

## SLAKE BITE

### Introduction

- in 1999–2001, there were a total of 19,335 admissions to hospitals throughout Malaysia due to venomous animal bites and stings. A significant numbers are due to snakebite and hymenoptera (bee) stings.
- not all snakes are venomous. In Malaysia there are approximately 40 species of venomous snakes (18 land snakes, all 22 of sea snakes) belonging to two families:
  - *Elapidae* – have short, fixed front fangs. The family includes cobras, kraits, coral snakes and sea snakes.
  - *Viperidae* – have a triangular shaped head and long, retractable fangs. The most important species in Malaysia are *Calloselasma rhodostoma* (Malayan pit viper) and *Trimeresurus genus* (green viper). The Malayan pit vipers are common in the northern part of Peninsular Malaysia but are not found in Sabah and Sarawak.
- cobra and Malayan pit vipers cause most of the cases of snakebites in Malaysia. Bites by sea snakes, coral snakes and kraits are uncommon.
- the snake venom is made up of procoagulant enzymes (activate coagulation cascade), phospholipase A2 (myotoxic, neurotoxic, cardiotoxic; causes haemolysis and increased vascular permeability), proteases (tissue necrosis), polypeptide toxins (disrupt neuromuscular transmissions) and other components.

Table 1. Venomous land snakes in Malaysia

Family	Scientific name	Common Malay name
<i>Viperidae</i>		
Malayan pit viper	<i>Calloselasma rhodostoma</i>	ular kapak bodoh
temple pit viper	<i>Trimeresurus wagleri</i>	ular kapak tokong
red-tailed pit viper	<i>Trimeresurus popeorum</i>	ular kapak ekor merah
mountain pit viper	<i>Trimeresurus monticola</i>	ular kapak gunung
Sumatran pit viper	<i>Trimeresurus sumatranus</i>	ular kapak sumatera
mangrove pit viper	<i>Trimeresurus purpureomaculatus</i>	ular kapak bakau
flat-nosed pit viper	<i>Trimeresurus puniceus</i>	ular kapak hidung pipeh
<i>Elapidae</i>		
common black cobra	<i>Naja naja</i>	ular senduk
king cobra	<i>Ophiophagus Hannah</i>	ular tedung selar
banded krait	<i>Bungarus fasciatus</i>	ular katang belang
Malayan krait	<i>Bungarus candidus</i>	ular katang tebu
red-headed krait	<i>Bungarus flaviceps</i>	ular katang kepala merah
spotted coral snake	<i>Callophis gracilis</i>	ular pantai bintik
small-spotted coral snake	<i>Callophis maculiceps</i>	ular pantai bintik kecil
blue Malayan coral snake	<i>Maticora bivirgata</i>	ular pantai biru biru
banded coral snake	<i>Maticora intestinalis</i>	ular pantai belang

### Clinical features

#### *Elapids*

- cobras usually cause pain and swelling at the bite site may progress to neurological dysfunction: ptosis, ophthalmoplegia, dysphagia, aphasia, respiratory paralysis
- Kraits cause minimal local effects but may cause central nervous system manifestations

- sea snakes cause minimal local effects and mainly musculoskeletal findings: myalgia, stiffness and paresis leading to myoglobinuria and renal failure. Paralysis can also occur.

### *Viperidae*

- pit vipers – cause extensive local effects: immediate pain, swelling, blisters and necrosis and systemic bleeding tendencies. The common sites of bleed are bite site, gingival sulci and venepuncture sites.

*Note: There may be overlap of clinical features caused by venoms of different species of snake. For example, some cobras can cause severe local envenoming (formerly thought to be due to only vipers).*

## Management

### *First aid*

The aims are to retard absorption of venom, provide basic life support and prevent further complications.

