Wilderness and Environmental Medicine, **20,** 275–282 (2009)

CONCEPT

The Anti Snake Venom Crisis in Africa: A Suggested Manufacturers Product Guide

Ian D. Simpson, BSc, PG (Dip); Roger S. M. Blaylock, MBChB (UCT), FRCS (Ed) FCS (SA) MMedSc, MD (Natal)

From the Pakistan Medical Research Council, Islamabad, Pakistan and the Anti Snake Venom Laboratory, Sindh Government, Nawabshah, Pakistan (Dr Simpson); and Potchefstroom Hospital, RSA (Dr Blaylock).

Considerable attention has been given to the shortage of anti snake venom in Africa. The current supply is reported to rest at crisis levels, and considerable attention has been given to reporting the crisis. What has been absent is a recommended list of anti snake venoms that suppliers can produce in order to alleviate the problem. Suppliers who may want to enter the market and provide new anti snake venoms are hampered by a lack of knowledge of which to provide, where to source the venoms necessary for production, and the likely volume levels required. Snakebite epidemiology is recognized as being poor, particularly in estimating the number of envenomations. Snakebite authorities and organizations such as the World Health Organisation have provided lists of medically significant species, but these are inadequate as a guide to production. This paper proposes a list of anti snake venoms that could be produced by suppliers and crucially lists relevant species by geographical area, venom sources for the target species, and likely production volumes to enable suppliers to develop a confident forecast of demand to ensure sustainability.

Key words: snake bites, antivenoms, Africa, envenoming, World Health Organisation, epidemiology

Introduction

Africa and Asia are the 2 key continents for which snakebite mortality and morbidity are critical, with South America also contributing to the total.[1] Both Africa and Asia are composed of developing countries with a high level of rural agricultural activity. While mortality figures are notoriously unreliable, it is estimated that Africa suffers approximately 20 000 snakebite fatalities per annum.[1,2] A contributory factor to this situation is the shortage of anti snake venom (ASV), which has now been reported to rest at ''crisis'' levels.[3–6] This has led to the demand for greater quantities of ASV to be produced and has generated many meetings to resolve the situation.

The critical question that has been overlooked, however, is more of what should be produced? The demand for greater quantities of product tacitly assumes that the product has been defined, and yet this is not the case. The assumption that manufacturers can refer to a required product list, detailing what species should be included and to which geographic area they should apply, is not substantiated by the facts. Instead product design is left to individual producers who achieve various levels of success.[7–9] The approach of detailing simple lists of medically significant species with no attention to sources of venom is not the solution.[10,11] Manufacturers that produce ASVs that do not cover the required species for Africa are described as ''unscrupulous,'' with the assumption that this activity is deliberate.[12] However, this pointedly overlooks the fact that a required product list that would guide manufacturers as to the required species and area of applicability is lacking.

The objective of this paper is to suggest a product array for Africa that gives effective coverage, sources of venom to develop the anti venoms, and data on the likely level of ASV demand to ensure that sustainable volumes of ASV are present.

A geographic approach to Africa

A single ASV approach to Africa is unattainable. The number of medically significant species across the continent is approximately 24. A single polyvalent

No grants were received in connection with this paper. Declaration of interest: R. S. M. Blaylock is a consultant to the Antivenom Unit of the National Health Laboratory Services, Johannesburg.

Corresponding author: Ian D. Simpson, Kooran House, Nayathode, Kerala, India 683572 (e-mail: iandsimpson@gmail.com).

Table 1. Country elements of zonal approach to African snakebite

Zone 1 South	*Zone 2 West*	*Zone 3 Northeast*
Angola Burundi	Benin Burkina Faso	Algeria Djibouti
Botswana Congo	Cameroon Cape Verde	Egypt Eritrea
D.R.C. Gabon	C.A R. Chad	Ethiopia Libya
Kenya Lesotho	Cote d'Ivoire Gambia	Morocco Sudan
Malawi Mozambique	Ghana Guinea	Somalia Tunisia
Namibia Rwanda	Guinea Bissau Liberia	
South Africa Swaziland	Mali Mauritania	
Tanzania Uganda	Niger Nigeria	
Zambia Zimbabwe	Senegal Sierra Leone	
	Togo Western Sahara	

ASV covering this number of species is impractical to develop, as titers for each species would be very low and would therefore require a large number of vials to be administered to achieve a neutralizing dose; monovalent antivenoms generally require a lesser dose. It is therefore necessary to segment Africa into useful subsections that enable ASVs to be developed, with definitive species included and with volumes that enable sustainability to be achieved.

