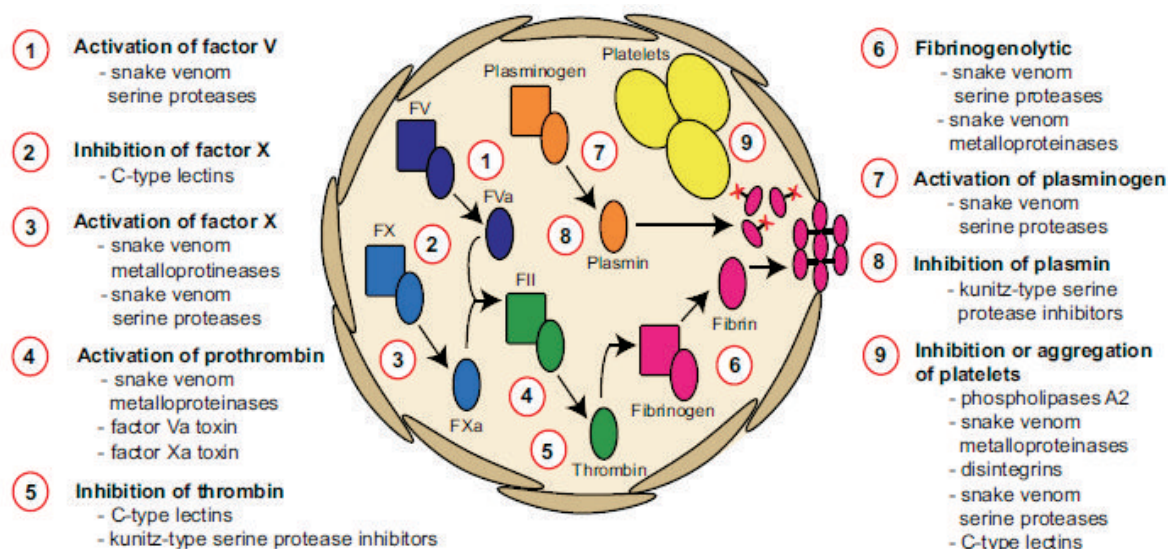


Figure 2. A schematic overview of the physiological targets of snake venom effect on haemostasis.

Figure 2 shows a schematic overview of the physiological targets of snake venom effect on haemostasis. Each physiological target is indicated by a red circle and the venom toxins type(s) that target these sites are listed. ACE, angiotensin-converting enzymes; FV- Factor v; FVa- Activated factor V; FX- Factor X; FXa- Activated factor X; FII- Prothrombin (Julien *et al.*, 2017).

Classification of Clinical Patterns of Snakebite Envenoming

Very broadly, venom components can lead to four main types of envenoming.

Cytotoxic Envenoming

This is characterized by painful and progressive swelling with blood-stained tissue fluid leaking from the bite wound and bruising. The victim will complain of severe pain at the site and throughout the affected limb and painful and tender enlargement of lymph glands draining the bite site. Irreversible death of tissue may occur (necrosis). Species that cause this type of envenoming include saw-scaled/carpet viper, puff adders and spitting cobras (WHO, 2010).

Haemorrhagic Envenoming

This is characterized by bleeding from the gums, gastro-intestinal and genitor-urinary tract and recent and partly healed wounds. Species include saw-scaled/carpet vipers, boomslang and vine snakes (WHO, 2010).

Neurotoxic Envenoming

This is characterized by moderate or absent local swelling, progressive descending paralysis starting with drooping eyelids and paralysis of eye movement causing double vision. These may be painful and tender enlargements of lymph glands draining the bite site. The patient may vomit, the saliva may become profuse and stringy and eventually there may be difficulties with swallowing and breathing. Species include black and green mambas, non-spitting cobras (WHO, 2010).

Myotoxic Envenoming

This is characterized by negligible local swelling, increasing generalized muscle pain and tenderness associated with features of neurotoxic envenoming and progressive descending paralysis culminating in paralysis of breathing. Species involved is the yellow-bellied sea snake (WHO, 2010).

Clinical Manifestation of Snakebite

Local Features

Fang marks: Generally, the presence of two puncture wounds indicates a bite by a poisonous snake. In the case of a non-venomous snakebite, small puncture wounds are seen arranged in an arc.

Pain: Burning, bursting pain may develop immediately after the bite and spread proximally up the bitten limb. Draining lymph nodes soon become painful.