- reassure the victim – anxiety state increases venom absorption.
- immobilise the bitten limb with splint or sling (retard venom absorption)
- apply a firm bandage for some elapid bites (delay absorption of neurotoxic venom) but not for viper bites whose venom cause local necrosis
- leave the wound alone - DO NOT incise, apply ice or other remedies
- tight (arterial) tourniquets are not recommended
- do not attempt to kill the snake. However, if it is killed bring the snake to hospital for identification. Do not handle the snake with bare hands: even a severed head can bite!
- transfer the victim quickly to the nearest health facility

### *Treatment in the hospital*

- do rapid clinical assessment and resuscitation including Airway, Breathing, Circulation and level of consciousness. Monitor vital signs (blood pressure, respiratory rate, pulse rate).
- establish IV access; give oxygen and other resuscitations as indicated.
- history: inquire part of body bitten, timing, type of snake and history of atopy.
- examine
  - bitten part for fang marks (sometimes invisible), swelling, tenderness, necrosis
  - distal pulses (reduced or absent in compartment syndrome)
  - patient for bleeding tendencies – tooth sockets, conjunctiva, puncture sites
  - patient for neurotoxicity – ptosis, ophthalmoplegia, bulbar and respiratory paralysis
  - patient for muscle tenderness, rigidity (sea snakes)
  - urine for myoglobinuria
- send blood investigations (full blood count, renal function tests, prothrombin time/partial thromboplastin time, group and cross matching)
- perform a 20-min Whole Blood Clotting Test. Put a few mls of blood in a clean, dry glass test tube, leave for 20 min, and then tipped once to see if it has clotted. Unclotted blood suggests hypofibrinogenaemia due to pit viper bite and rules out an elapid bite.
- review immunisation history: give booster antitetanus toxoid injection if indicated.
- venom detection kit is used in some countries to identify species of snake. However, it is not available in Malaysia.
- admit to ward for at least 24 hours (unless snake is definitely non-venomous).

### Antivenom treatment

Antivenom is the only specific treatment for envenomation. Give as early as indicated for best result. However, it can be given as long as the signs of systemic envenomation are still present. For local effect, antivenom is probably not effective if given more than a few hours after envenomation.

Indications for antivenom:

- haemostatic abnormalities, e.g. spontaneous systemic bleeding, incoagulable blood or thrombocytopenia ( $<100 \times 10^9/\text{litre}$ ).
- neurotoxicity.
- cardiovascular dysfunction, e.g. hypotension or shock.
- generalised rhabdomyolysis (muscle aches and pains).
- acute renal failure.
- significant local effect, e.g. local swelling more than half the bitten limb, extensive blistering or bruising, bites on digit or rapid progression of swelling.
- helpful laboratory investigations suggesting envenomation include anaemia, thrombocytopenia, leucocytosis, raised serum enzymes (creatinase kinase, aspartate aminotransferase, alanine aminotransferase), hyperkalaemia, and myoglobinuria.

### Choice of antivenom

- if biting species is known, give monospecific (monovalent) antivenom (more effective and less adverse reactions).
- if it is not known, clinical manifestations may suggest the offending species:
  - local swelling with neurological signs = cobra bites
  - extensive local swelling + bleeding tendency = Malayan Pit vipers
- if still uncertain, give polyvalent antivenom.
- no antivenom is available for Malayan kraits, coral snakes and some species of green pit vipers. Fortunately, bites by these species are rare and usually cause only trivial envenoming.

### Dosage and route of administration

Amount given is usually empirical. Recommendations from manufacturers are usually very conservative as they are mainly based on animal studies (Table 2).

- repeat antivenom administration until signs of envenomation resolved.
- give through IV route only. Dilute antivenom in any isotonic solution (5-10ml/kg, bigger children dilute in 500mls of IV solution) and infuse the whole amount in one hour.
- infusion may be discontinued when satisfactory clinical improvement occurs even if recommended dose has not been completed
- do not perform sensitivity test as it poorly predicts anaphylactic reactions.
- do not inject locally at the bite site.

Table 2: Guide to initial dosages of some important antivenoms

Species	Antivenom manufacturer	Initial dose
Malayan pit viper	Thai Red Cross (Monovalent)	100 mls
Cobra	Twyford Pharmaceuticals (monovalent)	50 mls (local) 100 mls (systemic)
	Serum Institute of India; Biological E. Limited, India (Polyvalent)	50 mls (local) 100 - 150 mls (systemic)
King Cobra	Thai Red Cross (Monovalent)	50 - 100 mls
Common sea snake	CSL, Australia (polyvalent)	1 000 units (1 vial)

- prepare adrenaline, hydrocortisone, antihistamine and resuscitative equipment and be ready if allergic reactions occur.
- pretreatment with SC adrenaline remains controversial. Small controlled studies in adults have shown it to be effective in reducing risk of reactions. However, its effectiveness and appropriate dosing in children have not been evaluated. There is no strong evidence to support the use of hydrocortisone/antihistamine as p  
remedications. Consider their use in the patient with history of atopy.

