# Plant Toxins:

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- Alcohols
- Alkaloids
- Glycosides – cyanogenetic
  - goitrogenic
  - irritant oils
  - Coumarins
  - Steroids & triterpenoids
- Oxalates
- Resins or resinoids
- Phytotoxins
- Minerals
- Nitrogen
- Polypeptides
- Amines

**Toxalbumen / Phytotoxin:** toxic protein which resembles a bacterial toxin in action & causes agglutination of red cells with some haemolysis & is antigenic.

Ex: abrin, ricin, crotin, ergot, calotropis

**Animal toxalbumens:** Snake venom & scorpion venom.

# Snake Bite:

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## Classification:

→ In India, there are 330 snake species.

→ Of the 330, 70 are venomous snakes [40 land snakes, 30 sea snakes]

→ Krait: most potent poison

→ Cobra: most dangerous due to high amount of injected poison.

| Feature | Venomous Snakes | Non-venomous Snakes |
|---|---|---|
| General appearance | Stout, dull coloured | Slender, brightly coloured |
| Head | Triangular | Rounded/oval |
| Belly scales | Large & cover entire breadth of belly | Small (may be large), but do not cover entire breadth of belly |
| Anal plate & subcaudal scales | Single row | Double rows |
| Teeth | Two long fangs with/without a row of smaller teeth | Several small teeth arranged in rows (No fangs) |
| Fangs | Canalized teeth (like hypodermic needles) | No fangs. Teeth are short & solid with no canal. |
| Poison glands | Present | Absent |
| Saliva | Contains toxic polypeptides & enzymes | No |
| Tail | • Rounded / flattened<br>• Tapers abruptly | • Always rounded<br>• Tapers gradually |
| Habits | Mainly nocturnal | Diurnal |

# Common Snakes in India:

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i) Saw-scaled viper (Echis carinatus)
ii) Russell viper (Daboia russelli)
iii) Common Krait (Bungarus caeruleus)
iv) Indian Cobra (Naja naja)

} Big Four

## ① Russell Viper:

→ Triangular head
→ V-shaped mark
→ 3 rows of diamond-shaped spots

## ② Saw-Scaled Viper:

→ Triangular head with birds' foot print mark
→ White mark resembling arrow
→ Wavy white line with diamond-shaped scales in between.

## ③ Indian Cobra:

→ has a broad hood
→ spectacle mark present on head
→ 3rd labial shield touches eye & nasal shield

## ④ King Cobra: (Ophiophagus hannah)

→ has a narrow hood, no spectacle mark
→ 3-4 metres long

## ⑤ Common Krait: (Bungarus caeruleus)

→ blue/black
→ white bands across the body
→ Dorsal scales are hexagonal

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⑥ Banded Krait: (Bungarus fasciatus)

→ black & deep yellow alternating bands

## 5 families of Venomous Snakes: V - CACHE

| | |
|---|---|
| i) Colubridae | Bird snake |
| ii) Elapidae | Cobra, Krait ⇒ neurotoxic & cardiotoxic |
| iii) Crotalidae | Rattle snake |
| iv) Viperidae | Viper ⇒ vasculotoxic |
| v) Hydrophidae | Sea snake ⇒ musculotoxic |
| vi) Atractaspididae | stilleto snakes |

Non-venomous snakes: - Pythons
- Boas

## Krait:

→ β bungarotoxin – Phospholipase A2

→ inhibits the release of Ach from the presynaptic membrane

→ Anti-snake venom has no effect (presynaptic nerve terminals are irreversibly damaged)

→ Recovery is dependent on regeneration of terminal axon.

## Cobra:

→ α Neurotoxins ⇒ Curare-mimetic toxin

→ prevent interaction between Ach & Ach receptors on postsynaptic membrane

→ prevents opening of $Na^+$ channels → Neuromuscular blockade

→ Anti-snake venom causes rapid reversal of paralysis (due to dissociation of toxin-receptor complex)

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# Toxins: Snake Venom

how to differentiate toxins?