Local swelling: Viper bites produce more intense local reaction than other snakes. Swelling may become apparent within 15 minutes and becomes massive in 2-3 days. It may persist for up to 3 weeks. The swelling spreads rapidly from the site of the bite and may involve the whole limb and adjacent trunk. Regional lymphadenopathy may develop. In case the envenomed tissue is contained in a tight fascial compartment like the pulp space of digits or anterior tibial compartment, ischaemia will develop. If there is no swelling 2 hours after a viper bite, it is safe to assume that there has been no envenoming.

Local necrosis: In viper bites, bruising, blistering and necrosis may appear over few days following the bite. Necrosis is marked following bites of Asian pit vipers, and some rattlesnakes.

Secondary infection: Bacterial flora in the oral cavity of the snakes contributes to secondary infection (Mehta and Sashindran, 2011).

General Features

Even in patients with 'dry bites', symptoms like flushing, breathlessness, palpitations, and dizziness, tightness in the chest and sweating are common. These are due to anxiety and sympathetic overactivity. Apart from these, early symptoms in elapid bites include vomiting, heaviness of eyelids, blurring of vision, hypersalivation, congested conjunctivae and 'gooseflesh'. It is important to remember that nausea and vomiting are common symptoms of all severe envenomation (Mehta and Sashindran, 2011).

Systemic Features

Clotting defects and haemolysis: Haemostatic abnormalities are characteristic of envenoming by Viperidae. Persistent bleeding from fang puncture wounds, venipuncture or injection sites, and other new and partially healed wounds suggest that the blood is incoagulable. Spontaneous systemic haemorrhage is most often detected in the gingival sulci. Epistaxis,

haematemesis, cutaneous ecchymoses, haemoptysis, subconjunctival, retroperitoneal and intracranial haemorrhages are also reported (Mehta and Sashindran, 2011).

Neurotoxicity: Some snake venoms have significant neurotoxicity. Following an elapid bite, paralysis is first detectable as ptosis and external ophthalmoplegia appearing as early as 15 minutes after the bite. Sometimes the onset maybe delayed for 10 hours or more. Later the face, palate, jaws, tongue, vocal cords, neck muscles, and muscles of deglutition become paralyzed. Airway obstruction or paralysis of the intercostal muscles and diaphragm cause respiratory failure. Neurotoxic effects are completely reversible either acutely in response to antivenom or anticholinesterases or may wear off spontaneously in 1 to 7 days. It is important to note that these neurotoxins do not cross blood brain barrier and do not alter consciousness

Cardiotoxicity: Viper and elapid venom can cause direct myocardial damage manifesting as arrhythmias, bradycardia, tachycardia or hypotension.

Nephrotoxicity: Renal failure is secondary to ischaemia in Viper bites (especially Russell's viper).

Shock: A variety of factors contribute to shock. They include fright, hypovolemia (due to extravasation of fluids and blood loss), myocardial depression, haemorrhage into the adrenals and pituitary and increased kinin production (Grenvik *et al.*, 2000).

Laboratory Investigation of Snakebite Haematological Investigation

Full blood count can be used to ascertain envenoming which is usually associated with a neutrophil leucocytosis counts above $20 \times 10^9/L$ indicate severe envenoming. Initially, there may be haemoconcentration (increased haemoglobin concentration or haematocrit), but later haemoglobin concentration and haematocrit may fall because of bleeding into the bitten limb and elsewhere and from intravascular haemolysis in patient with disseminated intravascular coagulation (Schneemann *et al.*, 2004).

Test of Haemostasis: Incoagulable blood is a cardinal sign of consumption coagulopathy from envenoming by most viperidae (in Africa especially saw-carpet scale vipers, puff adder and desert horned viper). According to (WHO 2010) diagnosis of snakebite is aided by a test known as the 20 Minute Whole Blood Clotting Test (20WBCT). A clean, dry glass bottle or vial into which 1-2 milliliters of venous blood is added, is allowed to stand at room temperature for 20 minutes, and is then inverted and the presence or absence of a complete clot is recorded. Where a blood clot is present, the test result is negative, whereas if no clot forms and the blood remain liquid, the test result is positive, indicating presence of a coagulopathy and the need for antivenom treatment. Where this test is used it is essential that it be appropriately standardized using uniform glassware, sample volume and temperature, and validated for accuracy using serial donor samples prior to routine use.

