Global Snakebite: India, South Asia and Global Issues in Handling Snakebite Emergencies

Ian D. Simpson

Tamil Nadu Snakebite Taskforce, Chennai, India, Advisory Board: Indian Journal of Emergency Pediatrics, Snakebite Adviser: Pakistan Medical Research Council, Islamabad, Pakistan

Kooran House, Nayathode, Kerala 683572, India, 0091-9947131374, iandsimpson@gmail.com,

Author Contribution, IDS planned and prepared the article.

Abstract

India and the South Asian countries constitute the majority of world snakebite deaths. Some of these countries have taken action in response by developing locally relevant protocols to overcome known dependency on western textbooks for medical education. There is more for Governments to do in ensuring that all doctors are availed of the best methods of treating snakebite in local settings. The world's largest and lowest priced producer of anti snake venom (ASV) is India and Indian ASV is used throughout the South Asian region. Affordable and sustainable ASV remains the goal across the world and yet Indian ASV is often criticized, with little justification. The view that western production methods are 'safer' and the answer to ASV shortages is not credible; lessons from South Asia and Indian production should be given more credence in the ASV debate. This editorial examines the current approach to snakebite and provides some thoughts on how the lessons learnt in India and South Asia can help other areas.

Key Words: Snake Bites, Developing World, India, World Health Organisation, Antivenoms

Introduction

The global approach to the snakebite 'crisis' remains in shambles, characterised by "differences with each other, our power plays and politics"; according to a meeting of experts, and "going nowhere" (1). The latest epidemiology 'estimate' provides a potential range of mortality and envenomings so wide as to cast major doubt on the veracity of the analysis; and experts admit that "our figures are so vulnerable" (1-2). Nevertheless it is clear that India has the highest snakebite mortality and together with other South Asian countries such as Pakistan, Sri Lanka and Bangladesh, all of whom use Indian ASV, constitute 70% of world snakebite mortality (2). South Asia and India can therefore, provide very valuable lessons for the global approach to snakebite management. Issues established here can and should form the basis of snakebite strategy in other areas.

Reprints Requests: Ian D. Simpson
Kooran House, Nayathode, Kerala 683572
Cell:0091-9947131374
E-mail: iandsimpson@gmail.com,

The Over Simplification of Concentrating on ASV

It is interesting that the concentration of experts and W.H.O. is on increasing ASV supply and quality issues, when neither of these issues are clear cut problems which if solved will drastically reduce snakebite mortality (3-4). For example, India produces approximately 1.4 million vials per annum, used in India, Bangladesh, Sri Lanka and Pakistan, and China produces 0.5 million vials. Four of these countries are present in the top 10 for snakebite mortality (2). Clearly therefore, the supply of large amounts of ASV alone is not enough to significantly reduce snakebite deaths.

Research has shown that in many cases, the doctor's ability to effectively treat snakebite, even when ASV is available, has been diminished by significant gaps in medical training (5-6). Snakebite management training is still largely dependent on western textbooks that is inapplicable in the developing world settings (5-7).

Regional protocols, for example, the WHO South East Asia Guidelines are little better (8).

Incredibly, despite containing no ASV dosage guidance, inapplicable ASV administration guidelines and drugs not widely found in the relevant region, it is described as 'pearls of the literature' by some and indeed recommended for other parts of the world where it clearly does not apply (8-9).

India and Pakistan have responded to the weakness in snakebite training in western medical textbooks by developing and approving National Snakebite Protocols, specifically designed with the local snake species, ASVs and infrastructure in mind (10-11). Both protocols have excellent details on improvised approaches when medical facilities are limited and tiered-support resulting from local hospital structure. Some States in India have already launched versions of the protocol and provided training workshops for local doctors. States such as Tamil Nadu, West Bengal and Madhya Pradesh have made significant commitments to training front line doctors in the new protocol. However, at the central government level, neither India nor Pakistan have disseminated the protocols widely enough. In September 2007, Government of India, Health & Family Welfare Department agreed to hold workshops in five key target States and distribute tiered bedside poster material specifically designed to help doctors effectively manage snakebite in the three main levels of health care (Figure 1&2), with funding provided by WHO India. To date, despite WHO funds being made available, this has not happened.

