PDP 406 CLINICAL TOXICOLOGY

Pharm.D

Fourth Year

Poisonous snake bite

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Introduction

A study of the current knowledge base in treating snake bite amongst doctors in the high-risk countries of India and Pakistan: does snake bite treatment training reflect local requirements?

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Table 1. Global Estimates of the Snakebite Envenomings in 2007 by Region

Region	Snakebite Envenomings per Year				Range for Wider Region
	Low Estimate	Incidence/100,000	High Estimate	Incidence/100,000	
Asia Pacific, high income	703	0.39	3,156	1.74	237,379–1,184,550
Asia, Central	228	0.29	1,213	1.55	
Asia, East	4,582	0.33	218,673	15.73	
Asia, South	121,333	7.84	463,350	29.94	
Asia, Southeast	110,533	18.82	498,158	84.65	
Australasia	1,099	4.41	1,260	5.06	1,099–1,260
Caribbean	1,098	2.82	8,039	20.66	1,098–8,039
Europe, Central	106	0.09	2,489	2.09	3,961–9,902
Europe, Eastern	795	0.38	795	0.38	
Europe, Western	3,060	0.74	6,618	1.61	
Latin America, Andean	6,548	12.90	27,653	54.47	80,329–129,084
Latin America, Central	42,087	19.04	67,373	30.47	
Latin America, Southern	2,058	3.46	2,163	3.63	
Latin America, Tropical	29,636	14.97	31,895	16.12	
North Africa/Middle East	3,017	0.71	80,191	18.88	3,017–80,191
North America, high income	2,683	0.79	3,858	1.14	2,683–3,858
Oceania	361	3.87	4,635	49.70	361–4,635
Sub-Saharan Africa, Central	18,176	20.28	47,820	53.37	90,622–419,639
Sub-Saharan Africa, East	42,834	12.94	74,823	22.61	
Sub-Saharan Africa, Southern	1,613	2.34	2,296	3.33	
Sub-Saharan Africa, West	27,999	8.87	294,700	93.34	
Total	**420,549**	**6.28**	**1,841,158**	**27.5**	**420,549–1,841 158**

The big four

Cobra

Krait

Russel's viper

Saw-scaled viper

***Naja naja* (•)**
***Naja oxiana* (o)**

Sheesh Nag, Kala Nag, Karo

Bungarus caeruleus **(•)**
Bungarus sindanus **(o)**
Bungarus sindanus razai **(x)**

Sung Choor

Daboia ruselii (●)

Koriwala

***Echis c. sochureki* (•)**
***Echis c. astole* (o)**
***Echis c. multisquamatus*(∗)**

Lundi, Khappra, Sindh khappra, Waziristan khappra, Astola khappra

Snake bite in Asia: epidemiological risk factors

- Children
- Agricultural workers, fishermen and other high risk occupations
- Seasonal (rains and harvests)
- Epidemics resulting from flooding and invasion of snakes' environment

Assesment

- Time of bite
- Activity at the time of bite
- First aid action taken since the bite
- Clinical examination
- 20 mn whole Blood Clotting Test

Local signs

- fang marks
- local pain
- local bleeding
- bruising
- lymphangitis
- lymph node enlargement
- inflammation (swelling, redness, heat)
- blistering
- local infection, abscess formation
- necrosis

General symtoms (1)

- ***General:*** Nausea, vomiting, malaise, abdominal pain, weakness, drowsiness, prostration
- ***Cardiovascular*** **(Viperidae):** Visual disturbances, dizziness, faintness, collapse, shock, hypotension, cardiac arrhythmias, pulmonary oedema,

General symtoms (2)

- ***Bleeding and clotting disorders*** **(Viperidae)**
  - bleeding from recent wounds (including fang marks, venepunctures etc) and from old partly-healed wounds
  - spontaneous systemic bleeding - from gums, epistaxis, bleeding into the tears, haemoptysis, haematemesis, rectal bleeding or melaena, haematuria, vaginal bleeding, bleeding into the skin (petechiae, purpura, ecchymoses) and mucosae (eg conjunctivae), intracranial haemorrhage..

