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UNLEASHING THE SECRETS OF SLITHERING SERPENTS

WAASIFA ANSARI[1*], Dr. R.SREERANJANI[2], E.L. AADHIE SHRIE[3], Dr. T. SATHYABAMA[4]
[1,2,3,4] DEPARTMENT OF VETERINARY PHYSIOLOGY, VCRI, NAMAKKAL.

***Corresponding Author**
WAASIFA ANSARI
DEPARTMENT OF VETERINARY PHYSIOLOGY, VCRI, NAMAKKAL.

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Abstract: Snakes are fascinating creatures which have evolved millions of years ago. They are adapted to various habitats and ecological niches. They belong to the suborder Serpentes and are characterized by their elongated, cylindrical bodies, limbless structure, and unique feeding habits.

Features like flexible jaws, heat-sensing organs, and the presence of fangs for delivering venom make them successful predators.

Venomous and non-venomous snakes make up the two primary categories into which snakes are generally classified. Via specialized glands, venomous snakes generate and inject venom, which can be a complex blend of proteins, peptides, and enzymes. These elements are essential for digesting and immobilizing prey.

A snake bite can cause a variety of symptoms, such as pain, swelling, bruises, and in more extreme situations, tissue necrosis or paralysis. Managing a snake bite requires immediate first aid techniques, such as immobilizing the afflicted limb, applying a constricting band, and obtaining medical assistance. We must be cautious of what should be done and what should not be done if someone is bitten by a snake. We must also be aware about our surroundings and should remove risk factors that favor hiding places for snakes. Many diagnostic tools based on immunology are present which can help in the detection of snake venom. They identify the specific type of venom and guide the appropriate treatment.

There are many myths about snakes and we must make sure not to trust the myth blindly and should know the truth about them.

It's true snake venom may be dangerous but it is found to have several medicinal properties including the development of medications for conditions such as heart disease and chronic pain. The main treatment for snakebite envenomation is antivenom, a specialized medication intended to neutralize snake venom. Managing snakebites also requires supportive therapy, which includes wound care, pain control, and ongoing observation for any consequences.

In conclusion, snakes possess unique evolutionary adaptations and features, including venomous capabilities, that have contributed to their success as a species. Understanding the composition of snake venom, the signs and management of snakebites, and the potential benefits of snake venom are critical in promoting effective treatment and conservation efforts for these remarkable reptiles.

Keywords: Snakes, Fangs, Venom, Enzymes, Myth, Antivenom, Therapy.

INTRODUCTION

Snakes are amazing animals. The earth is home to about 3,000 different species of snakes. They may be gigantic as Reticulated Python or be tiny as Barbados Thread Snake. Some are venomous and others are non-venomous. An estimated 5.4 million individuals are bitten a year, of which 2.7 million suffer from snake envenomation, according to estimates from the World Health Organization (WHO).

Not every bite from a poisonous snake causes envenomation. At least 25% of snakebite cases are thought to be "dry" bites. Even though a lot of people are bitten by snakes, the precise figure is still unknown.

EVOLUTION AND FEATURES OF SNAKES

Snakes first appeared some 135 million years ago, during the late Jurassic period.

Fish/Pisces →Amphibians →Reptiles → Snakes

Snakes are Vertebrates, that evolved from Lizards. They have separate movable jawbones connected by a ligament which helps

them to swallow the prey. Their body is cylindrical and they lack eyelids and limbs.

Venomous snakes have two large hollow fangs and a small hooked tooth, whereas in non-venomous snakes only teeth are present. The majority of snakes, including cobras and pythons, are oviparous; however, vipers and green vine snakes are viviparous. Certain snakes, like the Sand Boa, develop the embryo inside the egg and are ovo-viviparous, meaning they are born inside their mother's body. The parthenogenic nature of the Indian Blind Snake makes it special.