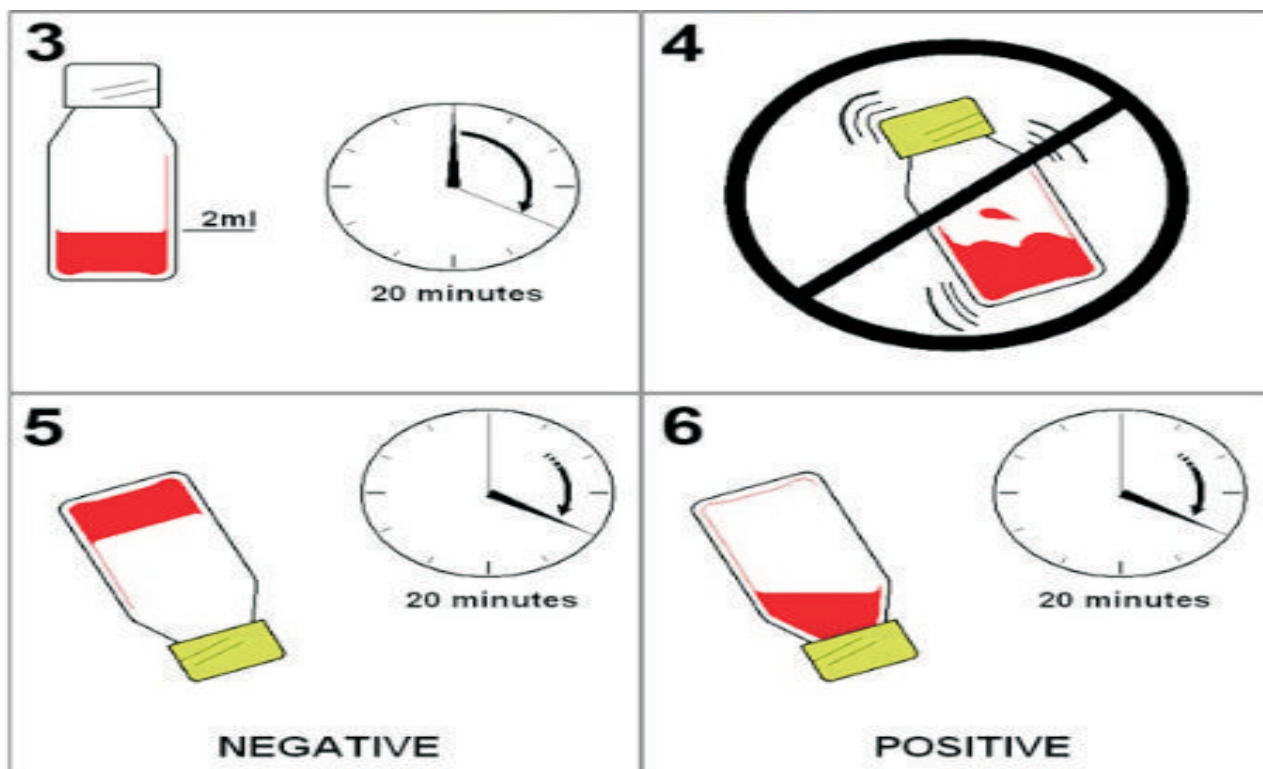


Figure 3. Illustration of the 20-minute whole blood clotting time test

Figure 3. Show an illustration for carrying out the 20-minute whole blood clotting time test and the expected result after the procedure (WHO, 2010). Other more sensitive tests haemostasis-related laboratory test includes Prothrombin time (PT), Thrombin and activated partial thromboplastin time and measurement of FDP and D-dimer concentration.

Biochemical Investigation

Biochemistry can reveal evidence of muscle damage. Serum concentrations of creatine kinase, aspartate aminotransferase and blood urea are commonly raised in patients with severe envenoming because of local muscle damage at the site of the bite. Blood urea, serum creatinine and potassium concentration should be measured in patients who become oliguric, especially in cases with a high risk of renal failure. A snake-bitten patient should be encouraged to empty his/her bladder on admission. Urine should be examined for blood, haemoglobin and protein and for microscopic haematuria and red cell cast.

Strategic Management of Snake Bite in Rural Nigeria

Essential First Aid Procedures

It is essential that first aid is carried out by bite victims themselves or bystanders, using material that are immediately available, while instituting the following first aid procedures, organize

transport to get the patient to a medical facility as soon as possible. The following evidenced based steps are recommended (WHO 2010):

1. Move the victim to safety from the area where they might be bitten again and remove the snake if it is still attached but not with your bare hands.
2. Reassure the victim, who maybe terrified. Reassurance is justified as most bites result in negligible or no envenoming and even if the patient is envenomed, there is usually ample time to transport them to medical care.
3. Removing constricting clothing, ring, bracelets, bands, shoes etc from the bitten limb.
4. Immobilize the whole patient, especially the bitten limb, using a sling or splint. Muscular constrictions anywhere in the body, but especially in the bitten limb will promote the adsorption and spread of venom from the site of the bite via veins and lymphatics. All movements should be avoided as far as possible.