General symtoms (3)

- ***Neurological*** **(Elapidae, Russell's viper):** Drowsiness, paraesthesiae, abnormalities of taste and smell, "heavy" eyelids, ptosis, external ophthalmoplegia, paralysis of facial muscles and other muscles innervated by the cranial nerves, aphonia, difficulty in swallowing secretions, respiratory and generalised flaccid paralysis

- ***Skeletal muscle breakdown*** **(sea snakes, Russell's viper):** Generalised pain, stiffness and tenderness of muscles, trismus, myoglobinuria (Fig 34), hyperkalaemia, cardiac arrest, acute renal failure

General symtoms (4)

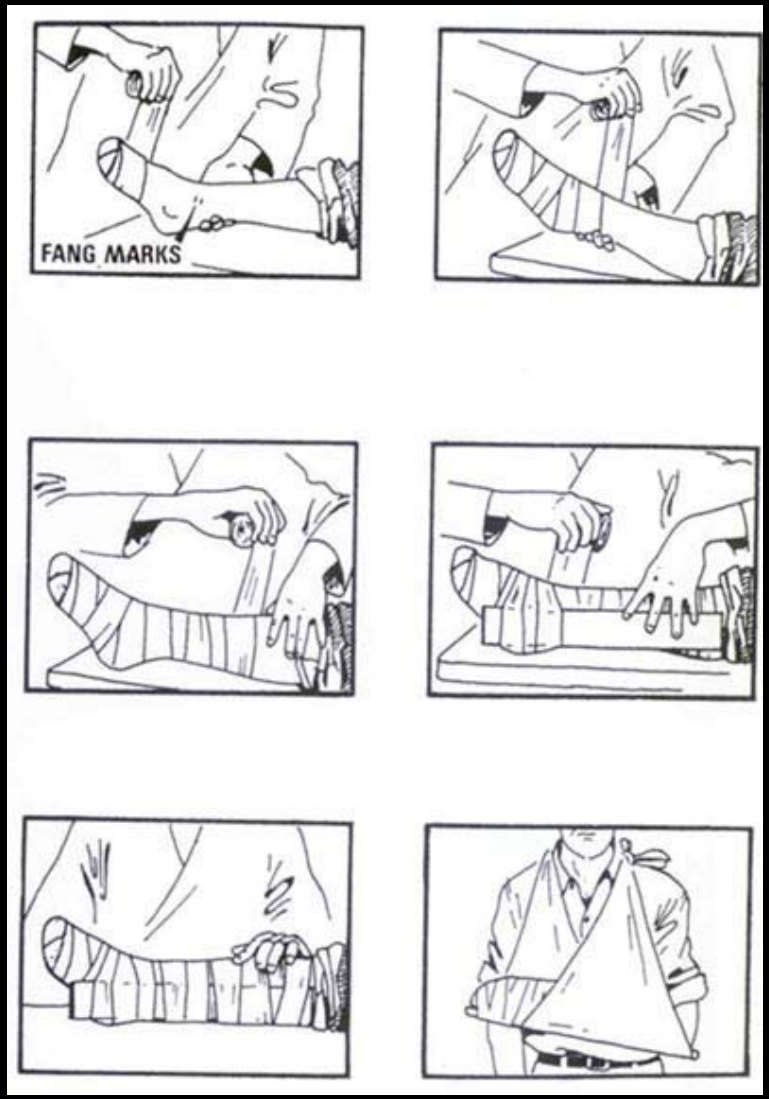
- ***Renal* (Viperidae, sea snakes):** Loin (lower back) pain, haematuria, haemoglobinuria, myoglobinuria, oliguria/anuria, symptoms and signs of uraemia (acidotic breathing, hiccups, nausea, pleuritic chest pain….)
- ***Endocrine*** (acute pituitary/adrenal insufficiency) (Russell's viper)
  - Acute phase: shock, hypoglycaemia
  - Chronic phase (months to years after the bite): weakness, loss of secondary sexual hair, amenorrhoea, testicular atrophy, hypothyroidism etc (Fig 35)

Syndromic approach to species diagnosis

- Descending paralysis + severe local envenoming = Naja spp.
- Bites at night while the victim is asleep + negligible local envenoming + severe abdominal pain = Bungarus spp.
- Rhabdomyolysis + renal failure = *D. russelii* (on land) or sea snakes (in river, estuary or sea)
- Shock, bleeding, coagulopathy, renal failure and local envenoming = classic viperid envenoming (Viperinae and Crotalinae)
- + neurotoxicity, rhabdomyolysis and haemolysis = *D. russelii*

Management

- ABCs
- Pressure immobilization
- Clinical assessment / 20WBCT
- ASV
- Neostigmine
- Supportive therapies (MV, dilaysis)
- Adequate referral



Pressure immobilisation is recommended for bites by neurotoxic elapid snakes, including sea snakes but should not be used for viper bites because of the danger of increasing the local effects of the necrotic venom.

