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#### **REVIEW ARTICLE**

## Snakebites and their Impact on Disability

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#### ABSTRACT

Snakebites represent one of the main causes of mortality and according to some estimations there are three times the number of disabilities in victims of poisoning by the bites.

Disability can be classified as total if it prevents the victim from performing his/her productive routine activities or requires long term physiotherapy to recover part of the function. Partial disability can be related to the time, or the degree of lost function related to her/his productive activity.

In general, snakebites are classified as neglected diseases, and its study focuses on the immediate morbidity or mortality while the consequences in the long term are less studied.

A neglected disability is related to mental health, wherein many victims suffer the effects of post-traumatic stress disorder (PTSD), or changes in self-image because of deformities left by the ophidic accident.

The review of the topic had the objective to identify the level of discussion of disability issues caused by snakebites and for this purpose publications in Medline (English literature) and Scielos (Spanish, Portuguese and English publications) were explored. The results were obtained around the terms Snakebites and disabilities, snakebites and permanent sequelae, and Snakebites and rehabilitation. The results were organized according to type of disability, world region and type of snake-species.

Disability can be the product of local damage (muscle and local tissue loss), or neurological loss reflected in different degrees of sensorial loss or partial/total loss of motricity.

Particular interest must be given to the loss of productivity of individuals affected in their muscular, neurological, and mental conditions. Mental health sequelae can also prevent people from restoring their productive activity.

Describing the consequences of snakebites in the long term serves a purpose as education to those affected by snakebites in often neglected areas of the world. Additionally, it serves as critical information for clinicians and health personnel in the rehabilitation and treatment of those affected.

**Keywords:** snakebites, disability, envenoming, organic and functional disorders.

#### Introduction

Snakebites, a neglected tropical disease, constitute a problem worldwide affecting poor populations in rural areas worldwide especially in Africa, South and Southeast Asia, and in the Americas<sup>1</sup>.

According to some authors every year there are from 1.2 million to 5.5 million snakebites and from 400,000 to 1.8 million people suffering from envenoming after having a snakebite. Of these, around 94,000 died<sup>2</sup>.

South Asia had the highest number of poisoning cases (121,000), followed by Southeast Asia (111,000) and sub-Saharan East Africa (43,000). The lowest numbers were estimated to be in Central Europe and Central Asia. South Asia had the highest number of snakebite deaths (14,000), followed by sub-Saharan West Africa (1,500) and sub-Saharan East Africa  $(1,400)^{2,3}$ .

Snakebites cause significant morbidity and mortality worldwide. The highest levels are in South Asia, Southeast Asia and Sub-Saharan Africa. India has the highest annual number of poisonings (81,000) and deaths (approximately 11,000). Other countries with high estimated annual envenoming numbers are Sri Lanka (33,000), Vietnam (30,000), Brazil (30,000), Mexico (28,000) and Nepal (20,000)<sup>3</sup>.

The lowest death tolls are estimated to be in Australia, South Latin America, and Western Europe. India has the highest number of snake deaths in the world, with about 11,000 people dying each year. More than 1,000 people died annually in Bangladesh and Pakistan<sup>3</sup>.

According to the World Health Organization (WHO), the number of amputations and other permanent disabilities brought on by snakebites is about three times higher than the recorded mortality worldwide from the same cause, a silent but real emergency for the affected populations<sup>4</sup>. The profile of the victim of venomous snake bites is a young adult male dedicated to agricultural activities<sup>5</sup>.

With systemic snake venom administration to humans the injected venom is absorbed and enters the systemic circulation, producing different clinical effects depending on the individual snake and the venoms components<sup>6</sup>. These manifestations can be acute (local or systemic) or can lead to lethal effects and death. The survivors can suffer diverse types of disabilities affecting the sensorial systems, motricity and sensibility, the integrity of tissues and the adequate irrigation and oxygenation of them<sup>2,4</sup>.

Currently, most of the conversation is centered around the accessibility of victims to anti- venom therapy and the need to have clinics closer to areas at high risk for accidental encounters of humans with venomous snakes. The possibility of access to therapy is limited by geographical, socio-economic, and cultural barriers of the victims and the availability of services and antivenom supply<sup>7</sup>.