5. Carryout pressure- immobilization techniques which is a safer alternative to the use of highly tight tourniquets that may cause many gangrenous limbs.
6. Transport the patient as quickly and as passively as possible to the nearest facility available for medical care.
7. Avoid the many harmful and time wasting traditional first aid treatments. Such as
 - Incision and Excision
 - Tattooing
 - Immediate prophylactic amputation of the bitten digits
 - Suction by mouth
 - Application of ice packs or electric shocks are absolutely contraindicated as they are potentially harmful and none has any proven benefit (Bush, 2004).
 - A tight (arterial) tourniquet should never be used. Tourniquets is one of the most popular first aid methods in Africa and continues to cause terrible morbidity and even mortality in snakebite victims. It should not be used. The dangers of torniquets are ischaemia and gangrene. Tourniquet if applied for more than about 2 hours can result to peripheral nerve damage, congestion and swelling and also increased bleeding.

Emergency Management of Snakebites

Snakebite is a medical emergency. Ideally, all patients bitten by snakes should be assessed by medically trained staff. Uncertainties, such as the species responsible, the amount of venom injected and the variable time course for development of signs, demand that patients be kept under observation for at least 24 hours. Medical staff must decide quickly whether the patient has been bitten by snake, whether there are signs of envenoming and whether antivenom or ancillary treatment is needed.

Rapid Clinical Assessment and Resuscitation

Rapid clinical assessment and resuscitation are essential. In Nigeria, patients may arrive hospital between hours and many days, after being bitten. They may, therefore show early or late signs of envenoming or its complications. It is essential that all patients with a history of snakebite be assessed rapidly. Although they may be moribund on presentation, they should still be salvaged by appropriate resuscitation.

Cardio-Pulmonary Resuscitation

Cardio-pulmonary resuscitation may be needed. This includes clearances of the airways, oxygen administration by face mask or nasal catheters and establishment of intravenous access to allow treatment of hypovolaemic shock with intravenous fluids and medicines. Airway, respiratory movements (Breathing) and arterial pulse (Circulation) must be checked immediately, vital signs must be recorded: blood pressure, pulse rate and respiratory rate. If the patient is unresponsive and no pulse or respiratory movement is detected, start cardio-pulmonary resuscitation (CPR) immediately. In case of respiratory distress/failure clear the airway (tongue, foreign bodies), lift the chin, give oxygen by facemask or nasal catheters with or mouth assisted ventilation and consider the need for endotracheal intubation.

Urgent Intervention

Patients bitten by venomous snakes in Nigeria may present with any of the following problems requiring urgent intervention:

1. Profound hypotension and shock:
 - Hypovolemia secondary to extravasation of plasma volume into the bitten limb, external or concealed blood loss, persistent vomiting and failure of adequate oral fluid intake.
 - Direct cardiovascular effects of the venom (for example after viper/adder bites).
 - Auto pharmacological effects of the venom (activation/inhibition of physiological vasomotor systems such as the angiotensin-renin-bradykinin system by venom toxins and rarely anaphylaxis provoked by antivenom given outside hospital or rarely provoked by venom in those who have been sensitized by previous exposure.
2. Sudden deterioration after release of a tourniquet or compression bandage, resulting in shock, bleeding or respiratory paralysis. These bands, bandages or ligatures are often removed too hastily by hospital staff before antivenom treatment has been initiated and appropriate staff and equipment are on hand in case resuscitation is need.
3. Airway obstruction resulting from aspirated vomits or the tongues blocking the upper

airway, especially in patients with evolving bulbar paralysis who have not been transported to hospital in the left lateral (recovery) position. Vomiting can be the result of systemic envenoming or ingestion of emetic traditional herbal remedies.

4. Terminal respiratory failures from progressive neurotoxic envenoming that has led to paralysis of the respiratory muscles.
5. Intracranial haemorrhage after envenoming by saw-scaled vipers, desert horned-vipers, some other vipers and boomslang. There will be characteristic lateralizing signs, dysphasia, impaired consciousness or neck rigidity.
6. Hours after the bite: cardiac arrest resulting from hyperkalaemia in patients with massive generalized skeletal muscles breakdown (rhabdomyolysis) after sea snakebite and neglected cytotoxic bites.
7. Days after the bite: Acute renal failure due to shock and rhabdomyolysis.
8. Days after the bite: Septicaemia from secondary infection of necrotic bite wounds or of incisions made at the site of the bite or complicating aspiration pneumonia.

