



Antivenom for snakebite envenoming in Sri Lanka: The need for geographically specific antivenom and improved efficacy



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ABSTRACT

Sri Lanka is a tropical developing island nation that endures significant economic and medical burden as a result of snakebite envenomation, having not only a high prevalence of envenomations, but also one of the highest incidence rates (200 snakebites/100,000 people/year) of venomous snakebite in the world (Kasturiratne et al., 2005). Ironically, the very snakes responsible for this human morbidity and mortality are a valuable biomedical and ecological national resource, despite the medical and economic consequences of envenomation. Currently, no snake antivenom is produced using venoms from native Sri Lankan snakes as immunogens, and there is a true need for an efficacious Sri Lanka, poly-specific snake antivenom. An approach to fulfilling this need via combining the scientific, technological and economical resources from Costa Rica and the United States with the knowledge and talent of Sri Lankan official governmental agencies, legal counsels, environmental, medical and veterinary academic institutions, and religious and cultural leaders has been initiated, coordinated and funded by Animal Venom Research International (AVRI), a nonprofit charity. This bridging of nations and the cooperative pooling of their resources represents a potential avenue for antivenom development in a developing country that suffers the consequences of few specific resources for the medical management of venomous snakebite. The desired final outcome of such an endeavor for Sri Lanka is, most importantly, improved medical outcomes for snakebite patients, with enhanced and expanded science and technology relating to snake venoms and antivenoms, and the collateral benefits of reduced economic cost for the country.

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1. Introduction

Despite the recognition of snakebite as a significant neglected public health issue by the World Health

Organization, and other agencies, progress to resolve the problem has been limited in tropical ecozone regions of the world where it is needed most (WHO, 2010; Gutiérrez et al., 2011). Additional efforts by toxinology leaders/scientists, and the recently established Global Snakebite Initiative (Williams et al., 2010, 2011) are in current pursuit of resolution, but are constrained by limited economic resources. In addition, the lack of recognition of the magnitude of this problem by regional and national health authorities in

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many parts of the world further complicates the solution of this problem (Williams et al., 2010; Gutiérrez, 2012).

Venomous snakebite patients all too frequently receive inadequate treatment due to a lack of antivenom availability, and in many instances due to the unavailability of antivenom with good pharmacotherapeutic effectiveness (Abubakar et al., 2010; de Silva et al., 2002; Theakston and Warrell, 2000; Gutiérrez, 2012). The native people of Sri Lanka suffer nearly 40,000 venomous snakebites annually, and the country has one of the highest snakebite mortality rates in the world (Sri Lankan Ministry of Health, 2008). The difficulty of treating snake envenomated patients with less than optimal therapy is frustrating for medical professionals, and of considerable health costs and personal loss to the patient.

Sri Lanka has been historically plagued with human suffering from venomous snakebite. The problem still persists, for it was estimated that 143,750 vials of antivenom would have been required to provide adequate treatment for the 37,100 snakebite patients in the year 2000 (Kasturiratne et al., 2005). Two years later, in 2002, an appeal for an effective, affordable antivenom with a minimal adverse reaction profile was made (de Silva et al., 2002), and recent studies have indicated that there is a continued need for developing higher quality antivenoms with greater efficacy (Isbister et al., 2012). However, despite collaborative efforts, the quest for a new, improved antivenom has not progressed to production and clinical use. Currently available antivenoms for Sri Lanka snakebite patients are produced and manufactured using the venoms of cobra (*Naja naja*), Russell's viper (*Daboia russelii*), common krait (*Bungarus caeruleus*), and the saw-scaled viper (*Echis carinatus*) from mainland Asia rather than with the venoms of these species from Sri Lanka's native snakes. Further, the hump-nosed viper (*Hypnale* spp.), common in Sri Lanka and Southeast Asia, is not included in the immunization mixtures used for the production of these antivenoms. Thus, the fact that antivenoms currently distributed in Sri Lanka do not include the *Hypnale* venom antigens, and are prepared by immunizing horses with venoms from other regions that are likely to differ from those of Sri Lankan snakes, represents a problem for the treatment of envenomations in this country (Sellaheewa et al., 1995). In addition, antivenom-induced adverse reactions are frequent, may be life-threatening, and often require further management (Gawarammana and Keyler, 2011; de Silva et al., 2011).