Many victims do not get medical treatment and antivenom in time, and they are a part of the mortality statistics that are not collected as part of the official records. Some of them survive but with some damage that is physical, functional, and often with a degree of irreversibility<sup>4,7</sup>.

It is expected that the main concern of the health system is the survival of the snakebite victim and the management of immediate health damage, but the management of subacute and chronic damages frequently remain out of the scope of the case management with few studies addressing the sequelae and needs of rehabilitation<sup>2</sup>.

Recent studies discuss the damage during the acute stage of the snakebites but the effects on the long term are discussed much less; countries like India and Sri Lanka have produced more research in this area, some studies of Sub- Saharan Africa, where the problem is endemic, also discuss the effect of snakebites on individuals and families<sup>8,9</sup>.

In the Americas, the concept of disability associated with snakebites is mentioned but, in less detail, while the priority is the acute effect and the need to access anti-venoms<sup>5</sup>.

Snakebites are a medical urgency during the acute phase, and they continue to be part of the global burden of disease. The additional dimension posed by disability is social and economic. Individuals are affected by their productivity, affecting their family and social role, and which is also important to their own self-care, and quality of life. Disability caused by these events should be addressed more actively in health debate<sup>7</sup>.

We'll center in this study in identifying some of the potential sequelae left by venomous snake bites and how they correspond to the described venoms effects. The sequelae will be reflected in specific types of disability corresponding to the organic systems affected by the venoms.

## Methods of the study

OBJECTIVES:

- 1. Identify the level of priority given to the disability caused by venomous snakebite
- Describe the characteristics of disabilities mentioned in association with snakebites and grouped according to three main types of toxicity and damage to the organic systems
- 3. Discuss what the impact of the referred disabilities is on the daily routines of the survivors of snakebites in the regions of study based on current knowledge

We conducted a literature review in the databases of Pubmed, Toxmed, Scielos including publications in the geographical areas of Africa, South Asia and the Americas where publications on the topic of snakebites have been written and the reported burden of disease is higher.

"snakebites The terms searched were and disability", "snakebites and sequelae", and "snakebites and long-term effects" which restricted the number of searched papers. Those papers mentioning only the generic term "disability" without providing further details were excluded, leaving only those that described details of the lesions and experiences of treating patients with disabilities caused by venomous snakebites. For this review, we included a variety of observational study designs. The consulted literature covered the last 40 years. (1985-2024) in the areas of higher risk (South and Southeast Asia, Subsaharan Africa and America).

### Results

#### SNAKE VENOMS IDENTIFIED WORLDWIDE

Snake venom is composed of a mixture of biologically active proteins and polypeptides (representing about 90-95% of the venom mass) and other non-protein components such as carbohydrates, lipids, amines and inorganic salts. Proteins and polypeptides are defined as enzymes for example; phospholipase A2 (PLA2), metalloproteases (SVMP (Snake venom metalloproteases)), serine proteases (Snake venom serine protease), L-amino acid oxidase (LAAO)] and non-enzymatic substances e.g., B. three-finger toxin (3FTx), Kunitz peptide (KUN) and disintegrin (DIS)]. The composition of snake venom depends on several factors, including the snake family, genus and species, geographical location, typical prey species, age and size of the snake<sup>10</sup>. For example, threefinger toxins (3FTx) and phospholipase A2 (PLA2) are predominantly found in elapid snakes, whereas phospholipase A2 (PLA2), snake venom metalloproteinases (SVMP), and snake venom serine proteases (SSPA) are most abundant in viperid snakes<sup>6,10</sup>. Venomous snakes are found in most parts of the world (including many oceans), except for some islands, icy environments, and highlands<sup>11</sup>. However, poisoning and death from snake bites is a serious public health problem. Many victims survive with lasting physical and psychological effects from localized tissue necrosis. (See table 1 at the end of the document)

## IMMEDIATE EFFECTS OF THE VENOMS IN HUMAN INDIVIDUALS

Snake envenoming typically causes a mixture of cytotoxic, myotoxic, hemotoxic and neurotoxic effects on those affected<sup>12</sup>. Cytotoxicity refers to a venom's cell injury/death causing properties and may cause equally or worse outcomes in patients. A common outcome of cytotoxic snake envenoming is necrosis (passive cell death), and this effect may have implications for both local and distal tissues and organs<sup>12</sup>.

