



Snake Venom and its Effects on Animal Health

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ABSTRACT

This review is based on snake venom, and aims at interspersing theory with a practical approach. Snakes have evolved a toxic concoction called venom or zootoxin which has helped them subdue and digest their prey, prior to ingestion. The first signs of venom in snakes date back to 28 million years ago. It was found to be composed of 90% water, lipids, proteins, amino acids, nucleosides, neurotransmitters, and carbohydrates. The various components of snake venom acted on different physiological systems within the victim's body, eventually subduing them and enabling the snake to consume its meal. Out of the 4,000 described species in the world, about 600 were believed to be venomous, and around 200 of them could cause life threatening symptoms in animals and humans. Following a bite from a venomous snake, first aid must be performed promptly and the individual must be rushed to a nearby hospital to increase their chances of survival. Based on the mode of action of the venom, it is classified into neurotoxic, hemotoxic, cytotoxic and myotoxic. India, home to the 'Big Four' comprising the Russell's viper, Saw-scaled viper, Spectacled cobra and Common krait, which are responsible for the majority of the 58,000 deaths that occurred annually as a result of snake envenomation. All the photos used in this article were collected from professionals in the field of herpetology. Some of the information came from actual practitioners who were interviewed either in person or via email.

KEYWORDS: Snake bite, Snake venom, metallo-proteinases, serine proteases

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1. INTRODUCTION

Some snakes secrete a poisonous cocktail of biomolecules called 'venom' or 'zootoxin' which is made up of 90% water, lipids, proteins, amino acids, nucleosides, neurotransmitters and carbohydrates. Proteins and peptides predominate among the several toxin families that make up animal venom. It interferes with critically important systems in the prey, resulting in serious harm or maybe death (Uktin, 2021). Venom is used to subdue its prey and assist in its digestion and serves as a protective defensive tool against its predators and enemies (Mebs, 2002). The toxicity of venom depends upon its composition (Ferraz et al., 2019). Various snake species have evolved different mixtures of this concoction that disrupt the vital systems of the prey in different ways. Creatures have evolved diverse ways of injecting venom into their prey: Fish employ poisonous spines, insects use stingers, male platypuses have 'venom spurs' on their hind legs, while snakes and spiders utilize modified teeth called fangs. In India, a group of snakes called the Big Four, comprising of the Russell's viper, Common krait, Spectacled cobra and Saw-scaled viper account for the majority of deaths due to snake bites. Snake bite though of global importance is classified by the WHO as a neglected tropical disease (Harrison et al., 2019). Snake venoms can be broadly classified as haemotoxic, neurotoxic or cytotoxic (Anonymous, 2010). Most of the viper venoms are predominately haemorrhagic and elapid venoms are neurotoxic. However, some vipers cause neurotoxicity (Silva et al, 2017) and some elapids causing bleeding disturbances (Berling et al, 2015). Hence, the variation in the venom is critical in understanding the pathology and in determining the treatment. Clinical findings show that neuro-toxic snake envenoming causes extensive flaccid paralysis (Silva et al., 2016). Anti-venom is the most effective treatment for envenomation, as reported by the World Health Organisation (Anonymous, 2018). How effective the antivenom is, is determined by its capacity to prevent the occurrence, or reverse the effects, of venom in the clinical setting (Isbister, 2009). It has been researched that cobra venomes (venom proteomes) present in the Indian cobra (*N. naja*) (Sintiprungsat et al., 2016) have post-synaptic α -neurotoxins in large quantities, but negligible amounts of phospholipase A₂ toxins that are potentially pre-synaptic toxins. In kraits (*Bungarus* spp.) and taipans (*Oxyuranus* spp.) snakes with primarily pre-synaptic neurotoxins, antivenom does not reverse established neurotoxicity, but early administration may be associated with decreased severity or prevent neurotoxicity (Silva et al., 2017). Snake venom is also researched intensively for the multiple therapeutic effects it is able to provide. Venom derived drugs are used in the pharmaceutical companies (Waheed et al., 2017) and venom serves as a strong pharmacological tool.

The characterization of non-enzymatic proteins from snake venom has led to the development of powerful research tools, diagnostic techniques, and pharmaceutical drugs (McCleary and Kini, 2013). Thus, this review was based on snake venom, and aims at interspersing theory with a practical approach.

2. WHAT IS THE DIFFERENCE BETWEEN VENOM AND POISON?

Poison has to be ingested or inhaled in order to have a negative impact on the body, while venom needs to be injected into the body. Animals like poison dart frogs, when ingested, would cause nausea, convulsions and even death. Similarly, there are a few species of poisonous snakes that, when ingested, can cause similar symptoms. eg: Tiger keelback, which happens to be both venomous as well as poisonous. They acquire their poison by consuming poisonous frogs, newts, etc. and store the poison in nuchal glands (Klauber, 1997). Poison is mainly secreted by the victim to protect it from predators, whereas venom is used to render its target unconscious and digest it. When needed, venom is often employed as a defensive tactic.