Eggshells from snakes are leathery rather than hard. Except for the Indian Cobra, most snakes don't care once the eggs are laid.
The only snake that constructs a nest on its own using ground-level leaves is the king cobra, which then coils around the eggs it lays to hatch.

CLASSIFICATION

VENOMOUS SNAKES	NON VENOMOUS SNAKES
Triangle shape head	Rounded head
The presence of fangs is grooved with canal	Absence of fangs
A single row of Scales after the anal plate	Double row of scales after anal plate
Bright body colour	Body Color not so bright
Presence of Hood	Absence of Hood
Presence of Poisonous glands	Absence of Poisonous glands
Teeth are not uniform	Teeth are uniform and solid
Killing by injecting venom	Killing by Constriction
Eg. King cobra, Russell's viper, Saw scaled viper	Eg. Indian Rock Python, Red Sand Boa, Common Vine Snake

FANGS:

Snake's teeth and fangs are not the same. Both venomous and non-venomous snakes have two rows of solid teeth on the bottom and four rows on the top, which are used for constriction of prey but not for injecting or delivering venom. Fang is present only in venomous snakes for injecting venom.

Snake fangs are modified teeth that are long, sharp, hollow, or grooved. They are larger than neighbouring teeth and can be found at the back or front of the mouth. They can be hinged to fold backward or fixed, and they are attached to a small sac that is located in the snake's head behind its eyes. Venom, a poisonous liquid, is released from these sacs.

Fang type determines the efficiency of venom delivery. *i.e.*, hollow fang delivers venom directly into prey without any residue. The following are the classifications based on Fang:

Fang type	Meaning	Examples
Aglyphous fang	No groove	Python
Solenoglyophous fang	Pipe groove	Puff adder, Gaboon viper
Proteroglyphous fang	Forward groove	Cobra
Opisthoglyphous fang	Rear groove	Boomslang

COMPOSITION OF VENOM

Snake venom is a clear, transparent, acidic (e.g. Russel's viper pH of 5.8, Cobra pH 6.6), straw-coloured fluid, soluble in water having a specific gravity of 1.030-1.070.

The venom produced in the modified parotid glands behind the eye gets deposited into the prey via the tubular structure called fangs/poison teeth. Snakes use their highly modified saliva, known as venom, to immobilize their prey as a defence mechanism

The proteinaceous nature of snake venom was initially demonstrated in 1843 by Napoleon's nephew Charles Lucien Bonaparte. Ninety per cent of the venom's dry weight is made up of a complex mixture of proteins, hydrolytic enzymes, and toxins like neurotoxins and hemotoxins.

Neurotoxins, hemotoxins, cardiotoxins, cytotoxins, and myotoxins are examples of snake toxins with specific actions. The toxic venom of a snake may either be hemotoxic causing defects in blood coagulation, decrease in blood pressure and lysis of cells or neurotoxic where it interferes with the impulse transmission between the nerves and muscles at the neuromuscular junction thus causing paralysis of muscles and various neurological disturbances. There is a variation in venom's composition according to species.

While the venom of snakes in the Viperidae family (Russel's viper, Sawscaled viper) is typically hemotoxic and myotoxic with some minor neurotoxic effects, that of snakes in the Elapidae family (Krat and Cobra) is primarily neurotoxic with some myotoxic effects.

The potency of snake venom varies due to species-to-species variations in its composition. It is said that the venom of Australian sea snakes and elapids is the strongest in the world. Venom serves a variety of purposes, such as predigestion, defence, and neutralization of prey.

Among the snakes, Elapidae contains 25% of enzymes whereas Viperidae contains 80-90% of enzymes. Based on their molecular weight, the components of snake venom are categorised as physiologically least active and most active. Low-molecular-weight (<1500 Da) venom components are the least active such as peptides, lipids, nucleosides, carbohydrates, amines, and metal ions whereas large molecular weight (13000–150000 Da), produces marked physiological effects.

