Snake bite: Prevention is best but antivenom treatment must also be improved

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Around 5.5 million people are bitten by snakes each year, resulting in some 400,000 amputations and between 20,000 and 125,000 deaths. Despite this, the burden of human suffering caused by snake bite remains largely invisible to the global health community. A Seminar and linked Viewpoint in this week's *Lancet* discuss how educating communities on how to avoid snake bite, or providing them with protective footwear, might reduce the risk. Yet when a bite occurs, the correct antivenom and the right training about how to use it can be lifesaving. Antivenom technologies and their use need to be improved, since organised training programmes in the rural tropics are virtually non-existent.

The Seminar is by Professor David A Warrell, University of Oxford, UK (who is also a co-author on the Viewpoint). He says: "For a long time, the specialty has had an inadequate evidence base, uncritical attitudes to results that scarcely deserved consideration as data, rigid adherence to outworn traditional ideas, poor understanding of pathophysiological mechanisms, and inadequate discussion and collaboration with laboratory scientists."

Venomous snakes are widely distributed in almost every country between latitudes 50°N and 50°S in the western hemisphere and 65°N (Scandinavia) and 50°S in the eastern hemisphere. Sea snakes are found in the Indian Ocean and Pacific Ocean between latitudes 30°N and 30°S. On land, venomous snakes have been found from sea level up to altitudes higher than 4000 m in the Americas and Himalayas, and sea

snakes dive to depths greater than 100 m in the oceans.

The venom of any species might contain more than 100 different toxic and non-toxic proteins and peptides, and also non-protein toxins, carbohydrates, fats, amines, and other small molecules. The toxins of most importance in human envenoming include those that affect the nervous, cardiovascular and haemostatic systems, and cause tissue death. Snake venom neurotoxins block or excite peripheral neuromuscular junctions by acting at various sites.

In 2009, snake bite was recognised for the first time by WHO as a neglected tropical disease. In tropical countries, it is largely an occupational disease for agricultural workers, and, as a result, can affect food production. Productive young men and women, as well as children are all too often the victims of snake bite, and their deaths, or disabilities contribute to communal poverty by depriving societies of some of their fittest, most productive members. Snake bite causes substantial human mortality and disability—physical and psychological—but its recognition as an important international public health issue has been hindered by insufficient epidemiological data. Various studies, each with their flaws, have reported a wide range of deaths. Yet in India, it is the Million Deaths Study, done during 2001-03 with household interviews combined with medical assessment, that may finally convince people about the importance of snake bite in this country (the results are not yet published but will show a very high mortality due to snakebite). In survivors of snake bite, the main cause of permanent disability is local tissue death, which can require skin grafts or amputation.

While several countries have paid snake 'bounty-hunters' (USA, India, Pakistan, Burma), this is unwise for ecological reasons since snakes control local rodent populations. Professor Warrell says: "Community education to reduce the risk of bites is a better approach than is the eradication of venomous snakes. It should be based on knowledge of the

circumstances in which most bites occur, the preferred habitats of dangerous species, and their peak periods of activity—ie, time of day, season, and climate. For example, people are bitten by kraits (genus Bungarus) in south Asia almost exclusively at night while lying asleep on the ground in their homes. Such distinctive epidemiology predicates a means of prevention. In a high-risk area of eastern Terai, Nepal, sleeping under a mosquito net afforded protection." In Burma, use of cheap protective footwear in paddy fields has protected workers from the bite of Russell's vipers.

When a bite occurs, the person needs to be quickly transported to professional medical care. In developing countries, traditional healers administer inappropriate, time-wasting, and sometimes harmful treatment—this should be discouraged. The victim and especially his/her bitten limb should be immobilised and, if equipment and skills are available, bandaging the limb at a pressure of 50-70mm Hg and splinting might delay fatal respiratory paralysis in the case of an elapid (cobra, krait, mamba, coral snake or Australasian snake). Educating paramedical staff about correct prehospital care of bitten patients, including resuscitation techniques, and teaching health workers how and when to treat snakebite with antivenom are also important.

Antivenom, the only antidote to snake venom, consists of concentrated immunoglobulins from the plasma of domestic animals such as horses or sheep that have been repeatedly immunised with one or more different snake venoms. These immunoglobulins include antibodies that specifically target venom toxins. When injected intravenously into the snake bite victim, the antibodies bind to and neutralise toxins of the venoms used in their production, preventing and in some cases reversing the dangerous effects of envenoming.

Antivenoms themselves can cause complications, including potentially fatal anaphylactic shock. Incorrect assessment of risk versus benefit can

lead to
the unnecessary use of antivenom in patients with mild or even no envenoming, and in those bitten by snakes whose venoms are not neutralised by available antivenoms. Conversely, antivenom might be withheld from a patient with severe envenoming, in whom the benefits of antivenom outweigh the risks of this treatment, because of an exaggerated fear of antivenom reactions.

The limitations of antivenom treatment must be clearly recognised. Patients with respiratory, circulatory or renal failure need supportive treatment such as assisted ventilation, ancillary drugs and renal dialysis as well as antivenom if they are to survive.
Professor Warrell says: "Improvement of the treatment of snake bite requires solutions to many economic, logistical, marketing, distribution, and storage difficulties associated with production and supply of antivenom, and provision of improved training for medical personnel so that the best possible use of antivenom and other treatments is achieved."

"The development of safe, effective, and affordable antivenoms is a priority addressed by WHO...A fundamental difficulty associated with antivenom use, and recognised since the early 20th century, is the absolute requirement for specificity. Therefore, appropriate venoms need to be used in the production of antivenoms, which means that the market for a particular antivenom is restricted to a geographical area for which its specificity is relevant, usually in impoverished developing countries. Attempts to overcome this difficulty by discovery of universal venom antigens or immunogens have so far been unsuccessful."

He concludes: "Snake bite is a neglected disease that afflicts the most impoverished inhabitants of rural areas in tropical developing countries. It is an unusually challenging medical problem that deserves further investigation after the prolonged neglect by medical science."

The Viewpoint is written by David Williams, Australian Venom Research Unit, University of Melbourne, Australia, and several colleagues from different countries. They discuss the Global Snake Bite Initiative, launched in Melbourne during November 2008.

The authors say: "As long as product safety and efficacy remain untested and unproven, cost effectiveness and market sizes are unquantified, and regulatory frameworks remain fragile, the demand for antivenom in countries around the world will continue to be insufficient and organisations such as the Global Alliance for Vaccination and Immunization will be reluctant to become actively involved in the issue."

They applaud the positive efforts of WHO's Department of Essential Medicines and Pharmaceutical Policies to develop standard guidelines for the production, regulation, and control of snake antivenoms , and coordinate their implementation and the efforts of WHO's Department of Neglected Tropical Diseases to recognise snake bite as an NTD. The authors add: "Snake bite is a neglected condition that, rather than competing for resources, can benefit from integration with programmes funded to address HIV/AIDS, tuberculosis, and malaria, and contribute to the achievement of Millennium Development Goals."

They conclude: "With powerful, passionate advocacy, and at the same time, greatly improved information about the burden of human suffering attributable to snake bite, and compliance with the requirements of organisations with the capacity to mobilise resources, we can give snake bite global public health recognition so that it is no longer an obscure, denied, and neglected condition. In so doing, we can protect, save, and repair millions of lives, relieve an enormous personal and collective economic burden, and provide sustainable contributions to improving health in some of the world's poorest regions.

"To quote Bill Gates: 'humanity's greatest advances are not in its

discoveries-but in how those discoveries are applied to reduce inequity'."

Provided by Lancet

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