3. EVOLUTION OF VENOM

It is believed that modern snake venom evolved gradually from mildly venomous ancestors, around 28 million years ago (McCartney, 2014). It is believed to be the result of constrictors like boas and pythons undergoing divergent evolution from other snakes (Bryner and Ghose, 2023).

4. PRODUCTION AND DELIVERY OF VENOM

4.1. Production of venom

The venom of a snake is synthesized in a modified parotid gland present on either side of the head, caudal and ventral to each eye. It is stored in alveoli which are connected to the fang via ducts and is secreted by the action of a compressor muscle (masseter muscle) present caudal to the parotid gland. Upon compression of the muscles, venom gushes out of the fangs of the snake.

4.2. Delivery of venom

The dentition in snakes has evolved in a way that allows them to secure their prey and prevent it from escaping. This is achieved with backward-facing teeth. This arrangement of teeth is known as 'Aglyphous' dentition (Bosch, 2017; Wynns, 2018). A venomous snake injects venom into its victim via fangs (two in number), which are modified teeth that are notably larger than the rest of the teeth. The remaining teeth (normal ones), have the potential to pierce skin and bruise the area where they bite. Fangs have developed over time to create grooves and, eventually, a hollow canal inside the teeth which allows the snake

to effectively inject venom into its victim, much like a hypodermic needle.

A snake injects venom into the muscles of the victim, and not the bloodstream. The injected venom then gets absorbed into lymph and spreads throughout the body of the victim not by the blood, but rather the lymphatic system. The spread of venom is only made worse by physical muscle movement like running, walking, bending the knees and arms.

5. CLASSIFICATION OF SNAKES BASED ON THE POSITION OF THE FANGS

Based on the position of their fangs, snakes can be classified as Rear-fanged snakes and Front-fanged snakes. Rear-fanged (Opisthoglyphous dentition)-the fangs are placed at the back of the upper jaw, and are grooved, as depicted in Figure 1. eg: Asian vine snakes, Mangrove snakes. Front-fanged snakes are classified as those with Proteroglyphous dentition-the fangs are placed at the front of the upper jaw, and are grooved, as depicted in Figure 1. eg: Elapids like Spectacled cobra and those with Solenoglyphous dentition-the fangs are much larger than the other teeth. They are folded backwards at rest, and upon opening the mouth, extend outward at a right angle, thus driving the teeth much deeper into the prey, as depicted in Figure 1. The teeth are hollow inside, just like a hypodermic needle that makes it the most ideal dentition for envenoming a target. eg: Viperids like Russell's viper.

6. COMMON VENOMOUS SNAKES FOUND IN INDIA

The majority of the venomous snakes in the world belong to the Viperidae and Elapidae families, with a smaller number belonging to Atractaspididae and Colubridae families. In India, about 34 venomous species of snakes are found, out of which 20 of these species cause significant harm to humans. All 20 of these snakes fall into the families of Elapidae and Viperidae. In India around 1.2 million people died from snake envenomation between 2000 – 2019 leading to an average death count per year of around 58,000 (Anonymous, 2023) (Figure 1 and Plate 1).

7. CLASSIFICATION OF VENOM AND MECHANISM OF ACTION

Based on the action of the venom, it can be divided into Neurotoxic, Haemotoxic, Cytotoxic and Myotoxic. Neurotoxic venom is the deadliest type of venom, causing damage to the brain and nervous system. They act either pre-synaptically or post-synaptically by interfering with neurotransmitters at the synaptic junction between two adjacent neurons. Haemotoxic venom affects the blood itself, by interfering with the clotting systems of the body,

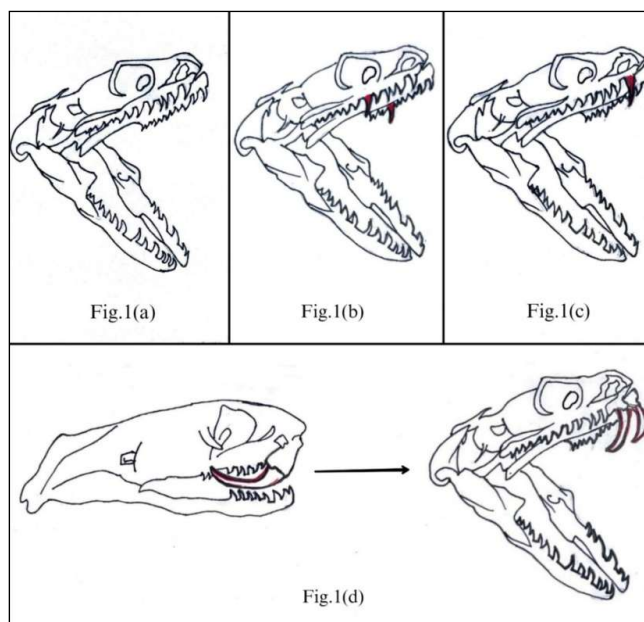


Figure 1: Dentitions in snakes- Illustration courtesy of Anika Palasamudram. 1a: Aglyphous dentition; 1b: Opisthoglyphous dentition; 1c: Proteroglyphous dentition; 1d: Solenoglyphous dentition