Potential threats to local ASV production

Keeping costs low in developing countries is essential if ASV supply is to be affordable. Developing economies cannot sustain high prices per vial and this leads to governments being unable to afford the required supply and victims being at greater risk.

Indian ASV is one of the cheapest available at approximately $8 per vial; contrasted with $80 per vial for ASV in Africa, $150 for ASV in China and $1,200 per vial in the U.S. A prime factor is that the bulk of Indian ASV is produced using the highly efficient caprylic acid fractionation method to capture the anti bodies that neutralise the venom, whereas many other suppliers utilise the less efficient ammonium sulphate precipitation method. As we have seen, India is the world's largest producer of ASV, unsurprisingly considering India has the largest snakebite problem.

However, possibly because of its low cost when compared to other manufacturers, critics take every opportunity to criticise Indian ASV and manufacturers for:

1. 'Quality issues' (12-13) which in a recent case were subsequently found to be due to poor product storage by the users. It is interesting that quality issues with western suppliers are not given such attention despite examples being available (14). Constant calls for increasing ASV quality by WHO and others, with no demonstrable need, exposes India and other low cost suppliers to significant price increases in ASV. At a recent snakebite meeting in India, an Indian supplier reassured the audience that quality could indeed be improved to closely resemble western standards and it would 'only double the price'!

2. 'Unscrupulous marketing' for which no evidence is presented, other than the fact that the Indian supplier clearly stated on the product that it was not effective against the local species and that Indian ASV had been found in a region where it was not effective (15-16).

There are certainly anecdotal stories that suggest that Indian ASV manufacturers on occasion have reduced the neutralising capacity of their ASV to reduce cost and that sample testing by regulatory authorities is not sufficiently random. However, properly produced Indian ASV is effective and provided at a cost level that is suitable for a developing country.

The critical approach to Indian ASV has worrying implications that need to be carefully monitored if affordable and sustainable ASV is to remain available in India and countries that rely on Indian ASV. The W.H.O. approach has suggested, "In developing countries the remaining producers of antisera are vulnerable…to the lack of financial investment to upgrade the facilities to comply with good manufacturing practices (GMP)" and "An international distribution of tasks can be envisaged. For example, some laboratories may be in charge of keeping collections of snakes" to

produce venom for "other laboratories to immunise animals and fractionate the hyperimmune plasma for antiserum production" (3). The implication that ASV production should be concentrated amongst a few western approved suppliers whilst other entities are relegated to the position of venom suppliers must be resisted.

There is an ominous precedent for western production standards used in an attempt to replace developing world produced ASV in Sri Lanka. Indian ASV was described as "inefficient in clearing Russell's viper venom antigenaemia" and also that it "frequently caused anaphylactoid reactions" (17). The conclusion was "There is therefore a need for effective and safe antivenom for treating Russell's viper bites in Sri Lanka" (17). The new ASV was a Fab ovine product, produced by the manufacturer of CroFab™ the US ASV, using venom collected from snakes at the WHO Collaborating Centre for the Control of Antivenoms (18). This is the model advocated by the WHO and experts to achieve 'good' anti venoms for use in developing countries (4).

However, the resulting ASV, was less effective than the Indian ASV in venom neutralisation, seemed to produce less adverse reactions but only at sub optimal doses and cost five times as much as the Indian ASV (19)! The use of western production methods and facilities presents the very real risk that not only will costs significantly increase to unaffordable levels but also that no greater benefit will accrue. Like so many false dawns that have been seen in ASV provision, the new ASV disappeared without trace.