Evidenced-based Management of Snakebite at Community Level and Different Health Care Facilities

In rural area where snakebite is most frequent, transfer to a hospital may not be feasible within a reasonable time frame of a few hours. In that case, a lower-level facility service must be equipped to cope with the emergency (WHO, 2010).

At Community Level

1. Check history of snakebite and look for obvious evidence of a bite (fang puncture marks, swelling of the bitten part).
2. Immobilize the whole patient as far as possible and especially the bitten limb and give reassurance.
3. Arrange transport of the patient to medical care quickly, safely and passively as possible by motor vehicle, boat, bicycle, stretcher etc. Ideally, the patient should lie in the recovery position (prone, on the left side) with the airway protected to minimize the risk of shock and inhalation of vomit.
4. Discourage time-wasting and potentially dangerous traditional treatments such as tight

ligatures (tourniquets), incisions, suction and application of herbs, ice, chemicals and snake stones.

At the Rural Clinic, Dispensary or Health Post

1. Simple medical assessment: history and simple physical examination-local swelling, painful tender enlarged local lymph glands, persistent bleeding from the bite wound, blood pressure, pulse rate, bleeding (gums, nose, vomit, stool or urine), level of consciousness, drooping eyelids and other signs of paralysis, 20-minute whole blood clotting time, urine examination (appearance, sticks testing for blood etc). identify the snake (if brought).
2. Assess need and feasibility of transporting the patient to a higher level of the health care.
3. Give analgesia by mouth if required: paracetamol (adult dose 1g maximum 4g in 24hours; children 15-20mg/kg. maximum 100mg/kg/day).
4. If the necessary skills, equipment, antivenom and other medicines are available give intravenous fluid to correct hypovolaemic shock and if the patient fulfils criteria for antivenom treatment, give antivenom. These skills include ability to diagnose local and system envenoming, set up intravenous infusion or intravenous injection, identify the early signs of anaphylaxis and treat it with intramuscular adrenaline/epinephrine. If no antivenom is available, transfer to a hospital.
5. If the patient has evidences of respiratory paralysis, give oxygen by mask and transfer to a hospital. It is assumed that assisted ventilation other than by a light-fitting face mask connected to an anaesthetic (Ambu) bag will not be possible at this level.
6. Discourage the use of ineffective and potentially harmful medicines (corticosteroids, antihistamines and heparin).

At District Hospital

1. More detailed clinical and laboratory assessment including biochemical and haematological measurements, ECG or radiography as indicated.
2. If no antivenom is available, transfer to a hospital that has antivenom or treat conservatively. This may require transfusion of blood or fresh frozen plasma.

3. Reassess analgesia and if requires, consider stronger parenteral opioid medicines as requires all with great caution.
4. If the patient has evidence of local necrosis (gangrene), give tetanus toxoid booster, antibiotics and consider surgical debridement of dead tissue.
5. If the patient has evidence of bulbar or respiratory paralysis, insert endotracheal tube or laryngeal mask airway. If there is evidence of reparatory failure, assist ventilation manually by anesthetic (Ambu) bag or mechanical ventilator.
6. If the patient has evidence of acute renal failure, treat with peritoneal dialysis. If this is not available, transfer to a specialized hospital.
7. If the patient is bleeding severely or is already seriously anaemic, consider blood transfusion.
8. Simple rehabilitation (exercising of bitten limb).

At Referral (Higher Level) Hospital

1. More advanced surgical management of local necrosis (e.g split skin grafting)
2. More advanced investigations including bacterial cultures and imaging (CT scans) as indicated.
3. If the patient has evidence of acute renal failure peritoneal or haemodialysis or haemofiltration.
4. Rehabilitation by physiotherapists.

Antivenom Treatment of Snakebite

Antivenom is the only specific antidote to snake venom. A most important decision in the management of a snake-bite victim is whether or not to administer antivenom.