Plate 1: The Big Four of India; 1a: Spectacled cobra, 1b: Common Indian krait, 1c: Russell's viper, 1d: Saw-scaled viper

thus inhibiting the blood from clotting. This causes severe internal bleeding, and prevents clots from plugging an external wound, thus causing the victim to bleed out. It also drastically affects the cardiovascular system. Cytotoxic venom affects the cells within our body on a molecular level, causing severe blisters and necrosis of the affected area. Myotoxic venom affects the muscle tissues in the body, destroying myosites and causing muscle paralysis (Banerjee, 2022).

Envenomation by snakes belonging to the family of Viperidae (Russell's viper, saw-scaled viper) leads to

hemotoxic and myotoxic symptoms, while envenomation by snakes belonging to the family Elapidae (spectacled cobra, common krait) leads to neurotoxic, cardiotoxic and cytotoxic symptoms. This however, does not mean that a bite from a cobra would purely result in neurotoxic symptoms, or vice versa. Bites from a viper are also known to have mild neurotoxic symptoms such as numbing or paralysis. This is because snake venom is just a cocktail of various toxic substances evolved to have different harmful effects based on the type of snake, the prey it's hunting, and the environmental conditions (Oliveria et al., 2022). Despite such toxic traits of venom, quite often, the result of death in a victim of snake bites is due to a hypersensitivity reaction (anaphylaxis) to the venom, rather than the toxicity of the venom itself.

8. TOXICITY OF VENOM

The toxicity of venom is measured in terms of Median Lethal dose (LD_{50}). It is the measure of dose of venom per unit body mass that can kill half of the test subjects used in the test. In the case of LD_{50} of snakes, rodents are used as test subjects. The venom is administered either subcutaneously (SC), intramuscular (IM), intravenous (IV) or intraperitoneally (IP). Results from tests administering the venom subcutaneously are considered to be more accurate, as only snakes with large fangs, like Viperids, are able to deliver the venom intramuscularly. Intravenous or intraperitoneal bites are extremely rare. For instance, the Spectacled cobra (*Naja naja*) injects its venom subcutaneously, but it is rapid in action. Brown (1973) found the SC LD_{50} for Southern American bushmaster (*Lachesis muta muta*) venom in mice to be 1.5 mg kg⁻¹ (intravenous), 1.6–6.2 mg kg⁻¹ (intraperitoneal) and 6.0 mg kg⁻¹ (subcutaneous). It is also worth noting that the average venom yield of *Naja naja* per bite is 169–250 mg. The most venomous snake in the world is the Inland taipan (*Oxyuranus microlepidotus*), belonging to the family Elapidae. With a SC LD_{50} of 0.025 mg kg⁻¹, it is capable of killing 100 adult men. Death can occur within 45 min of a bite. This snake, discovered by Frederick McCoy in 1879, is native to central and eastern Australia where it goes by several other names such as fierce snake, small-scaled snake, Lignum snake and western taipan (Fohlman, 1979) (Table 1).

9. DUVERNOY'S GLAND IN COLUBRIDAE

Generally, most species of Colubridae are not a threat to humans. However, a few snakes of this family possess a gland that is homologous to the venom gland in Elapidae and Viperidae. Herpetologists differ in their view regarding this gland, with some saying that the gland is functionally and anatomically distinct from the venom gland, while others claiming that it is a primitive form of the modern venom gland.

Table 1: Subcutaneous LD_{50} of the Big Four

Species	Zoological name	SCLD ₅₀ (mg kg ⁻¹)	Reference
Spectacled cobra	<i>Naja naja</i>	0.80	
Russell's viper	<i>Daboia russelii</i>	0.75	
Saw-scaled viper	<i>Echiscarinatus</i>	0.65	Gopalkrishnakone and Chou, 1990
Common krait	<i>Bungarus caeruleus</i>	0.365	

10. BIOCHEMISTRY OF SNAKE VENOM

Snake venom peptides are highly stable in nature, which makes them undetectable by the prey's immune system. Venom peptides are also resistant to some proteases. By surviving the proteolytic activity and bypassing immune mechanisms of the prey, the peptides bind to highly specific receptors and disrupt physiological mechanisms within the prey's body (Latinovic et al., 2020) (Table 2 and 3).