Monovalent antivenoms are used in Australia, where medically important snake species are fewer than in Africa and where venom detection kits are available,[13] which allows for identification of the offending snake species. There are about 24 medically important snakes in Africa, which would require the production of over 20 monovalent antivenoms. Further, offending snakes species identification is inaccurate as a result of patient descriptions of snakes, the use of snake pictures, the paucity of dead snakes brought to hospital, and the absence and expense of venom identification kits.[14,15] Polyvalent antivenoms are, hence, better suited to African conditions and allow syndromic management of snakebite.[16,17]

The South African Vaccine Producers[17] produce polyvalent antivenom using the venom of 10 different snake species. It is effective in stopping the progression of swelling, reversing paralysis, except in Cape Cobra bites, and stopping hemorrhage.[18] Using 10 venoms, as in the case of South African Vaccine Producers, to manufacture 1 ASV is clearly not deleterious to efficacy. It is suggested that venoms producing the same clinical syndrome, namely painful progressive swelling (PPS), progressive weakness (PW), or bleeding (B), be used to allow syndromic management, with possible benefit obtained from paraspecific antibody/antigen reactions. As B from medically important snakes is invariably preceded by PPS, venoms from snakes producing PPS alone and PPS with B can be combined to produce a single polyvalent antivenom. Envenomation from *Thelotornis* spp and *Dispholidus typus* leads to B without significant PPS, but bites from these snakes are uncommon, unless the snake is handled, and are hence excluded. The key to the objective of keeping the vial price low—to enable developing countries to afford the product—is to enable high volumes to be produced.[19]

Three zones with specific country ranges can be defined based on the distribution of the medically significant species, which cause the highest mortality or morbidity rate and frequently cause bites (Table 1). Snakes that infrequently bite or those whose bite uncommonly leads to mortality or significant morbidity are excluded.

In Zone 1 South, for example, the predominant species are *Bitis arietans* and *Naja nigricollis*. In Zone 2 West, the major biting species is *Echis ocellatus*, and in Zone 3 Northeast, the predominant species are *Cerastes cerastes* and *Echis pyramidium*. There are, of course, many other medically significant species in each area, but the character of snakebite in each of these zones is determined by these key species. It is therefore possible to view these areas as 3 discrete zones for ASV development. Such a clear demarcation of zones enables ASV to be sold in relevant areas, with a high confidence that the ASV is applicable to local species and can be derived from local venom sources.

For an ASV to be useful it must 1) be able to be administered with clear and unambiguous indications by the clinician, 2) cover all medically significant species in a clearly defined area, and 3) be immediately available and easily administered and possess acceptable levels of side effects.

The listed indications for ASV are for severe envenomation (anticipated or present), where life or limb is at risk. Lesser envenomation can usually be managed by supportive means, which spares the victim the possible adverse effects of ASV as well as the

expense associated with ASV. Nonspecific symptoms such as nausea and vomiting should be noted but are not an indication for ASV.

A clinical approach to snakebite symptoms in Africa

The 3 main clinical criteria allowing syndromic management of snakebite are apparent in Africa; these include PPS, PW, and B.[15,20–22]

Painful progressive swelling

Painful progressive swelling is the key symptom of many of the medically significant species in Africa. The cytotoxic cobras such as *Naja nigricollis* and *Naja mossambica*, in addition to some of the vipers, *B arietans* and *Bitis gabonica*, all present with PPS as the primary symptom. Later sequelae include blistering, necrosis, and hematoma caused by the action of cytotoxins, phospholipase A2 enzymes, and other toxins.

Anti snake venom administration criteria are included below for each ASV. Manufacturers provide guidelines related to administration on the ASV product insert, and it is important that these guidelines reflect the correct criteria for administration.

Anti snake venom is suggested in cases involving the following[22]: 1) swelling progressing 15 cm or more within 1 hour; swelling after bites to the extremities reaching the knee or elbow by 4 hours; swelling involving the whole limb within 8 hours; or swelling extending onto the trunk; 2) swelling threatening airway compromise or causing shortness of breath; 3) coagulopathy; or 4) compartment syndrome or major vessel entrapment.

Progressive weakness

Bites by nonspitting cobras such as *Naja melanoleuca* and *Naja haje* produce these PW symptoms, as do the mamba species (eg, *Dendroaspis polylepsis* and *Dendroaspis augusticeps*). The main contributors to this condition are postsynaptic toxins that inhibit acetylcholine binding, presynaptic toxins that inhibit acetylcholine release, toxins that increase acetylcholine levels, and other ill-understood mechanisms.