Sri Lanka's need for an optimally efficacious antivenom continues as antivenom is currently the most effective treatment for venomous snakebite globally (WHO, 2010), and it may be the most cost-effective treatment as well (Brown and Landon, 2010). Recent continued efforts, and the process to accomplish development of a poly-specific antivenom for the country using the venom from Sri Lanka's indigenous medically important snakes are discussed with respect to a currently active collaborative process to achieve this goal.

2. Epidemiology of snakebite in Sri Lanka

The island nation of Sri Lanka has a land area of 62,705 km², and lies in the Indian Ocean within the tropical

zone just north of the equator and south of the Indian peninsula. Ancient civilizations were predominantly agricultural and the fabric of human life was inexorably woven with the natural habitat of venomous snakes; and human encounters with serpents commonly resulted in envenoming, a frequent tragic medical emergency in that era. Despite the passing of considerable time, and a rapidly progressing technological world, Sri Lanka suffers this major medical problem still today (Kasturiratne et al., 2008). Ministry of Health data show that occurrence of snakebite covers all Districts of the country, and deaths continue to occur in most Districts; in addition, regional geographic variation in the distribution of venomous snakes is reflected by the distribution pattern of the number of snakebites geographically (Fig. 1) (Sri Lankan Ministry of Health, 2008). In the year 2007 there was a total of 39,321 hospital admissions from snakebite, and 91 in-hospital deaths were reported (Sri Lanka, Health Care at a Glance, 2008). However, it is likely that this is a gross underestimation of the actual reality. Deaths occurring outside hospitals are also inaccurately reported. Mortality in the country is one of the highest in the entire world. Epidemiological studies in the past have revealed 6 deaths per 100,000 population (de Silva and Ranasinghe, 1983). In 2008 there were 58 deaths out of 38,683 reported snakebites, males suffered 1.5 times more bites than females, and reported deaths were three times greater in males (Sri Lankan Ministry of Health, 2008). Although deaths have appeared to be trending downward in recent years, they continue to be a significant source of regional mortality (Fig. 2). Owing to inherent flaws and limitations of reporting, the magnitude of the problem of snakebite is likely to be far greater than what is reflected by the available limited statistical figures.

Sri Lanka provides favorable habitat to 96 species of land snakes, and its shores to 15 species of aquatic snakes. In the hill-country the majority of encounters with snakes have revealed bites are due to non-venomous species (K. Kularatne et al., 2011). There are 6 species of land snakes that are considered to be highly venomous or deadly venomous: the Sri Lankan cobra (*N. naja*), common krait (*B. caeruleus*), Ceylon krait (*Bungarus ceylonicus*), Russell's viper (*D. russelii*), hump nosed viper (*Hypnale* spp.), and the saw scaled viper (*E. carinatus*). The most common venomous snakebites across the country as a whole are due to the hump-nosed vipers (de Silva, 1981; Seneviratne et al., 2000; Kasturiratne et al., 2005). *Hypnale* is one of two crotalinae genera in Sri Lanka, *Trimeresurus* being the second. Taxonomic revision of the genus *Hypnale* was completed in 2009, and it was concluded that *H. walli* was synonymous with *H. nepa*, and that *H. zara* was different than *H. hypnale*. Hence, all three species of hump nosed vipers are now recognized (Maduwage et al., 2009). The green pit viper (*Trimeresurus trigonocephalus*) is a species that prefers mountainous habitats, bites are rare, and adverse clinical outcomes following bites are not known in the published literature. *B. ceylonicus* is a true endemic snake species that is geographically confined to the central hilly areas of the country and resembles *B. caeruleus*. However, they are not commonly encountered due to their nocturnal and timid behavior, and reported bites in Sri