Table 2: Classification of chemical composition of venom (Munawar et al., 2018)

Biomolecule type	Contents	Composition
Proteinaceous compounds	Proteins and peptides	90–95% of the dry weight
Non-proteinaceous compounds	Lipids, amino acids, carbohydrates, metal ions, nucleosides, amines	5–10% of the dry weight

Table 3: Classification of proteinaceous compounds in venom (Munawar et al., 2018)

Nature of protein	Protein family
Non-Enzymes	Kunitz-type serine Protease inhibitor (KSPI), Natriuretic peptide (NP), Three finger toxins (3FTx), C-type lectins (CTL), Nerve growth factor (NGF) and Vascular endothelial growth factor (VEGF), C-type lectin (CRiSPs), Cystatin, Myotoxins, Disintegrins (DIS)
Enzymes	Phospholipase A2 (PLA2s), L-amino acid oxidase (LAAOs), Paraoxonases, Arylamidases, Endonucleases, Hyaluronidase, Phosphodiesterases, Acetylcholinesterases, NAD Nucleosidases, Phosphomonoesterases, Heparinase Like Enzymes, Snake venom Metallo-Proteinases (SVMP) and Serine Proteinases (SVSP).

11. MECHANISM OF ACTION OF MAJOR PROTEIN FAMILIES

11.1. Phospholipase A2 (PLA2)

Active enzymes with an affinity for cell membranes rich in phospholipids. These compounds cause hydrolysis in the lipid bilayer of cells, thus causing holes or even destruction of the cell. They specifically act on the S_N2 acyl bond of phospholipids and cause hydrolysis (Oliveria et al., 2022; Ali et al., 2022).

11.2. 3 finger toxins (3FTx)

Group of proteins named aptly after their structure, containing 3 beta strand loops connected to a hydrophobic core made up of 4 conserved disulphide bonds. They show a *neurotoxic effect* by binding to N-acetylcholine receptors at neuromuscular junctions, thus interfering with transmission of a nerve impulse, leading to the paralysis of the particular muscle group. Some groups of this protein also exhibit a *cardiotoxic effect* by targeting cardiac myocytes and causing toxicity, and sometimes may damage the cell itself. This eventually leads to cardiac arrest.

11.3. Snake venom serine proteases (SVSP)

Enzymes that are hemotoxic in nature and disrupt blood pressure, blood fibrinogen levels, blood coagulation and platelet aggregation. They mimic the action of thrombin, which is a vital component in the clotting mechanism of blood. However, unlike thrombin, which activates a wide range of factors, like factor V, VII, XI, XIII and prothrombin, each type of SVSP is highly specific in its action and multiple isoforms exist to serve different functions in the clotting cascade (Oliveria et al., 2022).

11.4. Snake venom metallo-proteinases (SVMP)

Group of enzymes that are hemorrhagic in nature. It has 3 subgroups; PI, PII and PIII. Elapid venom contains all the 3 subgroups while Viperid venom primarily contains the PIII subgroup of SVMP. Each subgroup has a unique function with differing mechanisms of action, as elucidated in Table 4.

11.5. Disintegrins (DIS) (Cesar et al., 2019)

Non enzymatic proteins that interfere with signal transduction and cell to cell interactions. They cause the following effects on the body: Hemorrhages by acting on platelets, induce apoptosis, Cytotoxicity, Alter cellular processes such as adhesion, proliferation and migration

11.6. Kunitz-type serine protease inhibitor (KSPI)

Proteins that are capable of blocking ion channels, specifically, calcium and phosphorus ion channels (Oliveria et al., 2022; Hernández-Goenaga et al., 2019).

Table 4: Mode of action of subgroups of SVMP (Oliveria et al., 2022)

Subgroup	Action
PI group of SVMPs	Catalyze the hydrolysis of structural proteins that are physiologically significant. They cause hydrolysis of blood coagulation factors, fibrinogen and collagen IV. Hydrolysis of the first 2 causes inefficient clotting within the body, while hydrolysis of the latter causes thinning and eventually collapsing of capillary walls
PII group of SVMPs	Further reinforce the haemorrhagic activity of PI SVMPs by inhibiting platelet aggregation
PIII group of SVMPs	Contain a collagen binding catalytic domain, which binds to the capillary endothelium, further weakening it to cause hemorrhagic symptoms

11.7. Other major protein families present in snake venom (Oliveria et al., 2022)

L-amino acid oxidase (LAO) and Defensin (DEF). The composition and potency of each component of venom, as mentioned previously, is a consequence of evolution. A diagrammatic representation of the composition of venom in the Elapidae and Viperidae family is presented in Figure 2.

