**Supplementary file S1**

**Clinical and pathophysiological disturbances caused by snake venoms 1, 2-6**

**[H1] Viperidae** [including true Old World vipers and adders (Viperinae), and Asian pit-vipers, mamushis, habus and New World rattlesnakes, moccasins (cottonmouth and copperhead), bushmasters and lanceheads (Crotalinae)]

[H2] Classic syndrome

* Local: immediate radiating pain and rapidly-extending tender swelling with hot inflammatory erythema and lymphangitic lines, usually evident within two hours of the bite, prolonged bleeding from fang puncture wounds, bruising (ecchymosis), blistering (bullae), superficial soft tissue and muscle necrosis and secondary infection (cellulitis or abscess), and tender regional lymph node enlargement (Fig 6).
* Systemic: early syncope and collapse with transient loss of vision and consciousness, hypotension and shock, cardiac tachy- and brady- arrhythmias, severe bleeding diathesis, spontaneous systemic bleeding from nose gums, respiratory, gastrointestinal and genitourinary tracts, and sites of recent trauma or healing wounds, sub-arachnoid, cerebral, and ante- or post- partum haemorrhages, abortion and fetal death (Fig 6).

[H2] Variant syndromes (symptoms in addition to those above) associated with envenoming by some species:

* Early ‘anaphylactic’ (autonomic) symptoms (urticaria, angioedema, shock, sweating, vomiting, diarrhoea): e.g. bushmasters (*Lachesis*),1 Palestine viper (*Daboia palaestinae*),7 European adder (*Vipera berus*).8
* Acute kidney injury (AKI): e.g. Russell’s vipers (*Daboia*),9 and lance-headed vipers (*Bothrops*). With South American rattlesnakes (*Crotalus durissus terrificus***)1, 10** this is associated with rhabdomyolysis and withRussell’s vipers (*Daboia*), desert horned viper (*Cerastes cerastes*),11 andhump-nosed pit-viper (*Hypnale*)12 it is associated with microangiopathic haemolysis.12–
* Generalised increase in capillary permeability and acute/chronic pituitary/adrenal failure: *Daboia*.9,13,14 (Fig 6).
* Neuro-myotoxicity: e.g. *Daboia russelii*,15 Asian pit-vipers (*Gloydius*), *Crotalus durissus terrificus*,1 some populations of European asp vipers (e.g. *V. aspis, V. ammodytes*); with fasciculations (“myokymia”) - some North American rattlesnakes (e.g. *Cr. oreganus helleri, Cr. horridus, Cr. scutulatus*)16; with hyponatraemia and anosmia - berg adder (*Bitis atropos*).**17**
* In situ arterial thrombosis (causing ischaemic infarcts in brain, kidney, lungs, heart or elsewhere): e.g. Lesser Antilles pit-vipers (*Bothrops lanceolatus* and *B. caribbaeus*),18 terciopelo (*B. asper*),19 Russell’s vipers (*Daboia*),20 puff adder (*Bitis arietans*) (Paul Rollinson, Ngwelazana, South Africa, personal communication), *Hypnale*.

**[H1] Elapidae** (elapids) including cobras, kraits, mambas, coral snakes, Australian and Oceanian venomous snakes, and sea-snakes

[H2] Classic neurotoxic syndrome:

* Local: absent to moderate pain, paraesthesiae and local swelling, without blistering or necrosis.
* Systemic: flaccid paralysis is first evident as bilateral ptosis and external ophthalmoplegia (Fig 6) with dilated pupils, descending to involve muscles innervated by lower cranial nerves, neck flexors, bulbar, respiratory, trunk and limb muscles. Pooling of secretions in the pharynx, loss of the gag reflex, dyspnoea, declining ventilatory capacity, “paradoxical” abdominal respiration, use of accessory muscles and cyanosis are ominous signs of impending bulbar and respiratory paralysis. Paralysis is reversible in some cases by anticholinesterase drugs or specific antivenoms, and in all cases it is recoverable with time, provided that assisted pulmonary ventilation is adequate.

[H2] Variant syndromes (symptoms in addition to those above) associated with envenoming by some species:

* Severe local envenoming with immediate radiating pain and rapidly-extending tender swelling, blistering (bullae), superficial soft tissue necrosis with “skip lesions” and secondary infection, tender regional lymph node enlargement: African spitting cobras (Fig 6) and Asian spitting and non-spitting cobras (*Naja*).21
* Autonomic over-activity and fasciculations: Mambas (*Dendroaspis*).2
* Severe crescendo abdominal pain resembling renal or biliary colic: Indian krait (*Bungarus caeruleus*).22
* Excruciating pain radiating up the bitten limb: some coral snakes: some *Micrurus* species (*M. lemniscatus, M. tener*).23
* Rhabdomyolysis causing acute kidney injury: true sea-snakes (Hydrophiinae),24 greater black krait (*Bungarus niger*) and some other kraits,25 Indian spectacled cobra (*Naja naja*), some coral snakes (*Micrurus*),26 some Australian and Oceanian elapids (e.g. *Acanthophis, Oxyuranus, Pseudechis, Pseudonaja*).27
* Microangiopathic haemolysis causing haemolytic-uraemic-like syndrome (HUS) and acute kidney injury: Australasian and Oceanian elapids such as *Pseudonaja, Oxyuranus*.28
* Hyponatraemia: some kraits (*Bungarus candidus, B. multicinctus*).29-31
* Spontaneous bleeding and coagulopathy: some Australasian and Oceanian elapids.4,6,32
* Ophthalmia from venom spat into the eyes by spitting elapids - African and Asian spitting cobras (*Naja)*, and South African rinkhals (*Hemachatus haemachatus*).33 Intensely, painful chemical conjunctivitis with lacrimation and swelling of eyelids, risk of corneal ulceration, anterior uveitis, and secondary infection leading to permanent blindness.