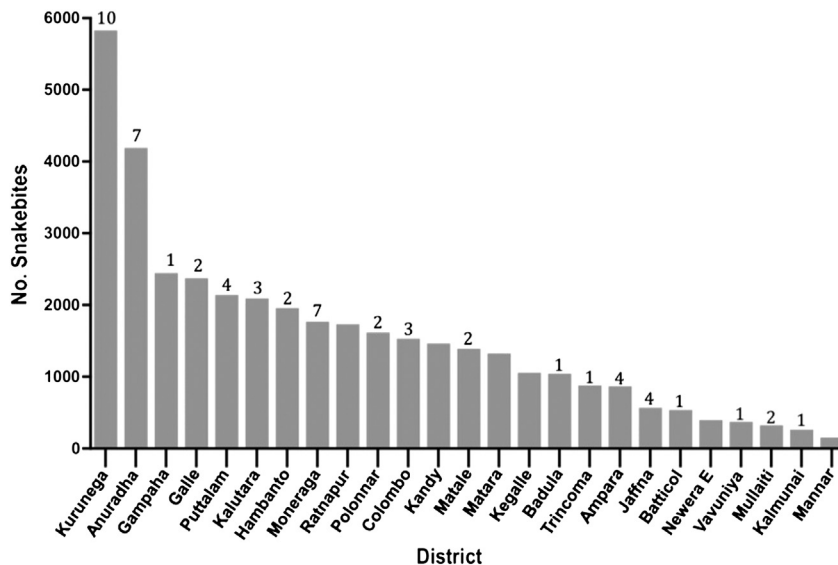


Fig. 1. Sri Lanka 2008 snakebite statistics for the country prioritized by decreasing number of cases per District. Numbers on bar caps represent the number of deaths (Sri Lankan Ministry of Health, 2008).

Lanka are very rare (de Silva et al., 1993). The hierarchy of genera responsible for envenomed patients requiring hospitalization, for the entire country of Sri Lanka, ranges from *Hypnale*, *Daboia*, *Bungarus*, and *Naja*, to *Echis* (Kasturiratne et al., 2005). Of all snakebite related deaths 97% are due only to three species: *N. naja*, *B. caeruleus*, and *D. russelii* (de Silva and Ranasinghe, 1983; de Silva et al., 2002; Kasturiratne et al., 2005).

Epidemiological significance with venomous snakebites in Sri Lanka relates to the different peneplains and climatic zones that support a diversity of fauna and flora in the island, with a resultant wide variation in the distribution of the different species of venomous snakes. These epidemiological attributes need to be addressed and incorporated in the planning of therapeutic interventions and development of a true Sri Lanka poly-specific antivenom.

2.1. Ecosystem

Sri Lanka has been reported to be one of the most biologically rich herpetofaunal countries in the world (Myers

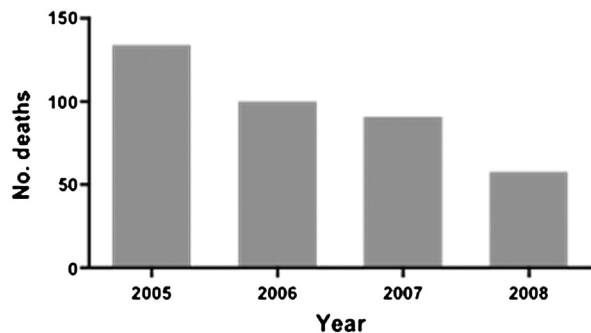


Fig. 2. Deaths from venomous snakebite in Sri Lanka 2004–2008, showing a downward trend over the four-year period (Sri Lanka, Health at a Glance, 2008).

et al., 2000; de Silva, 2006). Regional variation in rainfall and vegetation determine species distribution and there is correlation with these in the incidence of venomous snakebites. Dry, wet and intermediate climatic zones constitute 65%, 23% and 12% of the total land area of the island. There are also three peneplains, ranging from sea level to 270 m, 270 m to 1060 m, and from 910 m to 2420 m above sea level. The lowest peneplain constitutes the largest geographical distribution (de Silva and Ranasinghe, 1983; de Silva, 2005).