Family	Enzymes
Atractaspididae, Elapidae, Viperidae, Hydrophidae, Colubridae	Adenosine triphosphate, l-amino acid oxidase, amylase, catalase, deoxyribonuclease, hyaluronidase, NAD-nucleosidase, 5′-nucleotidase, Peptidase, phosphodiesterase, phospholipase A_2, phosphomonoesterase, ribonuclease
Elapidae and Hydrophidae	Acetylcholinesterase, dehydrogenase lactate, glycerophosphatase, phospholipase B
Viperidae	Argine ester hydrolase, collagenase, endopeptidase, factor X activator, fibrinogenase, kininogenase, metalloproteinase, prothrombin activator, serine protease, thrombin-like enzyme
Viperidae and Elapidae	Alkaline phosphatase, acid phosphatase, heparinase, lysophospholipase

Hyaluronidase: the adjacent cells are kept together by a cement substance called hyaluronic acid in the tissue. The hyaluronidase enzyme breaks down the acid, causing the tissue's integrity to be compromised and facilitating the spread of venom throughout tissues.

Phospholipase A2 (Lecithinase): The membrane of RBC, mitochondria, platelets, nerves and all other cells in our body is made up of Phospholipids. This enzyme causes lysis of the cell membrane and allows the contents of the cell into the blood and interstitium and also inhibits the electron transfer in mitochondria at Cytochrome C level.

Acetylcholine esterase is an enzyme that aids in the breakdown of neurotransmitters such as acetylcholine and other choline esters.

L-amino acid oxidase is an enzyme that gives venoms their yellow colour by using riboflavin 5'-phosphate as a prosthetic group.

α-Bungarotoxin and **cobra toxin** produced by **cobra snakes** are postsynaptic neurotoxins that attach themselves to the motor end plate's acetylcholine receptors.

β-Bungarotoxin, Crotoxin, and Taipoxin produced by **kraits** are presynaptic neurotoxins that damage nerve endings by the subsequent release of acetylcholine at the myoneural junction.

Zinc metalloprotein hemorrhagins in **crotalid** venoms are vasculotoxic causing haemorrhage and shock.

The polypeptide cytotoxic enzymes known as **cardiotoxins** (metalloproteinases, endopeptidases, or hydrolases) cause cardiotoxicity and increase vascular permeability, which in turn results in necrosis, blistering, bruising, and oedema at the bite site.

Anticoagulation factors interfere with the clotting factors and have fibrinolytic and fibrinogenolytic activity. They directly or indirectly activate plasminogen and prevent coagulation, thus it leads to Epistaxis.

SIGNS OF BEING BITTEN BY SNAKE

1. Presence of fang marks; two distinct fang marks about a half inch apart at the site of bite!
2. Bleeding may or may not occur.
3. Severe burning pain and the presence of swelling around fang marks.
4. Purplish discoloration and blood blisters around the bite usually within 2 to 10 hours.
5. Labored breath.
6. Fast heartbeat, feeble pulse, and reduced blood pressure.
7. Blurry vision.
8. Muscle twitching
9. Increased salivation and profuse sweating.
10. The lethal dose (LD_{50}) of Cobra (0.12g), Krait (0.06g), and Viper (0.15g).

DO'S

1. Seek medical attention or go to the hospital as soon as possible.
2. Try to memorize the appearance of the snake which will help to identify antivenom for treatment (or) take a photograph of the snake which will help to identify the antivenom.
3. Stay calm and don't be nervous.
4. Sit down in a neutral position.
5. Try to immobilize the victim.
6. Remove rings, watches, and bangles (anything which constricts the limbs) before swelling.
7. Use a clean, dry dressing to cover the bite.

DON'T'S

1. Never try to suck out of venom.
2. Never make an incision on the snake bite area.
3. Never go to traditional healers or any home remedies.
4. Never tie tourniquets or use ice.
5. Never clean out or tamper with the site of the bite.
6. Never try catching a snake.
7. Never try ineffective or dangerous treatments like application of corticosteroids or EDTA.