The Lessons of India and South Asia for the World

Closing the Knowledge Gap

Good local protocols, with relevant ASV advice, cognisance of local infrastructure, equipment and drugs work and should be implemented where snakebite is a significant medical condition! The Indian National Snakebite Protocol was subject to testing in a study in West Bengal (10,20). Significantly, the new protocol not only reduced mortality and patient bedtime; but also delivered a 19,000 vials saving in ASV in one year (20). This resulted from, clear criteria for when ASV should be given, rational criteria for giving additional ASV and clear clinical endpoints for when ASV should be stopped (20). ASV is a vital drug but in many cases across developing countries it is given when it is not necessary or dosages are too high and, due to a misunderstanding of its role, continued long after its therapeutic benefit has ceased (21).

The Government of India, Health and Family Welfare Department needs to rapidly implement the cascade and workshop programme for the snakebite protocol, as a new snakebite season will be starting in April. Although health provision is the State's responsibility, the central health department is responsible for guidelines and protocols. If the 11,000 people who are currently likely to die in 2010 are to be saved, action is required; now. State Governments can help by pressurising the centre to deliver on the programme. The clock for 11,000 victims is ticking!

Increasing ASV Supply

As an alternative to criticising Indian ASV, WHO and related experts should facilitate Indian ASV producers to contribute more ASV to regions with shortages (15-16). Instead of condemning Indian ASV for containing non-relevant species, clear guidelines as to which ASVs to produce, including detailed species guidance, venom sources and likely volumes should be published similar to those recently published for Africa (22). WHO, despite a reputation for favouring large pharmaceutical companies, should ensure that such guidance is widely available despite their advisory group consisting of a large number of current ASV suppliers (3-4,23)

If WHO and experts truly believe that snakebite is a crisis medical condition, this advice should be freely and comprehensively available and not subject to 'technology transfer agreements' where willing providers of ASV are charged additional costs for information that is claimed to be 'largely in the public domain' (3-4).

Many institutions that are quite happy for Bill Gates to donate funds to snakebite are less than enthusiastic when it comes to their institution donating guidance.