The island's rich and thick vegetation dissects to four forest types that have dwindled due to the development of agro-ecosystems over several thousands of years, resulting in the development and expansion of a selectively advantageous natural habitat for highly venomous snakes. The distribution, and hence the incidence of bites by the different species of snakes, is influenced to a large extent by a year-round favorable climate and vegetation cover. The accelerated Mahaweli program in 1978 resulted in the clear cutting of nearly 130,000 ha (1300 km²) of forested land. As a result the incidence of snakebite among the subsequent settlers in these areas increased, and human-related activities further augmented the abundance of rats, mice, amphibians, reptiles and other ideal food prey for displaced venomous snakes.

In the recent decades increased urbanization has necessitated the expansion of towns, which has led to further human encroachment into the snakes' environmental and terrain habitats (de Silva, 2006). Today, these continually evolving changes in the social dynamics of the country have resulted in snakebites occurring in urban and suburban areas that are not predominantly agricultural.

2.2. Occupational and social attributes

Risk of snakebite is closely correlated with occupation in Sri Lanka, being most common among those engaged in

agricultural pursuits such as farmers, gardeners and security duties (e.g. guarding plantations, paddy fields, and other cultivations). Consequently, there is an increase in the incidence of Russell's viper bite during paddy harvesting and paddy sowing (Kularatne, 2003). Krait bite is common among the *chena* (slash and burn) cultivators who live in watch huts and become vulnerable to nocturnal-biting kraits while guarding their fields. Sea snake envenomation has been reported only among fishermen during fishing or related activities. Gypsies and snake charmers have all been bitten while handling or attempting capture of venomous snakes. In general, adults and children living in rural villages frequently do not use foot ware, and snakebite is not uncommon; however, the majority of snakebite victims are adult males owing to their occupational predisposition (de Silva, 2005; Sellahewa, personal communication, 2012).

Climatic conditions in the North Central province of the country provide a favorable habitat for the common krait (*B. caeruleus*). Poor farmers who populate these areas and their impoverished dwelling conditions suffer a high incidence of krait bite. They live in wattle and daub huts and habitually sleep on the floor increasing the vulnerability to krait bite (de Silva, 2005; Sellahewa, personal communication, 2012).

Anatomical site of bites in the majority patients is below the knees. Walking barefooted on paddy field bunds, tank bunds, and foot-paths, and not using flashlights, are predisposing reasons for vulnerability of being bitten. The wearing of boots while working in paddy fields is considered to be unacceptable, uncomfortable, and impractical by most farmers and field workers (de Silva, 2005; Kularatne, 2003; Sellahewa, personal communication, 2012).

3. Etiology of venomous snakebite in Sri Lanka

Regional geographic variation in the distribution of venomous snake species and the distribution pattern of snakebites with certain species in the country also relate to human activities and behaviors associated with snake envenoming. Thus, environmental factors determine appropriate habitat for each snake species, and these same environmental factors influence the density of human activities in a given geographic region. When there is overlap or encroachment of environments, the competition between humans and snakes frequently results in medical consequences (Kasturiratne et al., 2005).

B. caeruleus is the primary krait species responsible for envenomations, and the species is widely distributed in the dry zone. Bites occur in the night while a person is often sleeping on the floor, and bites occur without any provocation. Consequently, krait bites have been inflicted on the unaware person on all parts of the body from head to toe, including even the genitalia (Ariaratnam et al., 2008a, 2009; Sellahewa, personal communication, 2012).