PREVENTION:

As always, prevention is better than cure.

1. Take care while cleaning the garden; supervise kids outdoors, especially in green neighbourhoods.
2. Use a torch/flash at night & and keep wearing shoes, check shoes before wearing them.
3. Watch your step and see before you sit.
4. Keep your backyard free of junk, and make your solid waste disposed of properly.
5. If you see a snake, do nothing, do not try to pick it up or kill it.
6. If a snake has entered your premises call professional snake rescuers.

TESTS FOR DETECTION OF SNAKE VENOM

Usually, identification or detection of snake venoms is done by immunological techniques due to the presence of active peptides and proteins present in the venom.

1. The use of particular monoclonal antibodies in radioimmunoassay (RIA) has shown to be extremely sensitive and dependable.
2. Purified rabbit antivenom IgG agarose tests are cheap, quick, and easy to use, but they have low sensitivity and instability.
3. Commercial ELISA method detection kits, such as the Avidin–Biotin microtiter ELISA (AB-microELISA) kit, are readily available and frequently used because of their specificity, sensitivity, speed, and simplicity. Incredibly sensitive and species-specific for detecting venom even up to 10 ng/ml of big 4 Indian snake species.
4. Immunosensor is highly effective for quantification of neurotoxin β-bungarotoxin.
5. Additional techniques, such as LC, LC-MS, CE, MS, and NMR, are used to analyze, separate, or study the structural makeup of these toxins.

MYTHS AND FACTS ABOUT SNAKE

1. **MYTH:** Green snake bites only in eye.

   FACT: They are arboreal, bites occur frequently on the head or upper body.

2. **MYTH:** Rat snakes mate with cobras.

   FACT: No snake, including rat snakes, will mate with another species. Rat snakes cannot mate with cobras because cobras consume other snakes.

3. **MYTH:** They gather to take revenge if their friend dies.

   FACT: Distress pheromones released by certain snakes draw in other snakes.

4. **MYTH:** The red sand boa has two heads**.**

   FACT: Its rounded tail is an anatomical adaptation that helps them to move through the sandy terrain simple and quick.

5. **MYTH:** Cobras, particularly the elderly, have valuable stones embedded in their heads.

   FACT: Snake catchers do not become wealthy overnight!

6. **MYTH:** Snakes are slimy to touch.

   FACT: They have dry skin.

7. **MYTH:** Snakes like to drink milk.

   FACT: It cannot enjoy milk because it is not a mammal.

8. **MYTH:** Snake bites, particularly those from sand boas, can result in skin conditions.

   FACT: As of yet, no scientific evidence.

9. **MYTH:** After a prey dies due to its bite, the Bronze Back Tree Snake ascends a tree relishes the funeral pyre.

   FACT: Since the snake is not poisonous, this cannot occur.

10. **MYTH:** Snakes have many heads.

    FACT: A two-headed snake is a rare phenomenon that occurs in snakes, turtles, tortoises, and geckos. It is known as bicephaly and is caused by a genetic mutation or deformity.

11. **MYTH:** Are snakes venomous or poisonous? (This is more of a misconception than a myth).

    FACT: Venom is a toxin that must come into contact with blood to affect the body. Therefore, the majority of snake species are venomous.

12. **MYTH:** Poisonous rat snakes exist.

    FACT: Rat snakes are rodent-eating, non-poisonous reptiles.

13. **MYTH:** As they age, some snakes develop a beard.

    FACT: Snakes are reptiles, and as such, they are hairless.

14. **MYTH:** No matter where you are, if one snake is killed, its partner will find you.

    FACT: Snakes are not hostile creatures and have no desire to seek out or track down those who have harmed them. They lack the cognitive and memory skills needed to recall individuals to follow.

15. **MYTH:** The charmer's music causes the cobra to sway its head.

    FACT: It's synchronized with the pipe's oscillations.