Antivenom treatment for snake-bite was first introduced by Albert Calmette at the Institut Pasteur in Saigon in the 1890s (Bon and Goyffon, 1996). Antivenom is immunoglobulin purified from the plasma of a horse, mule or donkey (equine) or sheep (ovine) that has been immunized with the venoms of one or more species of snake. "Specific" antivenom, implies that the antivenom has been raised against the venom of the snake that has bitten the patient and that it can therefore be expected to contain specific antibody that will neutralize that particular venom and perhaps the venoms of closely related species (Para specific neutralization). Monovalent (monospecific)

antivenom neutralizes the venom of only one species of snake. Polyvalent (polyspecific) antivenom neutralizes the venoms of several different species of snakes, usually the most important species.

Antivenom Use

Antivenom neutralizes a fixed amount of venom. Since snakes inject the same amount of venom into adults and children, the same dose/ volume of antivenom must be administered to children as to adults. Antivenom can be effective as long as venom is still active in the patient's body causing symptoms of systemic envenoming. These may persist for several days or even weeks after the bite.

Indications for Antivenom Treatment

Antivenom should be given only to patients in whom its benefits are considered likely to exceed its risks. Since antivenom is relatively costly and often in limited supply, it should not be used indiscriminately. The risk of reactions should always be taken into consideration. According to WHO (WHO, 2010) 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 (clinical), coagulopathy (20 WBCT or other laboratory tests such as prothrombin time) or thrombocytopenia ($<100 \times 10^9/L$ or 100 000/cu mm).
- Neurotoxic signs: ptosis, external ophthalmoplegia, paralysis etc.
- *Cardiovascular abnormalities*: hypotension, shock, cardiac arrhythmia and abnormal ECG.
- *Acute kidney injury (renal failure)*: oliguria/ anuria (clinical), rising blood creatinine/ urea.
- *Haemoglobin-/myoglobin-uria*: dark brown urine (clinical), urine dipsticks, other evidence of intravascular haemolysis or generalized rhabdomyolysis (muscle aches and pains, hyperkalaemia).
- Supporting laboratory evidence of systemic envenoming

Local envenoming

- Local swelling involving more than half of the bitten limb (in the absence of a tourniquet) within 48 hours of the bite.

Swelling after bites on the digits (toes and especially fingers).

- Rapid extension of swelling (for example, beyond the wrist or ankle within a few hours of bite on the hands or feet).
- Development of an enlarged tender lymph node draining the bitten limb.

Contraindications to Antivenom

There is no absolute contraindication to antivenom when a patient has life threatening systemic envenoming. However, patients with an atopic history (severe asthma, hay fever) and those with a history of previous reactions to equine antisera (anti-tetanus serum) have an increased risk of severe reactions. In these cases,

only, pretreatment with subcutaneous adrenaline and intravenous antihistamine and hydrocortisone is justified to prevent or diminish the reaction.

Timing of Antivenom Treatment

Antivenom should be given as soon as possible once signs of systemic or severe local envenoming are evident. It is almost never too late to try antivenom treatment for persistent systemic envenoming. It has been proved to be effective in reversing coagulopathy 10 days or more after Echis bites. Table 1 shows the guide to initial dosage of some important antivenoms for bites by common African snake (WHO 2010).

Genus species	English name	Manufacturer Antivenom	Approximate initial dose
Bitis arietans and B. gabonica	Puff adder	Sanofi-pasteur	50-100ml
Dendroaspis spp	Mambas	SAVP, Dendroaspis	40-200ml
Dispholidus typus	Boomslang	SAVP, Boomslang	20ml
Echis coloratus	Burton's carpet viper	SAVP, Echis monosp	20ml
E. Ocellatus	Ocellated carpet viper	SAVP, Echis monosp2	20ml
Naja haje	Egyptian cobra	SAVP, Polysp	50-120ml
N. mossambicaa	Mozambique spitting cobra	SAVP, Polysp4	100ml
N. nigricollis	Black-necked spitting cobra	SAVP, Polyp	550-100ml
N. nivea	Cape cobra	SAVP, Polysp6	80-120ml

Table 1: Guide to initial dosage of some important antivenoms for bites by common African snake

Key:

SAVP: South African Vaccine producers (SAVP).

Antivenom Specificity

If the species responsible for the bite is known for certain, monospecific antivenom is the optimal treatment. However, in areas where the venoms of a number of different species produce similar clinical effects, polyspecific antivenoms must be used in the majority of patients who do not bring the dead snake for identification. Polyspecific antivenoms can be just as effective as monospecific antivenoms for the prescribed range of venoms which they cover and may be less expensive.

Antivenom Administration

Antivenom is the most effective when given intravenously. Freeze-dried (lyophilized) antivenom should redissolve quickly (less than 10 minutes) in sterile water. Difficulty redissolving suggests faulty manufacture (WHO, 2010).