Grounds for administering ASV are the following[22]: 1) visible neurological signs (ie, ptosis, opthalmoplegia, excessive salivation, bulbar paralysis, inability to swallow, respiratory distress); 2) symptoms of 'pins and needles,' profuse sweating, and excessive salivation or a metallic taste in the mouth (mambas); and 3) general weakness in the presence of PPS (nonspitting cobras).

The physician's knowledge of local snakes and the symptomology of their bites is important, as cranial nerve palsies are not necessarily followed by respiratory muscle weakness in some snakebites (*Bitis peringueyi*, *Bitis xeropaga*, *Elapsoidea* spp, and *Aspidelaps* spp).

Bleeding

Bleeding and coagulopathy are caused by the viper family (eg, *E ocellatus* and *E pyramidium*). These symptoms primarily result from the activation of prothrombin and factor X, leading to consumption coagulopathy (*Echis*), thrombocytopenia, and activation of factor XIII (*B arietans* and *B gabonica*, respectively).[11]

Criteria for administering ASV include the following: 1) incoagulable blood determined by a 20-minute whole blood clotting test in a new, clean, dry, glass test tube as a bedside test[23]; 2) laboratory evidence of coagulopathy; 3) continual bleeding from the bite site, severe headaches, or convulsions (fainting is uncommon but should alert the physician to a possible intracranial bleed); and 4) systemic bleeding, not local bruising.

Criteria such as these allow ASV development so that antivenom choice can be made simply on the basis of the signs and symptoms manifested by the victim. There are examples in which an institution has designed a number of ASVs based on targeting individual species. This has resulted in an overlap of clinical symptoms between the ASVs, which renders them clinically unusable, as the physician is unable to determine which ASV to administer (I. D. Simpson, unpublished data).

The zonal approach to ASV design

ZONE 1: SOUTH AFRICAN PPS

In terms of populations at risk, Zone 1 represents the second largest of the African zones, with a population of approximately 328 million. The medically significant PPS species in this zone (Table 2) consist of primarily 2 families, either the cytotoxic spitting cobras (*Naja* spp) or the vipers (*Bitis* spp), with the addition of the Rinkhals (*Hemachatus haemachatus*).[15,22–30]

ZONE 1: VENOM SOURCES

Venom sources are available from a number of countries for the species to be included in the anti venom mix: *B arietans*: Republic of South Africa[31] and Kenya[32]; *B gabonica*: Burundi,[33] Republic of South Africa, Zimbabwe,[31] and Kenya[32]; *Bitis nasicornis*: Burundi[33] and Kenya[32]; *N nigricollis*: Tanzania[33] and Kenya[32]; *N*

Table 2. Zonal anti snake venoms (ASVs) for progressive painful swelling (PPS) and bleeding (B) symptoms

Zone 1 South	*Zone 2 West*	*Zone 3 Northeast*
Bitis arietans	*Bitis arietans*	*Naja nigricollis*
Bitis gabonica	*Bitis gabonica*	*Naja pallida*
Bitis nasicornis	*Bitis nasicornis*	*Naja nubiae*
Naja nigricollis	*Bitis rhinoceros*	*Naja ashei*
Naja mossambica	*Naja nigricollis*	*Echis leucogaster*
Naja nigricincta	*Naja katiensis*	*Echis pyrimidium*
Naja ashei	*Echis ocellatus*	*Echis ocellatus*
Naja pallida	*Echis leucogaster*	*Cerastes cerastes*
Hemachatus haemachatus		

mossambica: Tanzania[33] and Republic of South Africa[31]; *N nigricincta*[33] and *N ashei*: Kenya[32]; *N pallida*: Kenya[32,33]; and *H haemachatus*: Republic of South Africa.[31]

ZONE 1: ASV VOLUMES

As a result of the paucity of epidemiology data for African snakebite as a whole, it is difficult to determine the precise volumes of ASV vials required.[1,34] However, it is possible to estimate likely demand in the various zones and thus to ensure that a sustainable volume requirement is present. Two authors from Kenya and the Democratic Republic of Congo have given data for number of bites per 100 000 (ie, 13.8/100 000 per annum for Kenya and 80/100 000 per annum for the Democratic Republic of Congo).[29,35] Higher figures for numbers of bites have been shown for Kenya (ie, 151/100 000 per annum), but these were superseded by the later paper that included the same region of Kenya.[28,29] Based on population data for all of Zone 1, this would imply that the total bites per annum ranges between 45 264 and 262 400. Snow and colleagues[28] demonstrate that bites from venomous species constitute 19% of all bites, generating total Zonal bites from venomous species at 8600 to 49 856 per annum. Based on published work in this zone, 4 papers[14,15,36,37] (Table 3) provide data indicating that on average, 92% of bites from venomous species result in PPS and 8% in PW. This would imply that PPS bites account for 7912 to 45 878 bites per annum and that PW bites range between 688 and 3988 per annum. Utilizing ASV administration criteria from this region, the number of patients requiring ASV would be 10% of PPS bites (ie, 791–4587) and 70% of PW bites (ie, 482–3211). Assuming a similar level of neutralization in the new ASV compared to existing ASV would imply a requirement for PPS ASV of 23 000 vials per annum and a PW requirement of 32 110 vials per annum.[11,22] It is important to remember that this is not a precise estimate but rather a guide to the likely minimum levels of requirement based on published estimates and criteria of ASV usage for severe envenomation.