Many snake venoms also possess myotoxic characteristics, presenting a substantial concern for victims of envenoming. Phospholipase A2s, along with short chain amino acid (AA) residues, rapidly destroy myocytes through vacuolation, lysis and passive cell death (necrosis)<sup>13</sup>. Further, muscle fiber degradation may lead to rhabdomyolysis which is a life-threatening condition where degraded muscle components enter the bloodstream <sup>14</sup>.

Aside from snake venom metalloproteinases and other toxic snake venom compounds which may lead to local ischemia and local tissue damage<sup>15</sup>, other organs and tissues may be affected through alterations in the systemic vasculature. Snake venom of this kind, which affects the circulation and red blood cell characteristics is considered hemotoxic and may act in tandem with the other effects to potentiate adverse outcomes. For instance, the kidney has been shown to sustain acute damages as a result of renal hemodynamic changes leading to decreased renal blood flow<sup>16</sup>, these acute damages can result in chronic kidney failure in some cases<sup>17</sup>. On a molecular level, animal-model based research suggests envenomation from some species like Bothrops alternatus can cause increased oxidative stress and cytokine expression, along with degeneration in several parts of the kidney <sup>18</sup>.

Neurotoxicity in the context of snake envenomation typically describes alteration of neurotransmission at a synapse because of envenomation. These neurological changes occur because of cholinergic receptor antagonism and ion channel blockage preventing neurotransmission. At the neuromuscular junction (NMJ), this is a mechanism by which respiratory muscle, along with other muscle paralysis has been implicated in snake bite victims<sup>12</sup>.

## EVOLUTION OF THE VENOM EFFECTS FROM ACUTE EFFECTS TO LONG CHRONIC EFFECTS

The ways in which a victim of snake envenoming may be affected are concerning in an acutely affected time frame but should also be considered chronically. Prolonged necrosis of parts of the limb because of snake envenoming may lead to further complication in patients.

Secondary infections at the bite site present a serious concern that, if not managed correctly, may prolong recovery times, and cause significant structural injury in the form of necrosis<sup>19</sup>.

Amputation of the affected limb(s) may be necessary in these cases and in acute stages of snakebites. Importantly, both upper and lower limb amputations have profound implications as workplace injuries. Amputation at the level of the hands (fingers or whole) and feet can severely impede the completion of tasks in farming and tending to crop. On top of reducing workplace efficiency, amputation presents in itself a procedure in which patients will need some time off for proper healing of the limb(s)<sup>19, 20</sup>.

In the literature, chronic effects of snake envenoming and the disabilities that follow suit are a topic that has been significantly overlooked. Knowing that the victims of snake envenoming often live in developing countries and often as farmers, loss of function and/or amputation of a limb can place an unexpected financial burden on those affected, as well as their families and communities. Therefore, understanding the connection between disability and snakebite holds merit in both medical and socioeconomic fields<sup>19-21</sup>.

## REDUCTION OF MUSCLE POWER AND CHANGES IN THE BODY BALANCE AND GAIT.

Besides evident losses in mobility associated with amputation, chronic cases of snake envenomation may also lead to significant kinetic changes. Reduced muscle power, motion, balance and mobility have all been associated with snake envenoming sequelae. A cross- sectional study performed by Subashini Jayawardana et al. in 2016 examined 21 victims of snakebites leading to musculoskeletal disabilities. Range of movement was measured through a goniometer, muscle power through handheld dynamometers (grip strength) and manual muscle testing scale for other muscle groups. Finally, standing balance was measured using the functional reach test (FRT). A significant observation Snakebites and their Impact on Disability

of these patients on examination were that researchers found a prevalence of 3.2% for chronic musculoskeletal (MSK) disabilities in snake envenoming victims of a total sample size of 816 snakebite victims in a rural population in which snakebites are prevalent<sup>22</sup>.

In patients presenting complaints of pain during prolonged standing and walking and with foot bite sites, there was limited ankle dorsiflexion, however in those with Achilles tendon bite sites, there was limited ankle plantarflexion. These changes were seen anywhere from 3 months post bite - 34 years post bite, in both males and females, and ages ranging from 16 years old - 66 years old, indicating that snakebite envenoming may have lasting and chronic effects on mobility, regardless of the age of the patient. Although reductions in muscle power, range of motion and muscle wasting were present in many patients, only one patient displayed an abnormal gait pattern. The researchers suggest that these changes are likely because of distal neuropathic alterations as a result of the snakebite, wherein the venom can alter and damage nerve endings responsible for mediating a tight control on postural stability.