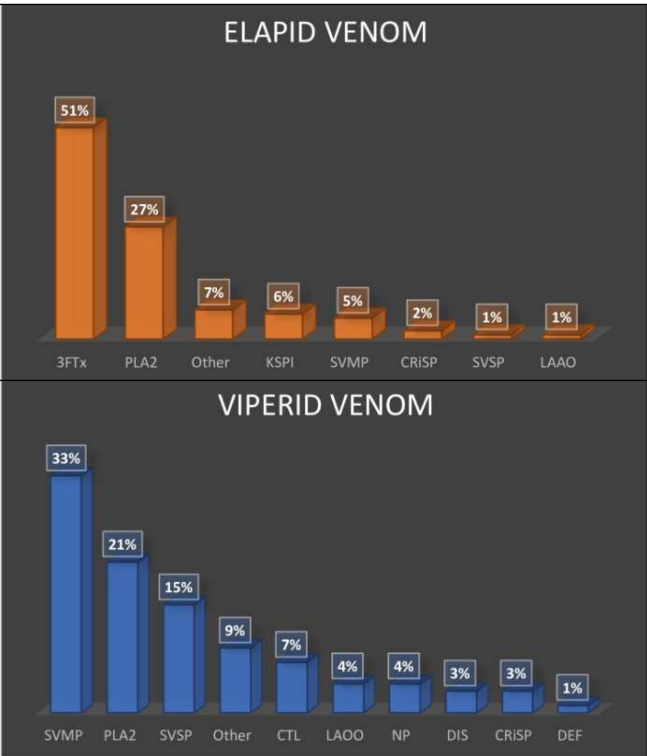


Figure 2: Composition of snake venom (Oliveria et al., 2022)

12. PATHOPHYSIOLOGICAL CONSEQUENCES OF A SNAKE BITE

12.1. *Elapidae* (Jayawardana et al., 2018) (Sarin et al., 2017; Chaudhari et al., 2014; Mittrakul et al., 1984)

Bites from snakes of family Elapidae mainly cause neurotoxic symptoms, alongside cardiotoxic and cytotoxic symptoms. Following a bite from an elapid, neurotoxins travel throughout the body via the vascular system and begin shutting the body down by inhibiting N-acetylcholine receptors at the neuromuscular junctions. An elevated heart rate, or a state of panic works in the favour of these neurotoxins and helps them travel throughout the body faster. At the same time, cytotoxins begin to hydrolyse the cells around the site of the bite causing severe blisters, severe pain, swelling and bleeding. These symptoms can be seen from the time of the bite, and up to 2 hours after. Immediate medical attention can reduce the harmful effects on the body, such as necrosis, paralysis, and respiratory failure.

Acute symptoms (Jayawardana et al., 2018) include nausea, ptosis, dizziness, frothy salivation, weakness of muscles in the neck region, loss of consciousness, incoherent speech, respiratory failure and paralysis of the heart. Death in most cases is due to respiratory failure and cardiac arrest which is accompanied by loss of consciousness. Even after seeking medical attention following an elapid bite, the body will suffer long term effects. Chronic effects (Jayawardana et al., 2018) include loss of muscle control, necrosis in the affected area, chronic renal failure, hyperpigmentation and fibrosis in the area of bite, migraine like syndrome and liver damage.

The most common Elapids that cause a high number of fatalities include spectacled cobra, common krait, and slender coral snake. These animals are prominent in rural areas and farms due to the high number of rodents that live alongside humans. The individuals who are bit by the snake are unable to feel it and go into a paralysis or comatose state. Respiratory paralysis soon follows, and the families are left helpless, as they cannot find the cause of their symptoms due to lack of awareness. Hospitals are also usually very distant in rural areas, so the affected individual is unable to get help in time.

12.2. *Viperidae and Colubridae* (Menon et al., 2015; Anuradhani et al., 2021; Barish et al., 2022)

Bites from snakes belonging to Viperidae and Colubridae families cause hemotoxic and myotoxic symptoms. In comparison to Elapid venom, Viperid and Colubrid venom is known to cause multiple organ failure, with death in most cases occurring due to capillary leak syndrome and acute respiratory distress syndrome.

Acute symptoms like severe bleeding from the site of the bite, serous membranes, mucosal membranes and even

internal organs are noted. Melena, hematuria, hypovolemic shock, intravascular coagulation, capillary leak syndrome, acute respiratory distress syndrome and acute kidney injury are some other life-threatening symptoms. Chronic effects seen are necrosis or deformities in the affected limb, squamous cell carcinoma at the site of bite, hypopituitarism, weakness in the limbs, and negative impact on cognitive ability, and liver damage.

12.3. *Atractaspididae*

Bites from snakes of this family are usually not life threatening to animals. However, cytotoxic symptoms can be seen. These include blisters in the affected area, necrosis, and sometimes loss of the tip of digits if bitten at the tip of the finger.

12.4. *Python bites*

Livestock especially small animals often fall prey to python. Python bites are non-venomous and they kill their prey by suffocating by crushing.