- Proteins & Peptides (90-95%)
  - Non-Enzymes
    - Protease inhibitors
    - Natriuretic peptide
    - Three-finger toxins
    - C-type Lectins
    - NGF & VEGF
    - CRISPs
    - Cystatin
    - Myotoxins
    - Disintegrins
  - Enzymes
    - $PLA_2$s
    - LAAOs
    - Paraoxonases
    - Arylamidase
    - Endonuclease
    - Hyaluronidase
    - Phosphodiesterase
    - Acetylcholinesterase
    - NAD nucleoside
    - Phosphomonoesterase
    - Hepatinase-like enzymes
    - Metallo & serine proteases
- Non-Proteinaceous Components (Lipids, Amino acids, Carbohydrates, Metal ions, nucleosides, amines)

Phospholipases A2: causes local & systemic myotoxicity, damage to lymphatic vessels, oedema, neurotoxicity, nephrotoxicity, haemolysis.

Snake venom metalloproteinases: haemorrhage, myonecrosis, ECM degradation, coagulopathy, pain, oedema

Hyaluronidases: ECM degradation → rapid spreading of venom

Three-finger toxins: cytotoxicity, necrosis & neurotoxicity.

Disintegrins: inhibition of platelet aggregation

Natriuretic peptide: hypotension

Ophioxidase: helps in autolysis

Protease: dissolution of vascular wall

# General Considerations of Snakebites:

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i) Season: venom output is more & is more toxic in summer

ii) Dry bite: when a snake bites but venom fails to get injected

→ approx. 20% of all snakebites are dry bites

→ Causes:
- layers of clothing or shoes over the bitten part
- when a snake bite does not inject venom
- superficial bite (venom is ejected superficially or externally without entering the wound)
- sideswipes (rather than head-on bites)

# Signs & Symptoms of Snake Bite:

Ophitoxemia: poisoning by snake venom

→ Signs & symptoms depend upon:
- Snake factors — species & size of snake
  - condition of fangs & venom glands
  - pathogens present in snake venom
  - location, number & depth of bite.
  - length of time the snake holds
  - amount of venom injected
- victim dependent factors — age & size of victim
  - victim's sensitivity to venom
- community dependent factors — first-aid & medical care given immediately

(i) General:

→ fright
- hypotension
- feeble pulse
- increased respiratory rate
- semiconsciousness
- cold clammy skin

→ gas gangrene

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→ tetanus

→ psychological shock & death

→ Fang marks

- two in number (most common)
- one mark (less common – seen in sideswipes)
- more than two (seen in multiple bites)
- depth: 2.5 – 4 cm (vipers generally cause deeper bites than Elapids)

(ii) Symptoms specific to Cobra:

| | Cobra | Krait | Viper |
|---|---|---|---|
| LS | ↓ | ↓↓↓ | ↑↑↑ |
| SS | ↑↑ | ↑↑ | vasculotoxic |

Local: manifestations start within 6-8 min

→ minimal local manifestations

→ small reddish wheal or bullae (at site of bite)

→ tenderness of bitten area with radiating burning pain & oozing of blood-stained fluid.

→ swelling: minimal/absent

Systemic: symptoms appear after 30 min

→ nausea, vomiting

→ excessive salivation, headache, vertigo, paresthesia around the mouth, myalgia, irritability

→ CNS depression: • drowsiness • slight intoxication
• weakness of legs • reluctance to stand/move

→ Paralyzing effect: First sign ⟹ ptosis & external ophthalmoplegia (since ocular muscles are most sensitive to neuromuscular blockade)

- blurring of vision, diplopia, dysconjugate gaze, strabismus
- paralysis of lower limbs, trunk, neck, head (head falls forward, inability to raise head), palate, vocal cords (dysphonia), jaws, tongue, muscles of deglutition (dysphagia)
- Absent gag reflex • Complete paralysis after 2 hours

→ Respiratory arrest: due to -
- paralysis of intercostal muscles & diaphragm
- obstruction of upper airway by paralyzed tongue
- inhaled vomitus

→ cardiac arrest

→ convulsions, coma

→ Cause of death: hypoxia & acidosis due to respiratory failure

→ in case of recovery: necrosis of skin & tissues around bite mark.

(iii) Specific Symptoms due to Krait:

Local: insignificant / minimal local signs

→ invisible / scarcely perceptible puncture marks

→ mild tenderness, itching, numbness, paresthesia

General: abdominal pain & fasciculations

→ drowsiness, intoxication

→ paralysis develops anytime before 12 hours

→ generalized rhabdomyolysis

→ albumin in urine

→ fatality is 75% in absence of ASV & assisted ventilation

(iv) Symptoms specific to Viper:

Local: (8)

→ swelling around bite; quickly spreads to entire limb & adjacent trunk

→ pain, paresthesia, tenderness, reddening

→ persistent bleeding from bite

→ regional lymphadenopathy

→ bruising over path of superficial lymphatics & over lymph nodes

→ blisters in & around the bite site start appearing within 12 hours & spread to entire limb

→ extensive necrosis of skin, subcutaneous tissue, muscle → extensive suppuration, sloughing

→ increased intracompartmental pressure due to edema (severe pain, anaesthesia, tense swelling)

Systemic:

→ haematologic abnormalities ⇒ Most characteristic.