Several factors, including the sample size of the study, and the use of only one test for measuring postural stability, underline the importance of further studies on the association between musculoskeletal alterations and snake envenoming sequelae. Despite the novelty of this kind of study, the mechanisms by which there may be impairments in muscular power and thereby the ability to maintain proper postural stability are clear (Neurotoxicity and Myotoxicity). Later research by Subashini Jayawardana et al. has also found that a unique adverse effect of snake envenomation in a rural Sri Lankan community is the development of vertigo and photosensitivity <sup>9</sup>. Vestibular system alterations also present a form in which standing balance may be potentially compromised in some snakebite victims. More research is needed in this area, however current research indicates musculoskeletal disabilities do occur with snake envenoming and affect varying aspects of human movement from postural control, to muscle power and range of motion.

#### DAMAGES IN LOCAL AND DISTAL TISSUES

Importantly, damage done to the tissues and nerves appears to be mostly local (ie. only those affected in the lower limbs experience lower limb alterations that may alter stability and balance). The pain caused at the site of the bite is also an important point to consider, as this may play the biggest role in patient work attrition, and thereby loss of productivity. Another cross-sectional study of a population affected by snake bites identified several musculoskeletal impairments, including swelling, muscle wasting, reduced motion, power, impaired balance and gait abnormalities <sup>22</sup>. The prevalent species in this study were Cobra, Russell's viper and hump

nosed viper. Cobra bites were associated with muscle wasting, reduced muscle power, joint stiffness, and deformities, while viper bite sequelae impaired standing balance and caused pain and swelling at the site of the bite. Other research has found that compared to healthy community controls, snakebite victims had a higher risk of an impaired joint function (9.8% vs. 3.2%; RR, 3.05; 95% CI, 1.25-7.47) <sup>23</sup>. Although snake envenoming may induce distal damage from the bite area, proper care should be placed to mending local damages to both musculature and inert structures where applicable. Physiotherapeutic interventions, especially in footto-ankle bites should be considered for proper management of the bite and mitigating any ensuing sequelae in the area.

## OCULAR DAMAGE MAY OCCUR BY DIFFERENT MECHANISMS.

In addition to causing musculoskeletal disabilities, snake envenoming of many species is known to induce ocular sequelae; the mechanisms by which it occurs are not understood for all conditions seen but have been linked to neurotoxicity and hemotoxicity of the venom<sup>24</sup>.

Neurotoxic effects on the eyes seen include

ophthalmoplegia, optic neuropathy and retinal toxicity. Hemotoxic effects seen include central retinal artery occlusion, cerebral visual impairment, vitreous hemorrhage, retrobulbar hemorrhage and anterior segment ischemia.

Other conditions, for which there was no clear mechanism, have also been identified. One of these conditions was found to be acute glaucoma and was also the most found visual impairment because of snake envenomation in patients in a meta-analysis<sup>24</sup>. This condition has been linked to reductions in a person's mobility performance in an age, gender and race matched control study <sup>17,24,25</sup>. (See table # 2).

Interestingly, some impairments because of snake envenoming appear to be equally dependent on the bite itself as it is on its management. For a condition such as optic neuropathy, researchers propose that this condition may arise as an adverse effect of antivenom rather than from the envenomation itself. Similarly, snake venom neurotoxicity from common krait bites have been found to induce ptosis in some patients which may also obstruct a person's visual field <sup>26</sup>. In these cases, the effects of the venom at the neuromuscular junction (impairing neuromuscular transmission) are the primary cause rather than myotoxicity, and unlike other envenoming sequelae, do not improve with antivenom administration.

Because there are several mechanisms by which victims can be affected, proper visual screening in a short term and long-term timeframe is paramount to identify and rule out all possible damage to vision.