13. SNAKE BITE IN LIVESTOCK

Animals can encounter snakes during grazing in the fields. Domestic animals like cattle, buffalo, sheep, goat and horses can be easily affected. Dogs are more prone to getting bitten by snakes. Dogs and cats because of their small size are more susceptible to fatal snake bites. Local swelling and pain at the site of bite (severity depending on the bite), muscle tremors, convulsions, respiratory difficulty, dilated pupils, immobility (paralysis), unsteady gait, saliva foaming at the mouth accompanied by dizziness and decreased vision are indicative signs of snake bite. One should also try to find the bite/fang mark on the limbs of the animals. Pigs due to their subcutaneous fat layer and thick skin are less susceptible to snake bites. Fatality rate is high when bites are on the muzzle, face or head. Snake bites can be diagnosed based on clinical symptoms, presence of bite marks, and identification of the snake (Gwaltney-Brant, 2022). Bolon et al., 2019 conducted the first global scoping of snake bite in domestic animals and reported that 69% of the literature was from North America, Europe and Australia and only 31% of the information came from central and south America, Africa and Asia. Because of its high population density, widespread agricultural activities, numerous venomous snake species and lack of functional snake bite control programs South Asia was identified as world's most heavily affected region (Alirol et al., 2010) and livestock like cattle, buffalo, sheep, goat, pigs and poultry are maintained by around 88% of the population (Anonymous, 2011).

14. TREATMENT OF SNAKE BITE IN ANIMALS

Snake envenomation requires prompt veterinary assistance due to its emergency. The faster the treatment is started,

better the chances for animals to survive. A polyvalent antivenom is mostly used as many times the species of snake that has bitten is not identifiable. Treatment depends on a number of factors viz. size and age of the animal, severity of the bite, location of the bite and species of the snake. To prevent secondary infection, anti-biotics like penicillin, streptomycin, oxytetracycline can be administered (Moses, 2023). Locally the bitten part should be immobilised to prevent or minimise the infection from spreading and the bitten area should be cleaned with a disinfectant (Moses, 2023).

15. HOW TO AVOID SNAKE BITE IN ANIMALS

Identify areas where snakes are present and avoid animals grazing in these areas especially areas with tall grasses. Most of the snakes bite only when provoked. Erect snake proof fencing and eliminate places or spots where snakes and hide like pile of bricks, wood or debris. Educate the farmers about the snakes and their habitats. Wearing of protective boots or foot wear by the farmers hinders direct snake bite (Moses, 2023).

16. ARE SNAKES VENOMOUS FROM THE MOMENT THEY ARE BORN?

Venomous snakes enter this world armed with venom and fully functional fangs, as it is their only means to procure a meal. They are capable of envenoming and subduing their prey the moment they hatch out of the egg. Young snakes cannot control the amount of venom they inject, so they tend to inject all of their venom at once. This however does not mean that they are more dangerous than adults, as adults possess a larger quantity of venom and are capable of controlling the amount injected in each bite (Shipman, 2015).

17. WARNING SIGNALS BY SNAKES

A snake's venom is very precious to it, since it depends on the functionality of its venom to subdue and eventually consume its prey. A snake derives the raw materials for its venom from its diet, so, the quantity of venom it can secrete is not infinite. Hence, a snake will try to avoid conflict as much as possible, as it must conserve its venom for the sole purpose of hunting. Generally, snakes tend to make a 'hissing' sound by rapidly inhaling and exhaling.

Cobras raise their hood, which are flaps of skin, by expanding muscles and ribs that are situated on either side of their necks. Doing so makes them appear more intimidating. If this boundary is crossed, the snake will further intimidate with warning strikes, which inject little to no venom. Failing to respect these boundaries leads to a fatal bite. *Russell's viper* inflates its body and makes a very loud hissing noise, which

is usually enough to ward off predators. *Saw-scaled viper* coil their bodies in the pattern of '8' and brush their rough and serrated scales against each other to create a sound similar to wood being cut by a saw (Plate 2).