BENEFITS OF SNAKE VENOM

Pharmaceutical agents

Snake type	Drug	Mode of action	Indications
Dusky pygmy rattlesnake and saw-scaled viper	Tirofiban (Aggrastat) and Eptifibatide (Integrillin)	Strong suppression of the integrin receptor α2β3, which stops platelets from clumping together.	Unstable angina and myocardial infarctions (Peerlinck *et al*, 1993; Scarborough, 1999).
Brazilian viper	Angiotensin-converting enzyme inhibitors	Toxins that block specific subtypes of voltage-dependent sodium or potassium channels in neurons, as well as muscarinic acetylcholine receptors.	Modulation of the heart rate, learning and memory and control of motor systems,
Thailand cobra	Alpha-neurotoxin Cobratoxin,	Blockade of receptors bearing α-7 NAchR, which prevents the release of glutamate, a known trigger for cell death.	Chronic pain to multiple sclerosis
Lancehead viper	Bradykinin potentiating factors, ACE inhibitor, captopril enalapril, lisinopril, perindopril and ramipril)	The conversion of angiotensin I into angiotensin II by the angiotensin-converting enzyme (ACE),	Reducing systemic blood pressure by preventing the production of a crucial vasoconstrictor. (Koh&Kini, 2012).
Elapid and Viperid snakes.	Factor X activators	Pro- and anticoagulant activity	Thrombosis and hemostasis of lupus anticoagulants (Takeya et al., 1992; Thiagarajan, Pengo, & Shapiro, 1986)
Saw-scaled Viper	Ecarin	Encourages the hirudin-inhibited conversion of prothrombin to meizothrombin.	For a clotting time assay for patients treated with hirudin(Nowak, 2003).
Viperidae	Thrombin-like enzymes (SVTLEs)	Cleavage at only one of the two fibrinogen chains resulting in the formation of loose fibrin clots.	Diagnostic labs to defibrinogenate blood samples (Koh&Kini, 2012).
Vipers and colubrids	Snake C-type lectin-like toxins	Platelet activation; anticoagulation factor I binds to coagulation factors IX and X, inhibiting clotting; additionally, it can bind directly to platelet glycoprotein receptors (e.g., convulxin) or indirectly through Von Willebrand factor (e.g., botrocetin, bitiscetin).	Activated partial thromboplastin time, prothrombin time, and thrombin time (Sajevic, Leonardi, & Križaj, 2011 and Zhang et al., 2012).
Brazilian lancehead viper	Batroxobin snake serine protease toxin (SVSP) venom serine proteases	Firstly, fibrinogenolytic activity causes defibrination; secondarily and indirectly, it triggers tissue plasminogen activator release and encourages clot degradation. Protease-activated receptors that are activated cause platelets to aggregate. Not inhibited by endogenous thrombocytin (e.g., hirudin) or exogenous serine protease inhibitors (e.g., antithrombin III).	Thrombotic disorders, ischaemic stroke, angina, myocardial and cerebral infarction and wound management after surgical interventions (Xu *et al*, 2007; Phillips *et al*, 2010). (Hutton & Warrell, 1993; McCleary&Kini, 2013 and McCleary *et al*, 2015).
Elapidae.	Three-finger toxins	Anticoagulant effects on the extrinsic pathway and factor VIIa inhibition consist of four to five disulfide bridges and three β-stranded loops	Thrombosis (Kini, 2006),
Black snake	Silica nanoparticles bearing venom	Owing to their proapoptotic characteristics, they both stimulate human prostate cancer cells to undergo apoptosis and improve the function of healthy lymphocytes.	Anticancer therapies (Al-Sadoon, Rabah, &Badr, 2013).