N. naja bites frequently occur near human dwellings and water reservoirs in the dry and intermediate zones of the country, with most bites occurring during the day (Ariaratnam et al., 2009). The bite site is usually to the lower limbs below the knees. These snakes bite only on provocation and most bites have occurred by accidental

treading directly on the snake. Many envenomations occur at the snakebite victim's home, and there have been accidental instances where cobras have fallen from the roof of thatched cottages and bitten the victim (Kularatne et al., 2009; Sellahewa, personal communication, 2012).

D. russelii bites are observed mostly in the dry zone, with most of the bites occurring during the early day and at dusk, when walking unprotected on footpaths and in paddy fields, or while clearing brush and shrubs (Ariaratnam et al., 2009). A distinct surge in the incidence of Russell's viper bites is observed during rice paddy harvesting. In the northern Anuradhapura region men more frequently (male:female = 5:1) suffer the consequences of envenomation than women, and the species is responsible for significant morbidity and mortality (Kularatne, 2003).

E. carinatus predominantly inhabits the dry arid zones where vegetation is sparse in the Northern and North Western provinces, and is the species responsible for the most common venomous snakebite in those regions. In a prospective, observational, hospital-based study done in the Jaffna hospital 45.6% of the bites were due to saw-scaled viper, with the majority having occurred to housewives, followed by school children and farmers. The majority of bites were to the feet (S.A. Kularatne et al., 2011). It has also been reported that most bites occur outside at night, and are sustained to the lower limbs from encounters while walking along footpaths (Gnanathanan et al., 2012).

Hypnale spp. are common in the wet zones. However, *Hypnale* spp. are ubiquitous in their distribution across all the three climatic zones, particularly in tea, rubber, and coconut plantations where hump-nosed viper bites are the most common of all the venomous snakebites (Ariaratnam et al., 2008b). Nearly two decades ago it was reported that the majority of people were bitten in the evening hours close to their dwellings, and the most frequent sites of bites were to the ankles and feet (Sellahewa and Kumararatne, 1994). A more recent prospective study also reports that *Hypnale* spp bites were primarily sustained to the lower limbs, but in contrast occurred during the daylight hours (Maduwage et al., 2013). *Hypnale* bites in the city of Kandy were reported to have involved the upper limb in 13 out of a total of 40 bites, and 61% of the bites occurred in home gardens to patients >15 years of age (K. Kularatne et al., 2011).

4. Primary envenomation clinical profiles

As discussed above, five snake genera (*Bungarus*, *Naja*, *Daboia*, *Echis* and *Hypnale*) in Sri Lanka are primarily responsible for envenoming leading to systemic toxicity. Elapid venoms induce predominantly neurotoxic manifestations, combined with local effects in the case of *N. naja*, whereas viperid venoms provoke local effects, bleeding, coagulopathy, cardiovascular shock and, in the cases of *D. russelii* and *Hypnale* spp, acute and chronic kidney damage (Herath et al., 2012).

B. caeruleus envenomation can rapidly lead to a classical occulo-facio-bulbar and respiratory muscle paralysis that requires mechanical ventilation in about half of all victims (Kularatne, 2002). Another important clinical presentation is deep coma with absent brain stem reflexes. These

complications are at least partly due to the presynaptic action of a neurotoxic phospholipase A₂ (β -bungarotoxin) present in the venom. The clinical manifestations are associated with delayed brain stem auditory and visual evoked potentials and abnormalities on electroencephalogram (Kularatne, 2002; Gawarammana et al., 2010).

N. naja envenomation predominantly results in local effects in about 80% of cases. Local reaction is severe in 33% of these patients. Some patients succumb to rapidly spreading skin and muscle necrosis. In contrast to *N. naja* bites in India, neurotoxicity following *N. naja* bites in Sri Lanka is less common (36%). Patients can develop respiratory paralysis, while few patients develop coagulopathy (12%) (Kularatne et al., 2009).