20WBCT

- Few ml of fresh venous blood placed in a NEW, CLEAN, DRY, GLASS test tube
- Left undisturbed for 20mn
- Gently tilted to 45° and examined
- If it has remained liquid: consumption coagulopathy $\rightarrow$ ASV required
- Clotted: ASV not necessary (at this stage)

Criteria for giving ASV

- ASV's only role is to bneutralize unbound free flowing venom
- 50% of Cobra bites inject no venom to the victim
- Criteria for Pakistan:
  - Incoagulable blood (20WBCT)
  - Visible neurological signs (ptosis, ophtalmoplegia, descending paralysis)
  - Clear evidence of current systemic bleeding
- ASV to be given only if one or more of this signs are present

Prevention of adverse reactions to ASV

- No intradermal test: targeted at IgE mediated reaction whereas ASV reactions are complement mediated
- Risk of pre sensitizing the patient and making the reaction more likely
- Waste of precious time
- Premedication with hydrocortsisone, anti-histamine or Sc adrenaline: only for the first dose, efficacy unproven

Treatment of adverse raction

- Usually within 20mn from start of ASV
- Drug of choice = Adrenaline, 0.5 mg IM, to be repeated if symptoms donot improve within 15mn
- 100 mg hydrocortisone + 25 mg Promethazine IM / 10 mg chlorphenimarine IV

Types of ASV available

- Liquid ASV (NIH)
- Lyophilized (imported from India)
- Liquid ASV requires no reconstitution but pb of cold chain
- Lyophylized ASV no refrigeration needed but 1h required for reconstitution with distilled water

Dose of ASV (1)

- Depending on the amount of venom injected by the snake
- Cobra and Russel's viper 60mg ≅
- Krait inject less venom but neurological symptoms similar to Cobra
- Each ASV vial neutralizes 6mg of Cobra and Russel's viper venom
- Initial dose 8-10 vials (NIH/indian ASV same neutalzing capacity)

Dose of ASV (2)

- Saw scaled viper (Echis carnatus, smaller, found in India) bite around 15 mg of venom
- Larger saw scaled viper (Echis sochureki) found in Pakistan: no studies
- Indian ASV made with Echis carinatus venom only (15 vials required to restore coagulation on average)
- Local experience in Sindh: higher requirements (25+ vials)
- ? Efficacy of Indian ASV on Echis sochureki
- NIH ASV produced with SSV from Sindh

NIH ASV guideline

- In all cases other than confirmed SSV bite, use 8-10 vials
- If confirmed SSV
  - give 4 vials if 20WBCT un coagulable
  - monitor coagulation and repeat ASV 6 hourly
  - Check series of patient
    - if 50-60% restore their coagulation, 4 vials is the correct starting dose
    - If 10-20% restore their coagulation after 6 hours increase the starting dose to all patients by one vial and monitor

Administration

- Over 1 hour maximum
- IV injection or continuous infusion
- SC, IM, around bite site : no

Repeat doses

- ASV should be given as late as blood is demonstrated incoagulable on 20WBCT performed 6 hourly (time required by the liver to restore clotting factors)
- Neurotoxic:atient reviewed 1 hour after initial dose:
  - if worsening, give 2nd dose of ASV
  - if not worsened, review again after 2 hours, if not improved, give 2nd dose of ASV
  - After 2 doses, ASV should be stopped, nor role for very large dose in neurotoxic bites

Neostigmine

- Cobra venom is a post synaptic neurotoxin and blocks the nicotinic receptor causing acetylcholine to be unable to bind
- Neostigmine prolongs the life of acetylcholine by inhibiting cholinesterase, increasing the likelywood of acetylcholine binding with unblocked receptor
- Baseline test: single breath count, time upward gaze
- 1.5 mg neostigmine methylsulfate + 0.6 mg Atropine
- Repeat the tests
- If objective improvement, repeat neostigmine + atropin eevery 30mn