Two methods of administration are recommended:

1. *Intravenous "push" injection:*
Reconstituted freeze-dried antivenom or

neat liquid antivenom is given by slow intravenous injection (not more than 2 ml/minute). This method has the advantage that the doctor, nurse or dispenser administering the antivenom must remain with the patient during the time when some early reactions may develop. It is also economical, saving the use of intravenous fluids, giving sets, cannula etc.

2. *Intravenous infusion*: Reconstituted freeze-dried or neat liquid antivenom is diluted in approximately 5-10 ml of isotonic fluid per kg body weight (250-500 ml of isotonic saline or 5% dextrose in the case of an adult patient) and is infused at a constant rate over a period of about one hour.

Local administration of antivenom at the site of the bite is not recommended: Although this route may seem rational, it should not be used as it is extremely painful, may increase intercompartmental pressure and has not been shown to be effective.

Intramuscular injection of antivenom: Antivenoms are large molecules (F(ab')₂ fragments or sometimes whole IgG) which, after intramuscular injection, are absorbed slowly via lymphatics. Bioavailability is poor, especially after intragluteal injection, and blood levels of antivenom never reach those achieved rapidly by intravenous administration. Other disadvantages are the pain of injection of large volumes of antivenom and the risk of haematoma formation in patients with haemostatic abnormalities.

The only situations in which intramuscular administration might be considered:

1. At a peripheral first aid station, before a patient with obvious envenoming is put in an ambulance for a journey to hospital that may last several hours.
2. On an expedition exploring a remote area very far from medical care.
3. When intravenous access has proved impossible (Win-Aung *et al.*, 1996).

Response to Antivenom Treatment

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

- (a). *General*: The patient feels better. Nausea, headache and generalized aches and pains may disappear very quickly. This may be partly attributable to a placebo effect.
- (b). *Spontaneous systemic bleeding* (e.g., from the gums): This usually stops within 15-30 minutes.
- (c). *Blood coagulability* (as measured by 20 WBCT): This is usually restored in 3-9 hours. Bleeding from new and partly healed wounds usually stops much sooner than this.
- (d). *In shocked patients*: Blood pressure may increase within the first 30-60 minutes and arrhythmias such as sinus bradycardia may resolve.
- (e). *Neurotoxic envenoming* of the post-synaptic type (cobra bites) may begin to improve as early as 30 minutes after antivenom, but usually takes several hours. Envenoming with presynaptic toxins (kraits and sea snakes) will not respond in this way.
- (f). *Active haemolysis and rhabdomyolysis* may cease within a few hours and the urine returns to its normal colour.

Antivenom Reactions

Early Reaction: Early reactions begin 3-60 minutes after starting intravenous administration of antivenom. Cough, tachycardia, itching, urticaria, fever, nausea, vomiting and headaches are common symptoms. More than 5% of patients with early reactions develop systemic anaphylaxis: hypotension, bronchospasm and angioedema.

Pyrogenic Reactions: Pyrogenic reactions result from pyrogen contamination of the antivenom during manufacture. They begin within 1-2 hours after treatment. There is an initial chill with cutaneous vasoconstriction, gooseflesh and shivering. Temperature rises sharply during the rigors and there is intense vasodilation, widening of the pulse pressure and eventual fall in mean arterial pressure. In children febrile convulsions may occur at the peak of the fever. Patients should be laid flat to prevent postural hypotension. Their temperature should be reduced by fanning and antipyretic medicines such as paracetamol given by mouth.

Late Reaction: Late (serum sickness type) reactions occur 5-24 (average 7) days after treatment. There is itching, urticaria, fever, arthralgia, periarticular swellings, proteinuria and sometimes neurological systems. Antihistamines are used for milder attacks, but in severe cases, including those with neurological symptoms, a short course of prednisolone should be given.

Prevention of Snake Bite in Rural Africa

The following preventative measure are indicated to prevent snakebite in rural Africa (WHO 2010):

- Be careful about where hands and feet are placed. For example, avoid reaching into spaces, holes, or underneath objects without first being sure a snake is not hiding underneath.
- Do not lie down or sit down in areas where snakes might be located
- Wear high-top leather boots when walking through or working in areas of dense vegetation.
- Do not attempt to capture, handle, or keep venomous snakes.
- Camp only in areas away from swamps, streams, dense foliage, and other places that snakes are known to inhabit.
- Slowly back away from and avoid touching any snake that is encountered.