D. russelii envenomations typically progress to a well characterized constellation of signs and symptoms including coagulopathy in 77%, local swelling in 92%, acute kidney injury in 18% and neurotoxicity in 78% of the cases (Kularatne, 2003). Coagulopathy manifests with spontaneous bleeding from mucosal surfaces, hematuria and intracerebral bleeding. Typical neurotoxic complications include external ophthalmoplegia, ptosis and rarely respiratory failure (Kularatne, 2003; Seneviratne and Dissanayake, 2002). These complications are due to the presynaptic action of secretory phospholipase A₂ present in the *D. russelii* venom (Priatelj et al., 2008). *D. russelii* bites are known to produce ischemic cerebral strokes possibly due to its activation of clotting factors (Gawarammana et al., 2009). Hypopituitarism has also been reported following bites by *D. russelii* (Antonypillai et al., 2010).

E. carinatus envenoming results in local effects in approximately 73% of patients, and a majority of patients (92%) develop coagulopathy. Acute kidney injury is rare (S.A. Kularatne et al., 2011). In a recently reported series of 48 cases, 65% had local envenoming signs, and incoagulable blood as a result of consumptive coagulopathy was observed in 71% of patients (Gnanathasan et al., 2012).

Hypnale spp envenomation frequently results in local clinical manifestations characterized by pain, swelling, induration, haemorrhagic blistering in the bitten site, and regional lymphadenopathy (Sellahewa and Kumararatne, 1994; Ariaratnam et al., 2008b; Joseph et al., 2007). Extensive gangrene development following bites to digits is rarely reported (Kularatne and Ratnatunga, 1999). Species-specific description of effects of *Hypnale* revealed that non-specific systemic effects are common following envenomation by all *Hypnale* species. *H. hypnale* envenomation leads to severe local envenoming in 13%, coagulopathy in 5% and acute renal failure in 1% of the cases, whereas *H. zara* envenomation leads to severe local envenoming in 25% of the cases, and deaths are rare (Maduwage et al., 2013, 2011).

Antivenom – the need for Sri Lanka geographically specific antivenom

The epidemiology, etiology, and medical significance of snake envenomation in Sri Lanka are all factors to be considered in antivenom design and development. However, despite previous (Ariaratnam et al., 1999) and current efforts by organized agencies and groups to develop

improved antivenoms for Sri Lanka, the greatest hurdle to overcome has been the lack of adequate economic support. Thus, efforts for improved antivenom development need to be continued, and modes of action may require alteration to the structure and process of more traditional models to achieve this goal. To this end, international partnerships constitute a valuable model to strengthen these efforts. The long-term objective should be the sustainable production of a poly-specific antivenom generated against the venoms of Sri Lankan snakes, and the accessibility of such antivenom to the public health system of the country.

6. A model for nonprofit charity and public institutional partnerships

It is widely recognized that there is a need for intervention in developing countries where the lack of resources causes suffering from conditions either long since remedied or non-existent in industrialized nations (Trouiller et al., 2001, 2002; Stirner, 2008; Hotez, 2011). The World Health Organization currently lists 17 conditions as ‘neglected tropical diseases’ (NTDs) requiring action, of which venomous snakebite has been recently included (WHO, 2012). However, despite acknowledgment of neglected disease issues, few advances have been made toward remediation. An article by Trouiller et al. (2002) written a decade ago stressed the lack of safe, effective and affordable pharmaceuticals aimed at neglected diseases and found a tremendous imbalance between research and development of drugs for NTDs versus other conditions. Their research identified a “13-fold greater chance of a drug being brought to market for central-nervous-system disorders or cancer than for a neglected disease.” Nearly a decade later, Cohen et al. (2010) reassessed the situation, covering the period investigated by Trouiller et al. (1975–1999) and including the period from 2000 to 2009. Cohen and colleagues claim the years evaluated by Trouiller et al. were not as grievous as stated, with 46 drugs approved for NTDs versus the 16 out of 1393 total drugs cited in that work. In addition, Cohen et al. argue that although some progress has been made, only certain well-funded initiatives have benefited. Of the \$2.5 billion contributed to neglected diseases during their study period, 80% of the funding was used toward HIV/AIDS, tuberculosis and malaria, while other conditions continued to remain generally underfunded.

