The biology of dangerous snakes: systematics and venom evolution. R. S. Thorpe, J. Daltry, W. Wuster, A. Malhotra and N. L. Thorpe (School of Biological Sciences, University of Wales, Bangor, Gwynedd LL57 2UW, U.K.).

The evolutionary biology of dangerous snakes can provide an important background to medical and toxicological studies as different species, and even geographic races and populations, may have different venoms. Snake systematics are not well understood so many are in a state of confusion exist. Four examples are given. (1) An example of a situation where classical taxonomy has obscured the existence of many species is provided by the Asian cobra, where instead of one species (Naja naja), multivariate and molecular studies have shown that there are nine (others remain to be described). (2) Numerous subspecies may be erected on inadequate, superficial study. These subspecies are almost always worthless and an example of this is provided by the very dangerous snake Daboia russelli. The five conventional subspecies of this snake are not supported by comprehensive multivariate analysis, or preliminary molecular studies. (3) An example of a cryptic species of venomous snake is provided by Trimeresurus where many species are superficially similar, but have different isoelectric venom profiles. Some species, i.e. T. stejnegeri and T. popeorum, are said to be only distinguishable by male hemipenal structures. However, DNA studies have shown these species to be distinct and not even closely related. (4) Calloselasma rhodostoma provides a model system in which to study the causes of venom evolution. There is ontogenetic, sexual and geographic variation in the isoelectric profile of venom. The geographic variation could be due to selectively neutral change and/or natural selection for specific environmental factors. Advanced simultaneous (partial regression) Mantel tests reveal that overall profile is not significantly related to neutral change (represented by patristic distances derived from enhanced RFLPs), seasonality, gender, size or geographic proximity, but is significantly associated with dietary differences.


There are currently five distinct subspecies of Russell's viper found erratically distributed from Pakistan (Daboia russelli russelli) in the west to China (D. russelli siamensis) and Taiwan (D. russelli formosensis) in the east. These snakes are clinically best known for their action of producing coagulation abnormalities (via the activation of factors V and X). However, there are some major differences between the symptoms produced by the different subspecies, such as acute renal failure, which is most frequently found in Burm and Sri Lanka. In Sri Lanka, however, there is also a neurotoxic action associated with bites by Daboia russelli pulchella. In Sri Lanka this snake kills more people than does any other species, with symptoms attributed to neurotoxicity being the most common sign of systemic envenoming. The two antivenoms used in Sri Lanka are imported from India and as a result raised against the native snakes of India (e.g. D. russelli russelli). This has resulted in the relative ineffectiveness of antivenoms such as those produced by the Hoffkine Biopharmaceutical Corporation which is the major antivenom used in Sri Lanka. At Therapeutic Antibodies Inc. (TAB) we have developed a low-cost ovine monospecific Fab antivenom raised against D. russelli pulchella venom that is papain free, using a new solid-phase papain digestion system. In order to assess this new antivenom, an in vitro assay demonstrating the neurotoxic action of this venom was required. The isolated mouse left phrenic nerve–pediatric preparation was chosen, and by the application of 12.5 mg/litre of D. russelli pulchella venom, it was possible to distinguish clearly between the neurotoxic and myotoxic actions of this venom over the course of a 3 hr period. The venom produced a definite neurotoxic action at lower doses (12.5–25 mg/litre), but at higher doses (50 mg/litre) the neurotoxic action became almost indistinguishable from the rapid myotoxic action. By premixing either the Hoffkine (1250 mg/litre) or TAB (500 mg/litre) antivenoms with 25 mg/litre of D. r. pulchella venom it was possible to show that the TAB antivenom was considerably better at neutralizing neurotoxicity using a dose of 1/4 that of the Hoffkine antivenom. In vivo neutralization using the standard mouse ELD₅₀ test showed that the TAB antivenom produced an ELD₅₀ of 1.5 mg/mouse (against 5 x ELD₅₀ = 1 mg/mouse); however, the Hoffkine product proved totally ineffective at the maximum dose of 16 mg/mouse. Owing to the inherently limited nature of biosynthetic, in the near future the new TAB antivenom will be compared clinically with the existing antivenoms found in Sri Lanka.