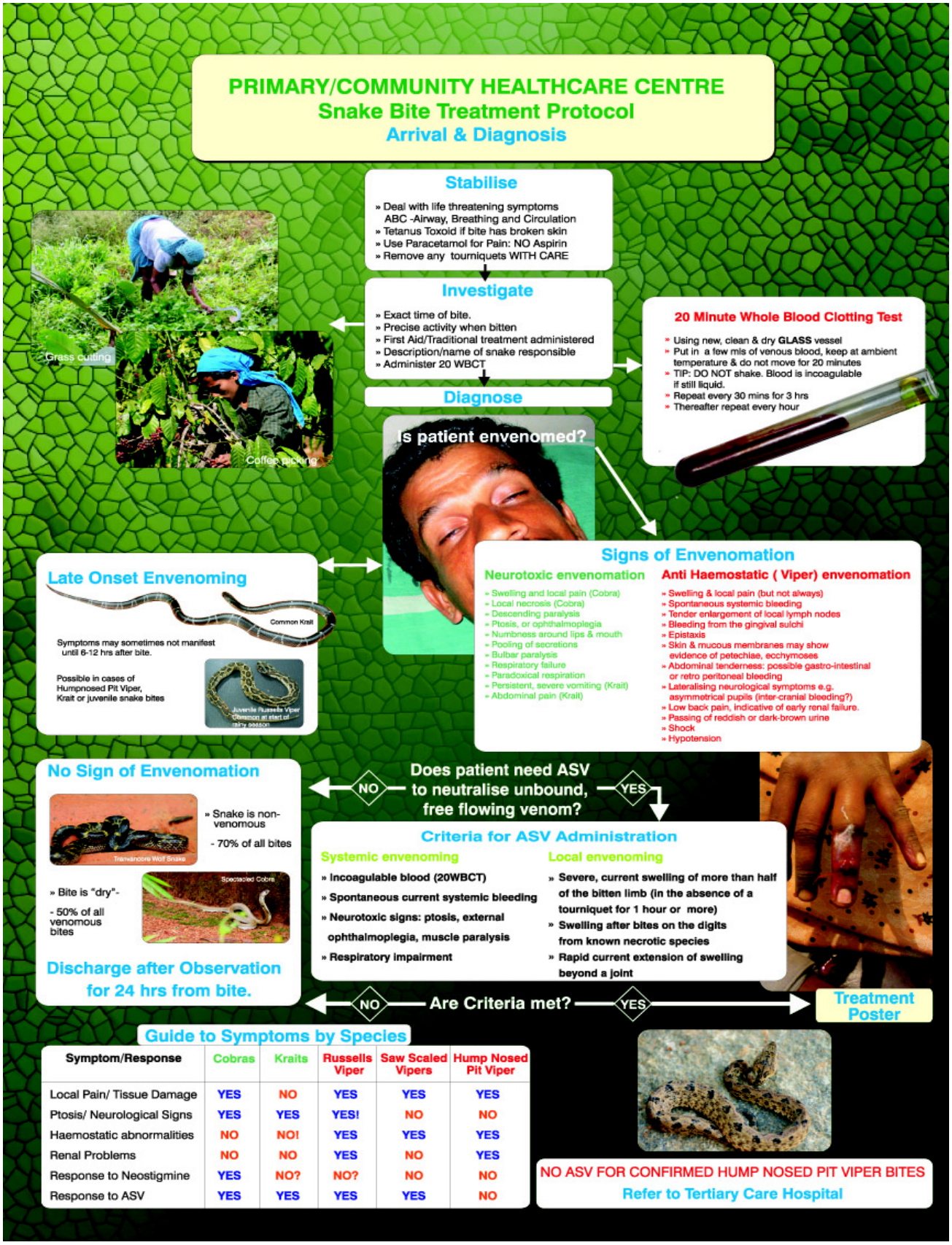

Fig 1. Arrival and Diagnosis Poster for Use in Primary Health Centres. Posters are available for District and Tertiary Hospitals with referral criteria.