Conclusion

Snake-bites are well-known medical emergencies in many parts of the world, especially in rural areas. The prevention of mortality and morbidity depend upon availability of antivenom in the health facilities in these settings and their rational use. There is the urgent need for the development of a national Snake Bite Strategy in Nigeria. Mechanisms need to be developed to ensure access to antivenom by all needy patients. The Nigerian health system needs to respond to this challenge and logistics must be put in place to ensure timely availability of antivenom at the point of use to reduce the incidence of preventable deaths and disability.

References

- Abdulrazaq, G.H. (2013). Public health aspects of snakebites care in West Africa: Perspective from Nigeria. *Journal of Venomous Animal and Toxin including Diseases*; 19:27.
- Alirol, E., Lechevalier, P., Zamatto, F., Chappuis, F., Alcoba, G. & Potet, J. (2015) Antivenoms for snakebite envenoming: what is in the research pipeline? *PLOS Neglected Tropical Diseases*; *PLoS Neglected Tropical Diseases*; 9(9): e0003896.
- Bush, S.P. (2004). Snakebite suction devices don't remove venom: they just suck. *Annals of Emerging Medicine*; 43(2): 187-188.
- Bon, C., and Goyffon, M. (1996). *Envenomings and their treatments*. Lyon: Editions Foundation Marcel Mérieux.
- Chippaux, J.P. (2011). Estimate of the burden of snakebites in sub-Saharan Africa: a meta-analytic approach. *Journal of Toxicon*; 57(4):586-99.
- Grenvik, A.K.E., Ayers, S.M., Holbrook, P.R. and Shoemaker, W.C. (2000). Injuries by venomous and poisonous animals. In: *Textbook of Critical Care 4th ed.*: 224-233.
- Harrison, R.A., Hargreaves, A., Wagstaff, S.C., Faragher, B. and Laloo, D.G. (2009). Snake envenoming: a disease of poverty. *PLoS Neglected Tropical Diseases*; 3(12): e569.
- James, A.P. and Van W. Snake. Facts and Types. *Encyclopedia Britannica*. November 05, 2020. <https://www.britannica.com/animal/snake>.
- Julian, W., Daniel, F.D., Stephen, J.T. and James, F.W. (2019). Snakebites worldwide; Management: *Bulletin of World Health Organization*; 76: 515.
- Julien, S., Jeroen, K., Robert, A.H. and Nicholas, R.C. (2017). Haemotoxic snake venoms: their functional activity, impact on snakebite victims and pharmaceutical promise: *British Journal of Haematology*; 177: 947-950.
- Kerkkamp, H.M.I., Casewell, N.R., and Vonk, F.J. (2015). Evolution of the Snake Venom Delivery System. In *Evolution of Venomous Animals and Their Toxins*, pp. 1-11. Living Reference Work, Springer, Dordrecht.
- Kasturiratne, A., Wickremasinghe, A.R., De Silva, N.R., Gunaardena, N.K.,

- Pathmeswaran, A. and Premaratna, R., (2008). The global burden of snakebite: a literature analysis and modelling based on regional estimates of envenoming and deaths. *PLoS Medicine*; 5(11): e218.
- Meyer, W.P., Habib, A.G., Onayade, A.A., Yakubu, A., Smith, D.C. and Nasidi, A. (1997): First clinical experience with a new ovine Fab *Echis ocellatus* snake bites antivenom in Nigeria: randomized comparative trial with Institute Pasteur Serum (Ipser) Africa antivenom. *Journal of Tropical Medicine and Hygiene*; 56(3):292–300.
- Mehta, S.R. and Sashindran, V.K. (2011). Clinical features and management of snake; *Medical Journal of Armed Forces of India*; 58(3): 247-249.
- Vonk, F.J., Casewell, N.R., Henkel, C.V., Heimberg, A.M., et al. (2013) The king cobra genome reveals dynamic gene evolution and adaptation in the snake venom system. *Proceedings of the National Academy of Sciences of the United States of America*; 110:20651-20656.
- Warrell, D.A. and Arnett, C. (1976). The importance of bites by the saw-scaled or carpet viper (*Echis carinatus*): epidemiological studies in Nigeria and a review of the world literature. *Acta Tropical*; 33(4):307–341.
- World Health Organization (2010). Guidelines for the prevention and clinical management of snakebite in Africa. (accessed November, 2019).
- Schneemann, M. (2004). Life-threatening envenoming by the Saharan horned viper causing micro-angiopathic haemolysis, coagulopathy and acute renal failure: clinical cases and review. *Quarterly Journal of Medicine*; 97(11):717-727.

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