**[H1] Colubroidea or Colubridae (*sensu lato*) back-fanged snakes**34, 35

African boomslang (*Dispholidus typus* Colubridae) and twig snakes (*Thelotornis* Colubridae)2; and Asian red-necked keelback and yamakagashi (*Rhabdophis* Natricidae)3have caused fatal envenoming. Local envenoming is usually trivial. Nausea, vomiting, colicky abdominal pain, and headache are followed by slowly or late evolving bruising (ecchymoses), systemic bleeding and coagulopathy causing intra-abdominal or intra-cranial haemorrhages and acute kidney injury. South America green racer (*Philodryas olfersii* Dipsadidae) and possibly other members of this genus can cause systemic haemostatic disturbance with ecchymoses distant from the bite. European Montpellier snake (*Malpolon monspessulanus* Psammophiidae) may cause mild neurotoxic envenoming.

An increasing variety of Colubroid species is reported to cause local pain, swelling, bruising, local bleeding, regional lymphadenopathy and mild constitutional symptoms. These species include *Boiga dendrophila* (Colubridae), *Rhamphiophis oxyrhynchus* (Lamprophiidae), *Leptodeira frenata* (Dipsadidae), and *Hydrodynastes gigas* (Dipsadidae).

**[H1] Atractaspidinae** (Lamprophiidae) burrowing asps (stiletto snakes or burrowing adders/vipers)

These are common causes of nocturnal bites in many parts of Africa and the Arabian Peninsula. *Atractaspis microlepidota*, *A. irregularis*, and *A. corpulenta* have caused fatal envenoming.

Local pain, swelling, blistering, necrosis, tender enlargement of local lymph nodes, local numbness, and paraesthesiae, fever. Rarely vomiting, profuse salivation, other autonomic symptoms, coma, anaphylaxis, ECG abnormalities and collapse.2

**Supplementary file S2**

The three-dimensional models presented in Fig 4 and illustrated by the crystallographic or NMR structures of some members of each protein family have been generated from the following spatial coordinates: 3DSL, PIII-snake venom metalloproteinase (SVMP) bothropasin from the jararaca, *Bothrops jararaca*; 1ND1, PI-SVMP BaP1 from the fer-de-lance *Bothrops asper*; 1TGM, monomeric snake venom phospholipase A2 (PLA2) from the Russell's viper *Daboia russelii*; 3R0L, heterodimeric β-neurotoxic PLA2 crotoxin from the venom of the South American rattlesnake *Crotalus durissus terrificus*; 1OP0, snake venom serine protease (SVSP) Dav-PA from the Chinese moccasin *Deinagkistrodon acutus*; 1IJC, three-finger toxin (3FTx) bucandin from the venom of the Malayan krait (*Bungarus candidus*); 1DTX, dendrotoxin (DenTx) from the green mamba (*Dendroaspis angusticeps*); 1IXX, coagulation factors IX/X-binding C-type lectin-like (CTL) protein from the habu snake *Protobothrops flavoviridis*; 3MZ8, cysteine-rich secretory protein (CRISP) natrin from the Chinese cobra *Naja atra*; 2IID, L-amino acid oxidase (LAO) from the Malayan pitviper *Calloselasma rhodostoma*; 4GV5, myotoxin (Myo) crotamine from the South American rattlesnake *Crotalus durissus terrificus*. Structural models were rendered with UCSF Chimera36. The photographs on the left of figure 4 are reproduced with permission of the photographers or under CC BY-NC 3.0 license, correspond, from top to bottom, to the following taxa: *Bothrops asper* (© Mahmood Sasa, Instituto Clodomiro Picado, Costa Rica), *Bothriechis bicolor* (© Manuel E. Azevedo, Universidad de San Carlos de Guatemala), *Crotalus durissus terrificus* (© Rodolfo Capdevielle, http://www.serpientes-snakes.com.ar), *Vipera aspis aspis* (© Felix Reimann, Wikimedia Commons), *Ophiophagus hannah* (© Freek J. Vonk, Naturalis Biodiversity Center, NL), *Pseudechis papuanus* (© David J Williams, University of Melbourne, Australia), *Micrurus tener* (© Chris Grünwald, Loma Alta, TX, USA), *Hydrophis platurus* (© William Flaxington, University of California, Berkeley, USA).

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