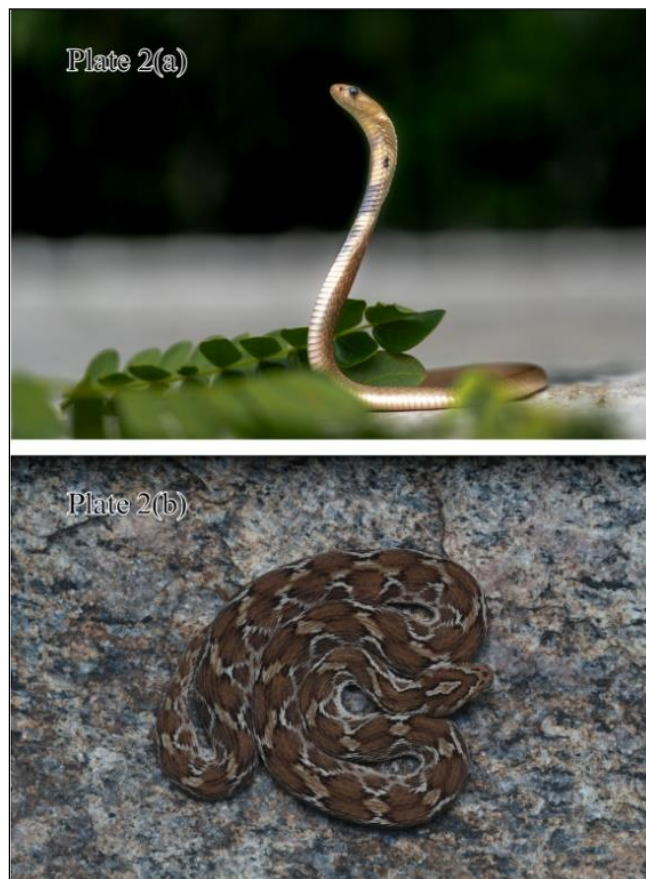


Plate 2: Warning signals by snakes; 2(a): A Spectacled cobra raises its hood to appear more intimidating and ward off predators. Photo courtesy of Vikas Kumar; 2(b): A Saw-scaled viper (*Echiscarinatus*) displaying its 'figure of 8' posture when threatened. Photo courtesy of Shashank G Bhat

18. WARNING SIGNALS BY SNAKES (Khair, 2018)

A snake bite becomes life threatening after approximately 1 hour. This is because the venom is allowed to circulate freely throughout the body and manifest its toxic effects. Many snake catchers refer to this time period as the 'golden hour', wherein, with the right type of first aid and care from an experienced veterinary medical professional, the bitten animal can be saved from death.

18.1. Precautions to be taken following a snake bite

Do not suck the venom out of the site of the bite. Doing this, does not extract the venom from the bite. Instead, it serves as a source of infection. Identify and ascertain the species of snake that caused the bite. Do not cut the affected area.

Unless one is sure of the species of snake that has bitten, applying pressure or tying a tourniquet to cut off blood flow is strictly advised against. Clean the wound with antiseptic solution or disinfectant. *Immediately contact the veterinarian* as he is well-versed in handling such situations.

18.2. First aid

18.2.1. Elapid bite

Following a snake bite, wash the area thoroughly with clean water. Tie a tourniquet or apply pressure near the area of the bite to avoid the neurotoxins from spreading. This keeps the neurotoxins from traveling throughout the body and causing paralysis. Applying pressure of tying a tourniquet however, will not stop the action of the cytotoxic component of the venom. There will be excruciating pain in the area along with redness, swelling, blisters and a burning sensation. Tie a cloth or a crepe bandage to the affected limb and keep it in a fixed position using a plank or a stick to immobilize it. This traps the venom within the lymphatic system and keeps it from traveling further. It is important to seek veterinary medical attention immediately.

18.2.2. Viperid and Colubrid bite (Khair, 2018)

Following a bite from a hemotoxic snake, wash the area thoroughly and seek medical attention immediately. One must not tie tourniquets or other constrictive objects to the affected area. Applying a crepe bandage or cloth is also strictly advised against. This is because isolating the venom in one area causes severe hemotoxic symptoms leading to loss of the limb (Figure 3).

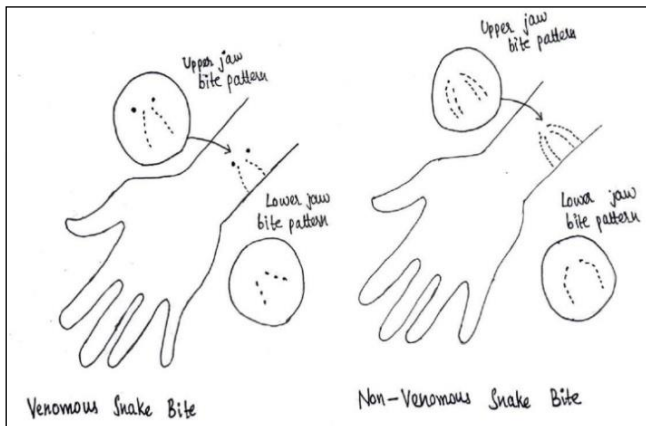


Figure 3: How to identify a venomous snake bite- Illustration courtesy of Anika Palasamudram

19. ARE SNAKES IMMUNE TO THEIR OWN VENOM?

Firstly, snake venom is toxic only when it enters the bloodstream. Hence, a snake will be completely fine if it consumes its prey which has been envenomed. Snakes produce antibodies against their own venom; however, these antibodies work only on small doses of venom. The King

cobra tends to hunt and feed on other snakes, including snakes of the same species (Eggleston, 2018). The bite of a king cobra is able to kill an elephant, let alone an individual of its own kind. To protect the snake from its own bite, the fangs are covered in retractable sheaths made of connective tissue.