ZONE 2: WEST AFRICA PPS AND B

In terms of demographics, this zone has the lowest population, at approximately 320 million; however, it is generally regarded as having the most significant snakebite problem.[11,12] Key biting species with PPS with possible B symptoms include 3 families (Table 2): the carpet vipers (*Echis* spp), the cytotoxic cobras (*Naja* spp), and the vipers (*Bitis* spp).[38–51]

ZONE 2: VENOM SOURCES

Venom sources are available from a number of countries for the species to be included in the anti venom mix: *B arietans*: Ghana[32]; *B gabonica*: Burundi[32]; *B nasicornis*: Ghana[32]; *B rhinoceros*: Ghana[32] and Togo[31]; *N nigricollis*: Cameroon[32] and Togo[31]; *N katiensis*: Burkina Faso[32]; *E ocellatus*: Cameroon[32] and Togo[31]; and *E leucogaster*: Mali.[32]

ZONE 2: ASV VOLUMES

To estimate ASV demand is difficult, again because of the lack of accurate figures on levels of envenoming.[1,34] However, using a case-based approach (ie, one based on hospital admissions), it is possible to estimate a case level of 60 per 100 000 per annum.[2] This would imply a level of cases of 191 880 per annum. Previous studies have shown that *E ocellatus*, the most significant biting species in this zone, accounts for 58% of bites, 99 778 (52%) of which result in envenomations and 12 088 (6%) of which result in dry bites.[45] Of the remaining non-*Echis* cases, it is credible to apply similar ratios, as outlined in Table 4. The result would generate dry or nonvenomous cases numbering 12 802, PPS cases numbering 61 611, and PW cases numbering 5601.

Table 3. Epidemiological data from 4 studies in Southern Africa providing syndromic split of envenomations and the percentage of nonenvenomations in hospital cases*

Place	*No. of patients*	*Envenomation absent (%)*	*PPS (%)*	*PW (%)*	*B (%)*	*Other (%)*
Eshowe[15] (RSA)	333	12	85	2	0	0.9
Empangeni[14] (RSA)	164	7	90	4	0	0
Kangwane[37] (RSA)	251	22	64	13	0.8	0
Triangle[36] (Zimbabwe)	250	21	70	4	0	4
Total	998	16	77	6	0.2	1

*Other indicates bites that are inconclusive with regard to symptoms because of minimal envenomation; PPS, painful progressive swelling; PW, progressive weakness; B, bleeding; and RSA, Republic of South Africa.

In terms of ASV requirement, again assuming similar neutralizing capability compared to existing ASVs, *Echis* envenomings would require 99 778 victims per year × 4 vials per victim = 400 000 vials per annum.[51] Progressive painful swelling cases would require 61 611 × 10% × 5 vials per victim = 30 805 per annum.[22] The total requirement for the Zone 2 PPS and B ASV would be approximately 460 000 vials per annum. Progressive weakness envenomations would generate 5601 victims per year × 70% (requiring ASV) × 10 vials per victim = 39 207 vials per annum.[11,14,15,18,22,36,37]

ZONE 3: NORTHEAST AFRICA PPS AND B

Interestingly, this zone has the highest population of the 3, with approximately 371 million, but being dominated by the Sahara, it suffers the least number of snakebites. The population is largely gathered around the coastal area, with huge portions of the region sparsely inhabited. The major medically significant species are grouped into 3 families (Table 2): the carpet vipers (*Echis* spp), the desert vipers (*C cerastes*), and the cytotoxic cobras (*Naja* spp).[30,52]

Table 4. All Africa anti snake venom (ASV) for progressive weakness (PW) symptoms: with listed species against which it is effective

Naja haje
Naja melanoleuca
Naja nivea
Naja annulifera
Dendroaspis polylepsis
Dendroaspis augusticeps
Dendroaspis jamesoni
Dendroaspis viridis
Hemachatus haemachatus