### *Antivenom reactions*

3 types of reactions may occur:

- early anaphylactic reactions
  - occur 10-180 minutes after starting antivenom
  - symptoms range from itching, urticaria, nausea, vomiting, and palpitation to severe systemic anaphylaxis: hypotension, bronchospasm and laryngeal oedema
  - stop antivenom infusion: give adrenaline IM (0.01ml/kg of 1 in 1000), antihistamine, e.g. chlorpheniramine 0.2mg/kg, hydrocortisone 4mg/kg/dose an IV fluid resuscitation (if hypotensive)
  - if only mild reactions, restart infusion at a slower rate
- pyrogenic reactions
  - occur 1-2 hours after treatment; are due to endotoxin compounds in antivenom
  - symptoms include fever, rigors, vomiting, tachycardia and hypotension
  - give treatment as above
  - treat fever with paracetamol and tepid sponging
- late reactions
  - occur about a week later
  - a serum sickness-like illness: fever, arthralgia, lymphadenopathy, etc.
  - treat with chlorpheniramine 0.2mg/kg/day in divided doses for 5 days
  - if severe, give oral prednisolone (0.7 – 1mg/kg/day) for 5-7 days

### *Anticholinesterases*

- should always be tried in severe neurotoxic envenoming, especially when no specific antivenom is available, e.g. bites by Malayan krait and coral snakes. The drugs have a variable but potentially useful effect.
- give test dose of IV edrophonium chloride (Tensilon) (0.25mg/kg, adult 10mg) with IV atropine sulphate (50µg/kg, adult 0.6mg)
- if patients respond convincingly, maintain with IV neostigmine methylsulphate (50-100µg/kg) and atropine, four hourly by continuous infusion

### Supportive/ancillary treatment

- clean wound with antiseptics
- give analgesia to relief pain (avoid aspirin). In severe pain, morphine may be administered with care. Watch closely for respiratory depression
- give antibiotics if the wound looks contaminated or necrosed  
e.g. IV crystalline penicillin +/- gentamicin, amoxicillin/clavulanic acid, erythromycin or a third generation cephalosporin
- respiratory support – respiratory failure may require assisted ventilation.
- watch for compartment syndrome – pain, swelling, cold distal limbs and muscle paresis. Get early orthopaedic/surgical opinion. Patient may require urgent fasciotomy. Correct coagulation abnormalities with fresh frozen plasma and platelets before any surgical intervention.
- desloughing of necrotic tissues should be carried out as required.
- for oliguria and renal failure, e.g. due to sea snake envenomation, measure daily urine output, serum creatinine, urea and electrolytes. If urine output fails to increase after rehydration and diuretics (e.g. frusemide), start renal dose of dopamine (2.5µg/kg/minute IV infusion) and place on strict fluid balance. Dialysis is rarely required.

### Pitfalls in management

- *giving antivenom 'prophylactically' to all snakebite victims.* Not all snakebites by venomous snakes will result in envenoming. On average, 30% bites by cobra, 50% by Malayan pit vipers and 75% by sea snakes DO NOT result in envenoming. Antivenom is expensive and carries the risk of causing severe anaphylactic reactions (as it is derived from horse or sheep serum). Hence, it should be used only in patients in whom the benefits of antivenom are considered to exceed the risks.
- *delaying in giving antivenom in district hospitals until victims are transferred to referral hospitals.* Antivenom should be given as soon as it is indicated to prevent morbidity and mortality. District hospitals should stock important antivenoms and must be equipped with facilities and staff to provide safe monitoring and care during the antivenom infusion.
- *giving polyvalent antivenom for envenoming by all type of snakes.* Polyvalent antivenom does not cover all types of snakes, e.g. Sii polyvalent (imported from India) is effective in cobra and some kraits envenoming but is not effective against Malayan pit viper. Refer to manufacturer drug insert for details.
- *giving smaller doses of antivenom for children.* The dose should be the same as for adults. Amount given depends on the amount of venom injected rather than the size of victim.
- *giving pretreatment with hydrocortisone / antihistamine for snakebite victims.* Snakebites do not cause allergic or anaphylactic reactions. These medications may be considered in those who are given ANTIVENOM.