20. ARE SNAKE BITES A NOTIFIABLE DISEASE?

With an average of 2.7 million envenomation year⁻¹, and approximately 81,410 to 138,000 deaths globally, snake bites are without doubt a life-threatening medical emergency with limited time to take appropriate action. Out of these deaths, approximately 58,000 are from India alone. With numerous awareness programmes being launched, targeted towards rural areas, and the boost in production of polyvalent anti-venom, India is taking numerous steps towards bringing the number of fatalities down (Gajbhiye, 2023). As of February 2024, the State of Karnataka has issued a directive to include snake bites as a notifiable disease under Section 3 of the Karnataka Epidemic Diseases Act, 2020 (Anonymous, 2024)

21. NATIONAL ACTION PLAN FOR PREVENTION AND CONTROL OF SNAKEBITE ENVENOMING (NAP-SE) (Anonymous, 2024)

The NAP-SE was launched by Shri Apurva Chandra, the Union Health Secretary on March 12th, 2024. Their vision is to halve the number of deaths caused due to snake envenoming by the year 2030. Through the 'One Health' approach, it provides a broad outline for states to create their own plan for the mitigation, prevention, management, and control of snakebites in the form of a guidance document. In order to ensure timely access to medical care and provide information to the general public, an initiative was made to pilot the 'Snakebite Helpline Number' (15400) in five states of India viz; Puducherry, Madhya Pradesh, Assam, Andhra Pradesh and Delhi. It is a vital resource that provides prompt guidance and support to individuals and their families affected by snakebite incidents.

22. SNAKE ANTIVENOM AND ITS PRODUCTION

Snake antivenom was discovered by French Physician Albert Calmette over 100 years ago, which even today, is the basis of production of modern antivenoms. Snake antivenom is a dried compound of antibodies raised in horses that is capable of neutralizing snake venom. Anti snake venom is prepared by first 'milking' the snake for its venom, which is then inoculated into equines, and antibodies against the venom are raised. Equines used for

this purpose are capable of producing powerful antibodies that bind to the venom and hence neutralize them. Eight million vials of snake antivenom (ASV) are produced in India annually by 7 companies. (Thiagarajan, 2024).

The 'Irula Co-op Venom Centre' produces the majority of snake venom used for these ASV vials. The Irula tribe is recognised as a scheduled tribe and inhabit the states of Tamil Nadu, Kerala and Karnataka. In 1978, Romulus Whitaker established the Irula Snake Catchers Co-Operative, which used the knowledge of the Irulas for snake conservation and snake antivenom production (Whitaker, 1995). Romulus Whitaker, an American born herpetologist, also known as the Snakeman of India, is the founder of the Madras snake park, the Andaman and Nicobar Environment Trust and the Madras Crocodile Bank Trust in 2008. He was awarded the Padma Shri in the year 2018. *Bungarus romulusi*, a species of krait has been named after him (c.f. Irulas: The snake trackers, 2003).

23. SIGNIFICANT CLINICAL USES OF SNAKE VENOM (Munawar et al., 2018)

Snake venom is being studied intensively for the multiple therapeutic effects that it is able to provide. The peptides present in snake venom are separated from each other by first milking a snake, and storing the venom at -20°C. The peptides are then separated by chromatographic methods, and the peptides of interest can be further studied.

23.1. A few instances include

Crotamine is used as a carrier for biomolecules. It acts as a tool for studies performed on cancer. It can penetrate the cell membrane by binding to heparan sulphate proteoglycans and is capable of electrostatically interacting with DNA (Oliveria et al., 2022). *Waglerin*, with its anti N-acetylcholine receptors properties, is used to produce anti-wrinkle creams due to its property to paralyze facial muscles. The active ingredient in this cream is a mimic peptide that was created by using waglerin as a template (Oliveria et al., 2022; Debono et al., 2017). *Disintegrins* are used in the development of thrombolytic and antitumor agents due to their ability to induce apoptosis and cytotoxicity by interfering with various cellular processes (Cesar et al., 2019). *Kunitz-typeserine protease inhibitor* are known for their therapeutic effects due to high binding specificity and high potency for their targets. They're also known for anti-tumoral and anti-metastatic effects (Morjen et al., 2014). *3 finger toxins* are used in cancer inhibitory studies. Using hydrostatic and electrostatic interaction, they physically perturb the plasma membranes of cells (Oliveria et al., 2022).

24. FUN FACT

The Caduceus and The Rod of Asclepius are used as the symbols of modern medicine. Wielded by the

messenger of the Gods, Hermes, the Caduceus consists of a staff with two snakes intertwined on it, and a pair of wings atop it. The Rod of Asclepius on the other hand, consists of a single snake entwining a rod. Although many medical professionals argue that the use of the Rod of Asclepius is a more fitting symbol for the field of medicine, the presence of serpents in both symbols holds the same meaning.

25. CONCLUSION

Snakes play a vital role in our ecosystem by feeding on pests like rodents, insects, frogs keeping their numbers in check. This has kept crops safe and protected us from vector borne diseases. Snake venom has been categorized into neurotoxic, hemotoxic, cytotoxic and myotoxic based on the mode of action on the victim's physiological systems. First aid must be performed promptly and accurately following a snake bite. Let us be respectful and protect these creatures by getting rid of our fear about them.

26. FUTURE PROSPECTS

Going forward, the use of snake venom in the medical field, due to the multiple therapeutic effects and cancer inhibitory properties need to be further researched upon.

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