Toxicity causing Ocular damage	Explanation	Species Involved
Neurotoxicity	and Retinal neurotoxicity	Gloydius family, Bitis atropos, Vipera aspis Trimeresurus macrops, Naja family (Nigricollis, Naja), Bungarus caeruleus, unspecified elapid, unspecified viper
Hemotoxicity	cerebral visual impairment, Vitreous	Echis carinatus, Dabola russelli, Naja Naja, Bothrops russelii, Bothrops athrox, Daboia russelii, Echis ocellatus, Unspecified vipers
	Acute glaucoma: The most commonly found visual impairment by meta- analysis (Jalink et al., 2023)	Unspecified viper, Macrovipera lebetinus, Naja naja

 Table #2. Mechanisms causing Ocular damage after a Snakebite<sup>24</sup>.

#### IMPACT ON DAILY ACTIVITY AND ROUTINE

Neurotoxic and hemotoxic effects may cause direct damage to limbs and tissues which may require surgical intervention and debilitate a victim's capacity to work and live their lives as they had prior<sup>27,28</sup>. In addition, envenomation has been shown to cause musculoskeletal disabilities. These span from reductions in range of motion of joints and muscular power, to visual and psychological deteriorations. Though studies to this point have only found chronic disabilities in a fraction of snake envenomation victims, the severity of the disabilities caused presents a major concern. Because snake envenomation often occurs in rural areas in which proper treatment is not as easily accessible, disabilities caused by snake envenomation have the potential to lead to significant monetary losses in the form of lost time at work. In rural areas where farming and crop tending is common, a person inflicted with a snake venom induced disability may have trouble moving due to musculoskeletal disabilities or may not be able to perform tasks properly due to visual reductions<sup>23</sup>. In addition, other sequelae seen such as photosensitivity presents a serious problem, knowing many patients affected by snake envenomation work outdoors in often sunny conditions<sup>9</sup>.

#### **Psychological damage**

Besides physical deficits, snake envenomation presents serious psychological risks for victims; workplace bites may cause hesitation or attrition altogether from those working at the same place<sup>29</sup>. Psychological conditions that may occur as result of snakebites include but are not limited to posttraumatic stress disorder (PTSD) and symptoms of depression and somatization.

Although not visible, the psychological effects onset by the experience of a snake bite are significant as they may directly impact a person's cognition, productivity, and overall quality of life <sup>19,28</sup>. Moreover, disability in this aspect may be more difficult to quantify and may have profound implications in psychosocial and socioeconomic perspectives <sup>30,31</sup>. Unlike other adverse outcomes of snakebites, psychological sequelae in particular is unique in that often many rural areas where snakebites are prevalent either do not acknowledge psychological conditions, have accessibility to proper mental health interventions, or both. Therefore, this kind of damage should be keenly examined and treated, as it can often be overlooked.

THINKING BEYOND THE IMMEDIATE SNAKEBITE International health organizations stress the need of

immediate care which is important but not realistic. It is important to limit the damage to local effect (pain, inflammation, bleeding, and damage to local tissue) saving the victim from systemic and more extensive effect. The availability of antivenom in clinics closer to the areas of high risk can reduce the impact of the toxins in the tissue, and the systemic distribution to distal tissues and organs<sup>32</sup>.

However, most patients in isolated areas currently don't have immediate access to treatment, they and their families and local health provider should know about the short and long term effects of venoms and be prepared to engage in efforts to save their lives protecting key organs from further damage: kidney (dialysis should be available to victims of disorders/clotting), hemorrhagic respiratory airways (artificial respirators to assist with different levels of respiratory paralysis), and providing musculoskeletal follow υp to impairments (physiotherapeutic training should be given to personnel in clinics and hospitals receiving survivors of snakebites) <sup>32,33</sup>.

#### ARE THESE DISABILITIES AND THEIR MANAGEMENT A PART OF HEALTHCARE MANAGEMENT AND THE SOCIAL SECURITY AND PREVISION SYSTEM?

In most countries Snakebites as, other Neglected tropical diseases have the potential to lead individuals and their families to poverty, isolation and practically to a non-entity life after their relative or total impossibility to continue being productive. The component of mental health support cannot be ignored to a population that becomes destitute in their own places. There is a need to develop social networks of support for them and to implement plans of gradual rehabilitation, "primary research to understand and address the long-term healthcare needs of snakebite survivors and increased health systems research and implementation research for the development of care delivery models that incorporate survivors' needs" <sup>33 34</sup>.