The finding of only 46 products out of 1393 still proves a gross inequity. Moreover, the disparity in levels of funding for certain diseases and conditions over others leaves a tremendous gap in response to the issues. New and innovative approaches are required to make progress toward solving the problems with NTDs, snakebite envenomations included. A number of interventions and strategies are currently in effect attempting to close the gap between resources and areas of need including: policy interventions, government action, private industry involvement and public-private partnerships (PPP). While all of these means have achieved some successes, they are not without difficulties. Private industry alone has had

little incentive to assist with neglected diseases, where minimal to no commercial returns are expected. Although some multinational companies have contributed to NTDs, there is usually an underlying long term motive: protection of reputation under public pressure, trends in social responsibility, or strategic considerations to position themselves for potential new markets (Moran, 2005). The majority of multinational companies working on neglected disease R&D are doing so in PPPs, where the public funder subsidizes costs and shares the risks. It has been said that continued success with PPPs is likely to depend on a health policy environment that promotes the appropriate levels of engagement from all participants (Gustavsen and Hanson, 2009).

Here we propose a sustainable solution to the issue of snakebite envenomation through a nonprofit charity and public institutional partnership. The advantage of a partnership of this kind is the elimination of a for-profit motive among collaborators and true emphasis on the issue to be solved. The main disadvantage is assurance of continued public funding sources, but this could be circumvented by innovative fund-raising strategies by the involved organizations. Collaborations of this type have not been widely explored and only two are known to the authors at this time, namely the Sabin Vaccine Institute and the Infectious Disease Research Institute (Hotez, 2011). Both of these nonprofit organizations are working with university laboratories and public sector manufacturers for vaccine development in Latin America with purported success. A similar collaborative model has emerged for the Sri Lanka Antivenom Development project.

7. A tripartite partnership with a common goal

In this project, a public nonprofit charity from the USA, a public university from Costa Rica devoted to research and antivenom manufacture, and public institutions in Sri Lanka, have constituted an international partnership aimed at the development and long-term production of a poly-specific antivenom for treating snakebite envenoming in Sri Lanka (Fig. 3).

Nonprofit Charity and Public Institutional Partnership Model

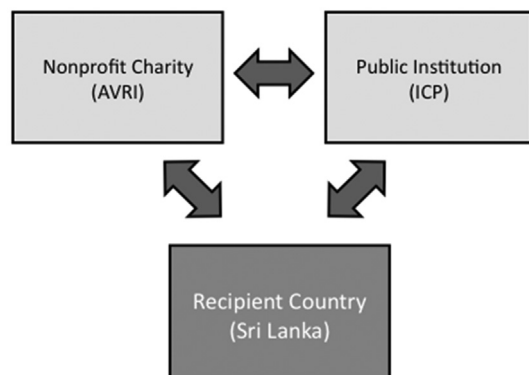


Fig. 3. Tripartite partnership model: international collaborational scheme.