Use of blood product

- Primary mean of restoring clotting factors is by ASV
- Once veom has been adequately neutralized, liver will begin to restore factors to normal levels
- Exceptionally used in case of severe bleeding, after coagulation has been restored

Others

- No heparin
- Prefer paracetamol to aspirin for pain
- No routine antibiotic
- Antibiotic if necrosis
- Tetanus passive + active immunization

Referral criteria

- Occult systemic bleeding / renal failure
- Neurotoxic envinemation requiring longer term mechnaical ventilation
- Surgical cases requiring debridement of necrotic tissue

Transport

- Viperine envenimation: give ASV then 6 hours before the next dose provides time to transport the patient
- Neurotoxic: need for mechanical ventilatory support ? Inability to perform neck lift suggests imminent respiratory failure
- Transportation of the patient: NPA + bag mask ventilation

Prevention (1)

- Education ! Know your local snakes, know the sort of places where they like to live and hide, know at what times of year, at what times of day/night or in what kinds of weather they are most likely to be active.
- Be specially vigilant about snake bites after rains, during flooding, at harvest time and at night.
- Try to wear proper shoes or boots and long trousers, especially when walking in the dark or in undergrowth.

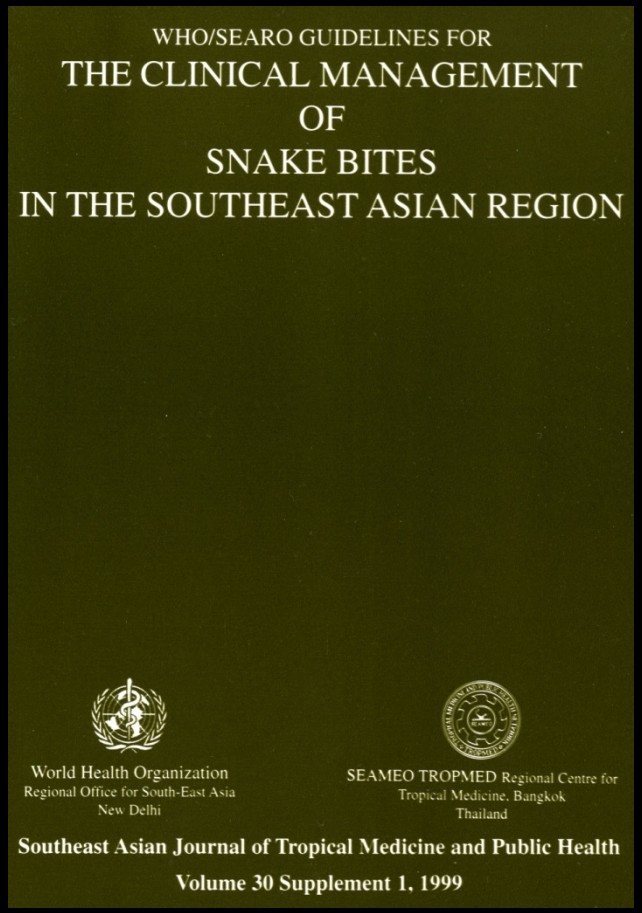
Prevention (2)

- Use a light (torch, flashlight or lamp) when walking at night.
- Avoid snakes as far as possible, including snakes performing for snake charmers. Never handle, threaten or attack a snake and never intentionally trap or corner a snake in an enclosed space.
- If at all possible, try to avoid sleeping on the ground.
- Keep young children away from areas known to be snake-infested.
- Avoid or take great care handling dead snakes, or snakes that appear to be dead.

Prevention (3)

- Avoid having rubble, rubbish, termite mounds or domestic animals close to human dwellings, as all of these attract snakes.
- Frequently check houses for snakes and, if possible, avoid types of house construction that will provide snakes with hiding places (eg thatched rooves with open eaves, mud and straw walls with large cracks and cavities, large unsealed spaces beneath floorboards).
- To prevent sea snake bites, fishermen should avoid touching sea snakes caught in nets and on lines. The head and tail are not easily distinguishable. There is a risk of bites to bathers and those washing clothes in muddy water of estuaries, river mouths and some coastlines.

References



Special Communication

A Contextual Approach to Managing Snake Bite in Pakistan: Snake Bite Treatment with Particular Reference to Neurotoxicity and the Ideal Hospital Snake Bite Kit

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Thank You !