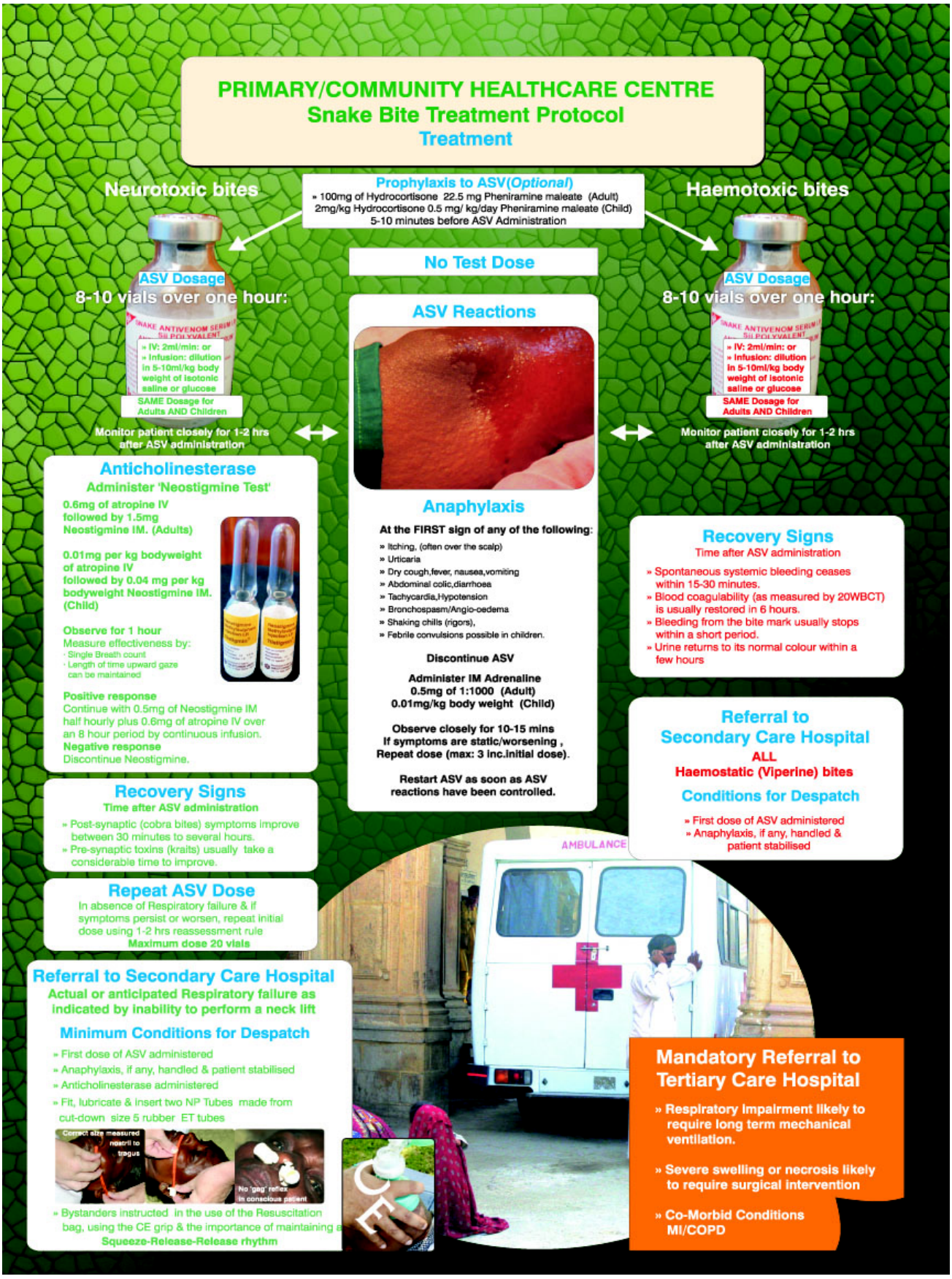

Fig 2. Treatment Poster for Use In Primary Health Centres including improvised airway devices

References

1. Global Snakebite Initiative. Open discussion of the global snakebite initiative concept., 1. 1. Melbourne, (2008) Available from: http://www.snakebiteinitiative.org/files/GICT%20Conference%202008/Audio/Session%2016%20audio/Session%2016%20Open%20Discussion.mp3 [Accessed 11th April 2009].
2. Kasturiratne A, Wickremasinghe AR, de Silva N, Gunawardena NK, Pathmeswaran A, Premaratna, R et al. Estimating the global burden of snakebite: A literature analysis and modelling based on regional estimates of envenoming and deaths. PLoS Med 2008, 5: e218. doi:10.1371/journal.pmed.0050218,
3. World Health Organisation. Rabies and envenomings: a neglected public health issue. Geneva, World Health Organisation; 2007.
4. World Health Organisation. Proposed WHO guidelines for the production, control and regulation of snake antivenom immunoglobulins. Geneva,World Health Organisation WHO/BS/08.2088, 2008.
5. Simpson ID. A study of the current knowledge base in treating snakebite amongst doctors in the high risk countries of India and Pakistan – does snakebite treatment training reflect the local requirement? Trans Roy Soc Trop Med Hyg 2008, doi:10.1016/j.trstmh.2008.04.013.
6. Fung HTJ, Lam SKT, Lam KK, Lam CW, Simpson ID. A Survey of Snakebite Management Knowledge Amongst Physicians in Hong Kong and the Implications for Snakebite Training. Wilderness and Environmental Medicine 2009; In press.
7. Auerbach P.S., Norris R.L. Disorders caused by reptile bites and marine animal exposures. In: Kaspar D.L., Fauci A.S., Longo D.L., Braunwald E., Hauser S.L., Jameson J.L., ed. Harrison's Principles of Internal Medicine 16th Ed. New York. McGraw-Hill; 2005:2593-2600.
8. Warrell DA. WHO/SEARO Guidelines for the clinical management of snakebite in the Southeast Asian Region. SE Asian J. Trop. Med. Pub. Hlth. 1999;1:1-85.
9. Ahmed SM, Ahmed M, Nadeem A, Mahajan J, Choudhary A, Pal J. Emergency treatment of a snake bite: Pearls from literature. J Emerg Trauma Shock. 2008 Jul;1(2):97-105.
10. Government of India. National Snakebite Protocol. New Delhi: Health & Family Welfare Department:2007.
11. Simpson ID , Quraishi NA, Qureshi HI,. Snakebite management in Pakistan – A guide to the latest methods of treatment. Pakistan Medical Research Council. Islamabad; 2008.
12. Abeyratne DS. Tough Action against Indian companies. Daily News. Available at: http://www.dailynews.lk/2009/11/05/news12.asp. [Accessed 18th November 2009].
13. Sri Lankan Guardian. Minister becomes protector of drug producer: doctors' union. Available at http://www.srilankaguardian.org/2009/10/minister-becomes-protector-of-drug.html [Accessed 18th November 2009].
14. Isbister GK, Tankel AS, White J, Little M, Brown SG, Spain DJ et al. High rate of immediate systemic hypersensitivity reactions to tiger snake antivenom. MJA 2006;184(8):419-20.
15. Warrell DA. Unscrupulous marketing of snake bite antivenoms in Africa and Papua New Guinea: choosing the right product—'what's in a name?. Trans R Soc Trop Med Hyg.2008;102(5):397-9.
16. Warrell DA, Williams D. Response to comment on: Failure of a new antivenom to treat Echis ocellatus snake bite in rural Ghana: the importance of quality surveillance. Trans R Soc Trop Med Hyg (2009),doi:10.1016/j.trstmh.2009.06.004.
17. Ariaratnam CA, Sjostrom L, Raziek Z, Abeyasinghe S, Kularatne M, Kondikara et al. An open randomised comparative trial of two antivenoms for the treatment of envenoming by Sri Lankan Russell's viper (Daboia russelii russelii). Trans R Soc Trop Med Hyg. 2001;95:74-80.