With the current emphasis on the reduction of snakebites by 50% in its mortality and morbidity there is an opportunity to channel resources (human, logistic and financial) to improve the health systems to support the victims of envenoming by snakebites once they are prioritize in rehabilitation plans. Further work should continue to identify disabilities that may arise from snake envenomation past the initial treatment time; such insights would hold merit in implementing comprehensive rehabilitation strategies. Moreover, this would prove critical for mitigating the impact these unfortunate events may have on an individual and their families and communities.

#### Conclusions

Neglected populations suffer a high proportion of Snakebites and have less access to health care in the long term, which means disabilities can affect them for a longer period and reduce their capacity to participate in productive lives.

Limitations caused by snakebites to the integrity of the body and its functions have been identified and described relative to different venoms and snake species. As such, there is a need to use this not only in a patient's medical follow-up but also in their rehabilitation by professionals and family members.

It's important to remember that neglected populations suffer from isolation and their access to health care in acute and urgent needs is limited. In the case of snakebites, effective medical management should be provided as soon as possible, ideally within a few hours of the event.

The current management of snakebites is centered around the use of antivenoms. However, this is not enough, and a careful assessment of the victims is also important to evaluate the needs to rehabilitate lost abilities. Further, health personnel need to be trained to provide basic treatment and therapy for potential disabilities. A multifaceted treatment approach must be taken in the management of envenomation sequelae, as sequelae can vary significantly due to the variability in snake venom composition. Neurotoxic, hemotoxic, myotoxic and cytotoxic compounds in snake venom all present cause for concerns as they manifest as a variety of different sequelae in those affected.

The aim of this review was to compile and interpret information related to snake envenoming sequelae and disabilities that may result from the lasting effects of these events. Although some areas in this field such as acute tissue damages and amputations are well characterized outcomes of envenomation, many others have yet to be fully elucidated. From what is currently known, human movement and mobility can deteriorate through both physical and psychological impairments following a snakebite. The species of snake, along with the bite area plays a key role in what kind of disability (if any) may occur.

A limitation of this review was that an insufficient amount of information was found for key topics relating to important parameters related to human disability. The chronic effect of envenomation of various species on a person's postural control and visual acuity are two important concepts of human movement which require further investigation.

#### **Recommendations**

It is necessary to emphasize the knowledge of Snakebites in the toxicologic and therapeutic dimensions to the medical teams and those staff and volunteer teams in areas of high endemicity of snakebites.

The acute and long-term effects of venoms should be the basis for approaching the management of cases without reducing attention to the disabling psychological effects of these encounters with snakes and the post-encounter reality of physical and functional changes.

Making physiotherapy accessible to this rural population afflicted by cases must be part of the long- term plans.

### **Conflict of Interest**

The authors declared they don't have any conflict of interest

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Snake species	Main toxins	Mode of action	Geographic area
Rattlesnake Crotalus spp.	Crotoxin, Phospholipase A2 1 in C. durissus Mojave toxin, Phospholipase A2 Species: C. scutulatus	Neurological effect 1.Pre-synaptic block 2. Post-synaptic effect by desensitization of nAChR Pre-synaptic ion channel blocker	South America Found in the deserts of the Southwestern United States and central Mexico.
Bothrops atrox	Thrombin-like enzymes (SVTLEs) (Batroxobin, Reptilase).	Hemorrhagic 1) Deactivate factor XIII and the clots produced can easily be broken down. 2) Local damage, such as edema, hemorrhage and necrosis, apart from systemic effects, including blood coagulation disorders Myotoxic.	Found in the tropical lowlands of northern South America east of the Andes, as well as the Caribbean Island of Trinidad.
Viperid and crotalid venoms	PLA2s	Cause rapid necrosis of skeletal muscle fibers, referred to as myotoxic PLA2	Found throughout the continental United States and Canada
Brazilian viper (Bothrops jararaca)	Angiotensin converting enzyme (ACE) inhibitor	Hypo tensor Causes sudden, massive drop in blood pressure	Endemic to South America in <b>southern</b> <b>Brazil, Paraguay, and</b> <b>northern Argentina.</b>

Table 1: Common snake species causing envenomation in the Americas, Africa, and Asia. Illustrative list