7.1. Public nonprofit

The public nonprofit charity, in this case Animal Venom Research International (AVRI), has developed a network of collaborators within and outside of the country in need or 'recipient country' (Sri Lanka). AVRI has sufficient interaction with Sri Lanka health care professionals and related personnel to appreciate an accurate understanding of the country's problems and needs with respect to the medical significance and consequences of snake envenoming. Furthermore, AVRI has established resources on the ground through time built relationships and associations that an outside organization may be unable to access. Members of AVRI are also cognizant of the socio-cultural and religious climate of the country and how to operate appropriately. Within Sri Lanka, AVRI has worked in cooperation with the University of Peradeniya to secure necessary permissions for the project. In addition, AVRI has identified and brought together partners and key stakeholders to collaboratively form agreements toward implementing the project. As a nonprofit public charity, AVRI is actively involved in fund-seeking to support research and development and cover program costs. The organization works in an operative capacity, building the necessary infrastructure, and will oversee quality control of the project as it moves forward. AVRI will ensure sustainability through continued oversight and program development. To date AVRI has successfully acted upon the identified need of a solution for venomous snakebite by: securing permits to build a serpentarium to house the snakes necessary for venom collection needed for antivenom production; organizing field collection of the snakes, and serpentarium staff. Serpentarium staff was trained in Sri Lanka by AVRI consultants from the Kentucky Reptile Zoo, United States, to safely and properly extract venom. Venom extraction has been conducted and the venom lyophilized through partnership with the University of Peradeniya, Sri Lanka, for forwarding to Costa Rica.

7.2. Public academic institution

The public academic institution, Instituto Clodomiro Picado (ICP) of the University of Costa Rica, will move the antivenom project to the next phase, i.e. research and development of an antivenom product. ICP has long-standing experience in scientific research on snake venoms, in the development of antivenoms for Latin America and other regions and in the preclinical assessment of antivenom neutralizing ability (Gutiérrez and Rojas, 1999). As an academic institution with proven success in antivenom research and production, ICP will conduct the R&D for creation of a species- and geographic-specific antivenom formulated against Sri Lankan snake venoms. ICP will further assist by providing the skills and knowledge base necessary to transfer the technology of antivenom development through AVRI to Sri Lanka. ICP will also contribute by mentoring and training of staff through each phase of the technology transfer program, building project capacity. Collaboration between ICP and AVRI via formulated agreement will allow for the sharing of resources, and jointly represent a strong unit for joint fund-seeking.

7.3. Recipient country

Sri Lanka, as the recipient country, will support the project through supplying the local educated workforce and materials, as well as through the involvement on a technology transfer process with the long term goal of establishing local antivenom production in Sri Lanka. The inclusion of Sri Lankan academic institutions and researchers will guarantee the project sustainability and the strengthening of the local scientific and technological capacity. Government cooperation and approval are imperative for smooth operations. The University of Peradeniya in Sri Lanka is currently working with AVRI to ensure that knowledge of worker and legal needs are met.

7.4. Outcomes for recipient country

The positive outcomes for the recipient country will include the alleviation of suffering through provision of resources, and eventually the access to a quality and life-saving antivenom at a reasonable cost, manufactured in the country. Moreover, the project will build indigenous innovation capacity and increased exchange of academic knowledge between Sri Lankan and foreign institutions. In addition, the country will benefit economically through not expending resources to purchase products from an outside source and increased self-reliance in a sustainable program.

8. Conclusion

Snakebite is a major medical problem in Sri Lanka responsible for significant morbidity and mortality. It affects predominantly the poor rural community with under reporting of the true incidence of snakebite. Mortality has declined over the last two decades owing to better patient education, changes in the health seeking behavior, improvements in medical attention to victims, and better access to medical intensive care facilities. Nevertheless, an unacceptably high death rate still prevails mainly due to the non-availability of an optimally efficacious and safe antivenom. Thus, it is timely to advance current collaborative efforts to develop and produce a poly-specific antivenom, derived from the venom of indigenous medically important Sri Lankan snakes. These collaborations demonstrate the relevance and potential impact of science and technology to medicine with a humanitarian benefit.

Ethical statement

No research animals were required or used for the provision of data presented in the manuscript. All components of the submitted manuscript have been gathered with integrity, and there are no individual persons that were patients, and no breaches of confidentiality.

Conflict of interest

Nothing to declare.

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