18. Theakston RDG, Warrell DA, Griffiths. Report of a W.H.O. workshop on the standardization and control of antivenoms. Toxicon 2003;41:541-557.
19. De Silva HJ, Fonseka MMD, Gunatilake SB, Kularatne SAM, Sellahewa KH. Anti-venom for snakebite in Sri Lanka. CMJ. 2002;(2):43-45.
20. Ghosh S, Maisnam I, Murmu BK, Mitra PK, Roy A, Simpson ID. A locally developed snakebite management protocol significantly reduces overall anti snake venom utilization in West Bengal, India. Wilderness Environ Med; 2008;19;267-74.
21. Pandey D. Snake bite first aid education and its impact in rural Madi Valley, Central-South lowland Nepal. Available at http://www.snakebiteinitiative.org/files/GICT%20Conference%202008/Session%204/Mr%20Deb%20Pandey.ppt [Accessed 19th November 2009]
22. Simpson ID, Blaylock RS. The anti snake venom crisis in Africa: A suggested manufacturers product guide. Wilderness and Environmental Medicine 2009;20:275-82.
23. McCoy D, editor. Global Health Watch 2. London: Zed; 2008.

Editor's Comments

Management protocols, by their very nature, are designed to assist doctors and patients at various levels of health care about the appropriate care for the specific clinical condition. The National Protocol for snakebite management, developed and approved by Government of India, has guidelines that are need based rather than follow a foreign model. The International Experts had a great role in encouraging and energising this protocol.

Emergency care for children in India with snake envenomation should not suffer due to misguided notions or policies on ASV. Ensuring availability of ASV and allocating resources in a sustainable manner to meet wider demand are indeed important. With an acceptable standard of Quality care and better Evidence-based outcomes published, wider dissemination and implementation of this National Protocol is our immediate need. The gaps in medical training for this rural medical emergency require effective plugging. I am confident that this Editorial, invited from Ian Simpson, will help our perceptions on snakebite management scale greater heights.

Professor (Dr.) S. Mahadevan
Editor-in-Chief