Therapeutic Development

Company	Product	Source	Application
Abbots Labs	Ancord	Malayan pit viper	Stroke
Astra Zeneca	Exanta	Cobra	Atrial fibrillation
Bristol Myers Squib	Captopril	Bothrops	Antihypertensive
Celtic Biotech	CrotoxinCardiotoxin	Rattlesnake Cobra	Cancer
COR/Schlering	Intergilin	Pygmy rattlesnake	Cancer
Kunming Institute	Cobrotoxin	Cobra	Drug addiction and pain
Merck	Aggrastat	Saw-scaled viper	Coronary application
PentaPharm	DefibraseHaemocoagulase	Bothrops	Acute cerebral infarction Hemorrhage
ReceptoPharm Reception	PepteronCobratoxin	Cobra	Antiviral Pain
TransmolecularVernalis	Chlorotoxin Marimastat	Scorpion Viper	Cancer

ANTIVENOM DOSAGE

A polyvalent equine antiserum is the anti-venom that is available to the armed forces. This works well against the four most significant venomous snakes in India: the saw-scaled viper, cobra, common krait, and russell's viper. The antiserum is supplied in lyophilized form, which requires reconstitution for injection using 10 millilitres of sterile water.

The antivenom is infused slowly over a one to two-hour period intravenously after being diluted in roughly 5 millilitres per kilogram of body weight in isotonic saline or 5% dextrose. This approach is better than the "push" technique, which involves injecting 4 millilitres of undiluted serum per minute.

Antivenom works in patients who are still defibrinated weeks after a viper bite and for up to two days following a sea snake bite. The dose required depends on the clinical state. The following dosage is needed for a viper bite:

a) Progressive local swelling without systemic signs:50 mL.

b) Mild systemic symptoms with or without haematological and coagulation abnormalities: 50-100mL.

c) Severe poisoning resulting in overt hemolysis or coagulopathy, progressing quickly: 150–200 mL.

Since Elapid absorbs more quickly and is less antigenic, higher dosages are recommended for bites. An initial dose of 100 - 200 ml is given. The adult and pediatric doses are the same.

Antivenom causes a sudden and dramatic reaction. While they typically take several hours, neurotoxic signs can improve in as little as 30 minutes. As long as a neutralizing dose has been administered, spontaneous systemic bleeding typically stops within 15 to 30 minutes and blood coagulability returns within 6 hours of antivenom.

If severe symptoms continue after one to two hours or if blood coagulability does not return in six hours, antivenom therapy should be administered again.

If the neurotoxicity is severe, the dose might need to be repeated every thirty minutes until the weakness stops progressing. In the case of viper bites, the antivenom should be repeated every six hours until the local swelling stops progressing and the clotting profile returns to normal.

A horse serum used as an antivenom is used to treat hypersensitivity reactions. Sensitivity testing has limited utility and is unreliable. Antivenom responds to treatment within 10 to 180 minutes of the beginning of the reaction. Itching, urticaria, nausea, vomiting, coughing, abdominal pain, fever, and tachycardia are among the symptoms. Patients with these symptoms may progress to bronchospasm, angioedema, and hypotension in up to 40% of cases. After treatment, a pyrogen reaction might appear one to two hours later. The late reaction, which appears 5–24 (mean 7) days after antivenom is administered, is a common serum sickness reaction. Therefore, when administering antivenom, an anaphylactic tray for allergic reactions should be available.

SUPPORTIVE THERAPY

1. Tetanus prophylaxis.
2. Only in cases of severe envenomation with a notable local reaction antibiotics are indicated.
3. Surgically removing dead tissue.
4. Fasciotomy for compartment syndromes.
5. Handling respiratory paralysis

   Ventilatory support needs to be thought about and started right away. This is how the "Tensilon test" ought to be conducted: Edrophonium chloride (10 mg for adults and 0.25 mg for children) should be administered intravenously (IV) after atropine sulphate (0.6 mg for adults and 0.02-0.05 mg/Kg for children). Patients who show a convincing response can be kept on atropine for four hours a day or by continuous infusion, along with neostigmine methyl sulphate (50–100 µg/Kg body weight).
6. Fresh frozen plasma, cryoprecipitates, and platelet concentrates might be needed in cases of severe bleeding. Heparin has no function.

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