Agkistrodon spp. (American copperheads) Bothrops spp. Includes Bothriechis, Cerriphidion (Pitvipers)	Metalloproteins Phospholipases A2 Serine proteases (SVSPs) Metalloproteins Phospholipases	Coagulopathy and Haemorrhage Coagulopathy and Haemorrhage	North America, ranging from the Southern USA to northern Costa Rica Southern Mexico and Guatemala
Crotalus spp. Common Name: North American Rattlesnakes Lachesis spp (known as Bushmaster)	PLA2, SVMP P-III, SVSP, Dis, LAAO, CRiSP, CTL, SVMP P-I, BPP, Hya, and PDE Bradykinin potentiating peptides (BPPs), serine proteinases, metalloproteinases and phospholipases A2 (PLA2)	Coagulopathy and Haemorrhage Coagulopathy and Haemorrhage	Found only in the Americas from southern Canada to northern Argentina Found in South America, and in the island of Trinidad in the Caribbean
Micrurus (Coral Snakes) M. nigrocinctus	Postsynaptic α- neurotoxins	Neurologic effects: Pain, nausea, Paresthesia, cranial	North, Central and South America
Cobra (Naja spp)	Alpha-Cobra toxin (Long-chain Alpha- neurotoxin or 3FTX) Cobrotoxin, short chain	nerve involvement, altered mental status, and respiratory failure. Binds to post-synaptic muscle nAChRs- produce reversible non-depolarizing block; and bind to neuronal α7nAChRs	South and Southeast Asia
	alpha-neurotoxin 3FTX (Present in the species N. atra) N.nigricollis Cardiotoxin, 3FTX	Post-synaptic non- depolarizing block Blocks axonal conduction, citotoxicity	This species is present in Southern China and some neighboring countries and islands. Sub Saharan Africa

	"Weak toxin"WTX, Non-conventional Alpha-neurotoxin 3FTX in the N. kaouthia	Bind to post-synaptic muscle nAChRs-cause irreversible,non- depolarizing block and bind to neuronal α7 nAChRs	ldem Indian spitting Cobra in <b>South and Southeast</b> <b>Asia</b>
Krait (Bungarus spp)	Alpha-bungarotoxin, long-chain alpha- neurotoxin(3FTX) Species: B. multicinctus	Bind to post-synaptic muscle nAChRs- produce irreversible, non-depolarizing block	Many-banded krait known as Taiwanese Krait or Chinese krait, found <b>in central</b> , <b>Southern China and</b>
	Beta-bungarotoxin, Phospholipase A2 Kappa-Bungarotoxin,	Pre-synaptic block	Southeast Asia Found in South and South-east Asia
	Kappa-neurotoxin (3FTX)	Block neuronal nAChRs in autonomic ganglia	Taiwanese Krait range
	Candoxin, non- conventional alpha- neurotoxin (3FTX) In B. candidus	Bind to post-synaptic muscle nAChRs- produce reversible, non-depolarizing block Bind to neuronal α7 nAChRs	Southeast Asia from Indochina south to Java and Bali in Indonesia
Rusell's viper (Dabola spp.)	Phospholipase A2 activity Species : D. ruselli	Pre-synaptic block	South-Asia ( <b>Indian</b> <b>subcontinent)</b>
300.7	Dabola Neurotoxin-1 (DNX-1), short-chain neurotoxin D.ruselli	Post-synaptic block	Native to <b>the Indian</b> subcontinent
	Viperotoxin-F Phospholipase A2 D. ruselli	Pre-synaptic block	Native to <b>Indian</b> subcontinent
Mamba (Dendroapis spp)	Dendrotoxins-alpha, delta, I,K, 3FTX Species : D. angusticeps, D. polylepis	Block neuronal voltage- gated potassium	Dendroaspis polylepis is native to <b>parts of</b> <b>Sub-Saharan Africa.</b>

Fasciculins, 3FTX	channels-presynaptic	
D.angusticeps,	+/-post synaptic effects	
D. polylepis	Inhibits AChE	
Muscarinic toxins, 3FTX		Dendroaspis
D.angusticeps	Muscarinic effects by binding to muscarinic AchRs	angusticeps. Native to the coastal regions of Southern East Africa
Calciseptine D. polylepis	Inhibit voltage-gated calcium channels	

**Sources:** Adapted from White (2005). Snake venoms and coagulopathy and Ranawaka (2013) Neurotoxicity in snakebite—The limits of our knowledge. <sup>5.35.36.</sup>