→ DIC → fibrin is used up → defibrination → blood becomes incoagulable
- primary pathological fibrinolysis (PPF)
- microthrombi formation

→ blood findings: • early hemoconcentration • ↑ clotting time • ↑ bleeding time • urine contains blood, protein & sugar

→ Main haemorrhagic manifestations: • bleeding anterior pituitary, floor of the mouth, genitourinary & GI tracts, tympanic membrane
- ecchymoses & petechiae over entire body • epistaxis • gingival bleeding
- hematuria • hemoptysis • subarachnoid/intracerebral haemorrhage
- intravascular hemolysis → hemoglobinuria, acute renal failure • rectal bleeding
- retroperitoneal & intraperitoneal haemorrhages ⇒ abdominal distension, tenderness
- subconjunctival haemorrhages

→ headache, dizziness, weakness

→ CVS: • Hypotension • Haemorrhagic shock • Tachycardia

→ Pupils: dilated

→ respiratory depression

→ abortions in pregnant females

→ Cause of death: haemorrhagic shock

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(v) Symptoms specific to Sea Snakes:

→ little / no local reaction
→ after ½ - 1 hour : pain, stiffness & weakness of skeletal muscles
→ marked polymyositis
→ trismus (in early stage)
→ later: flaccid paralysis (starts with ptosis)
→ myoglobinuria, renal failure
→ Death: cardiac arrest / paralysis of respiratory muscles.

## Fatal Period:

i) Common cobra = ½ - 6 hours
ii) Common Krait = 18 hours
iii) Russell's viper = 3 days
iv) Saw-scaled viper = 5 days.

| | | |
|---|---|---|
| C | 6 h | 15 |
| K | 18 h | 6 |
| R | 3 d | 20 |
| S | 5 d | 8 |

## Cause of Death:

i) Cobra = Respiratory paralysis
ii) Viper = Hemolysis, haemorrhage

| Snake | Fatal dose in terms of dried venom | Total yield in 1 bite in terms of dried venom |
|---|---|---|
| Krait | 6 mg | 20 mg |
| Saw-scaled viper | 8 mg | 25 mg |
| Cobra | 15 mg | 200 - 350 mg |
| Russell's viper | 20 mg | 150 - 200 mg. |

# Diagnosis:

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1] detection of snake specific venom antigens in wound swabs, aspirates or serum, CSF.
2] Radioimmunoassay (most sensitive & specific) for venom detection (from bitten area of skin)
3] Enzyme immunoassay
4] ELISA for venom antigen detection in body fluids
5] Swab taken from wound site / extract from skin is injected into a frog for evidence of toxicity.

# First - Aid:

- Assure the patient
- Apply firm pressure over bitten area (pressure immobilization is recommended for elapid & sea snakes, but not for vipers)
- Apply a broad firm bandage (Sutherland wrap) on bitten area & around limb. (pressure to be maintained: 50-70 mm Hg)
- Immobilize the limb (movement can accelerate spread of venom)
- No local incision / suction.
- Do not suck venom out of the wounds.
- Clean the wound with soap & water or iodine & cover with a sterile dressing
- Make patient lie on one side, so that airway is clear (in case of vomiting / fainting)

# Treatment:

1] Polyvalent Antisnake Venom: (PAV) useful when given within 4 hours, less useful if delayed for 8 hours.
→ each vial of PAV neutralizes 6-8 mg of venom (available as lyophilised powder in ampoules)

Dose: minimal symptoms (local swelling but no systemic reaction) ⇒ 5 vials
moderate symptoms (swelling beyond site of bite + systemic Rx) ⇒ 10 vials
severe symptoms (marked systemic Rx) → 10-15 vials

→ lyophilized powder is diluted in 500 ml of distilled water / NS & infused over a period of 1 hour.

→ In neurotoxic poisoning ⇒ 2nd dose of 10 vials must be given after 1 hour.

2] 20 minutes blood clotting test: Few ml of fresh venous blood is put in a clean dry glass tube & left undisturbed for 20 minutes & then gently tilted.

→ If blood is still liquid ⟶ viper bite (haematotoxic / vasculotoxic)

→ repeat the test every 6 hours

→ normalization of clotting point = end point of therapy

3] Anaphylactic Reaction to PAV: at first sign of any of these: utricaria, itching, shivering, chills, nausea / vomiting, hypotension, bronchospasm, angio-oedema

→ stop PAV infusion

→ administer 0.5 mg 1:1000 adrenaline IM (0.01 mg/kg for children)

→ hydrocortisone, anti-histamines

→ If no improvement after 10-15 minutes ⇒ give second dose of adrenaline

→ after improvement of condition ⇒ start antiserum infusion.

→ If there are signs of neuroparalysis ⇒ give 1.5 mg neostigmine for adults IM + 0.6 mg atropine

⇒ repeat twice at 10 min intervals

→ In case of clotting abnormalities ⇒ Heparin 1000 – 5000 IU

# Post Mortem Appearance after Snake Bite:

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i) Common to all poisonous snakes:

→ 1 or 2 or more fang marks ⇒ 1·5 cm – 2·5 cm deep.

→ washings from the site of bite & tissues underneath ⇒ show venom components (cholinesterase, thromboplastin)

→ Internal organs – congested

→ purpuric spots on pericardium, haemorrhage in lungs

ii) Elapids:

→ minimal local changes

→ Brain – congested

iii) Vipers:

→ Local changes: extensive local cellulitis, discolouration & swelling

→ Haemorrhages: Prominent

- occur from puncture, mucus membranes into bowel, lungs & all other tissues
- purpuric spots on pericardium

→ Kidneys: inflamed, haemorrhagic

iv) Sea snakes:

→ Signs of rhabdomyolysis

→ Kidneys: congested, tubules blocked with myoglobin.

# MLI:

i) Manner of death:

→ accidental ⇒ most common

→ homicidal • throwing snake on the bed of a sleeping person (method of infanticide)

→ suicidal ⇒ very rare (Queen Cleopatra committed suicide by snake bite)

ii) Cattle poison: cobra is shut up in an earthen vessel containing a banana → heat is applied to the vessel → snake is irritated → bites fruit → venom is injected into banana pulp → pulp is taken out → pulp is smeared on a rag → rag is thrust into animal's rectum using a split bamboo

iii) Excretion: occurs through milk, saliva, urine & mucus surfaces
→ case of a young child who died after suckling mother's breast who was bitten by a poisonous snake.

iv) Ingested venom: snake venom is not poisonous when ingested (since venom proteins are digested)
→ animals killed by snake venom may be eaten without ill effects
→ a rescuer who sucks snake venom from the wound may not be poisoned if he swallows the poison.

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# Scorpions: about 100 scorpion species are found in India (out of 1250)

→ 8-legged arthropods — have a hollow sting in the last joint of their tail

→ venom is clear, colourless toxalbumen — can be haemolytic or neurotoxic.

→ toxicity of poison: scorpion > snake bite; but only a small quantity is injected

→ venom is potent autonomic stimulator ⟹ release of massive amounts of catecholamines from adrenals.

→ most scorpion stings occur on extremities.

## Signs & Symptoms:

Haemolytic Venom: local reaction mainly (simulates viper snake bite)

→ Scorpion sting: only one hole in the centre of reddened area

→ oedema, pain, reddening ⟹ usually lasts for 1-2 hours.

Neurotoxic Venom: simulates cobra bite.

→ no marked local reaction
→ nausea, vomiting, restlessness
→ fever, paralysis
→ death: pulmonary oedema & cardiac failure.
→ cardiac arrhythmias
→ convulsions, coma
→ cyanosis, respiratory depression

Diagnosis is confirmed by ELISA

**Treatment:** 1] Immobilize the limb & apply tourniquet above the site of sting

2] Pack sting in ice & incise & use suction & wash wound with a weak solution of ammonia / borax / $KMnO_4$

3] Local anaesthetic to reduce pain is injected at the site — 2% novocaine or — 5% cocaine.

4] Specific antivenin (available for most species)

5] Calcium gluconate IV (to control swelling)

6] Barbiturates (to reduce excitement & convulsions) [Morphine is C/I]

7] Atropine (to prevent pulmonary oedema)