ZONE 3: VENOM SOURCES

Venom sources are available from a number of countries for the species to be included in the anti venom mix: *N nigricollis*: Cameroon[33] and Togo[31]; *N pallida*: Kenya[32,33]; *N nubiae*: Egypt[31,33]; *E ocellatus*: Cameroon[33] and Togo[31]; *E leucogaster*: Mali[33]; *E pyramidium*: Egypt[31,33]; *C cerastes*: Egypt and Tunisia[33]; and *N ashei*: Kenya.[32]

ZONE 3: ASV VOLUMES

Epidemiological data for the area are almost nonexistent, and, thus, close surrogate data must be employed from Saudi Arabia and Oman.[53,54] The work of Hanssens et al[54] details 2.1 cases per 100 000 annually, which would imply a total Zonal case load from snakebite of 7797. Assuming that *E pyramidium* and *C cerastes* are the key biting species, a similar model to that of Zone 1 can be adopted to determine likely ASV volume requirement. This would identify 4054 envenomations per annum from *E pyramidium*, with 468 dry bites not requiring ASV. In addition, 2521 bites annually would be probable from *C cerastes*, 524 bites from nonvenomous species, and 230 from PW species.[14,15,22,25,36,37]

The required volume of Zone 3 PPS and B ASV would be 4054 victims per annum × 5 vials per victim = 20 270 vials per annum, plus 2521 × 10% = 252 × 5 vials per victim = 1260 vials per annum. This would generate a requirement of 21 530 vials per annum of Zone 3 PPS/B ASV. In the case of PW bites, 230 × 70% would indicate 161 victims with a need for ASV, which would imply a requirement of 1610 vials of PW ASV per annum.[11,22]

ALL-AFRICA PW POLYVALENT

There is ample evidence that species causing PW as the key symptom are responsible for a smaller number of bites in Africa than are species causing PPS and

B.[14,15,36,37] However, these bites are significant and cause significant mortality because of the rapidity of action of the venoms. The PW species are also widely distributed across the continent. Two major families represent the PW species (Table 4): the neurotoxic cobras (*Naja* spp), the mambas (*Dendroaspis* spp), and also the Rinkals (*H haemachatus*).[15,18,24,28,29,36,37,55–58] As a result of the wide distribution of similar species and the desirability of maximizing volumes of any one ASV to aid sustainability, a pan-African PW ASV is recommended. It is also worth noting that *H haemachatus* is included in both the Zone 1 PPS and the all-Africa PW, as it has been reported to cause both syndromes.

ALL-AFRICA PW ASV: VENOM SOURCES

Venom sources for an all-Africa PW antivenom are fortunately many and widespread, enabling a good venom pool to be utilized in ASV production, thus: *N haje*: Egypt, Mali, Morocco, Tunisia,[33] and Kenya[32]; *N melanoleuca*: Ghana, Uganda, Cameroon,[33] Kenya,[32] and Zimbabwe[31]; *N nivea*: Republic of South Africa[31,33]; *N annulifera*: Mozambique[33] and Republic of South Africa[31]; *D polylepsis*: Kenya[32,33] and Republic of South Africa[31–33]; *D augusticeps*: Tanzania[33], Zimbabwe,[31] and Kenya[32]; *D jamesoni*: Cameroon,[33] Uganda,[31] and Kenya[32]; *D viridis*: Ghana[33] and Togo[31]; and *H haemachatus* Republic of South Africa.[31]

ALL-AFRICA PW ASV: VOLUMES

Based on the analysis of the 3 zones, the total annual requirement for the all-Africa PW ASV vials would be 72 927 vials per annum (Zone 1 South [32 110], Zone 2 West [39 207], and Zone 3 Northeast [1610]).

Discussion

The crisis in ASV supply is multifactorial, with contributions to the crisis including the cost of production, the reduction in the number of suppliers, the lack of key data, unclear guidelines on the most efficient methods of production (until recently), and unclear guidance on the required ASV products.[6,10,12,19,59]

The inability of manufacturers to refer to a specific model of, for example, African ASVs that contains the correct species, as related to a clearly defined geographic area, is a key factor. Anti snake venom manufacturers have made various attempts, which range from generally acceptable, with some species omissions, to the completely inappropriate.[7–9,16,17] Some of these ASVs are clearly inappropriate, as they relate to species from Asia and not Africa.[7] The response of snakebite experts to this specific issue, however, has been tardy, despite the fact that this has been a known problem since 2005.[12]

Producing general lists of medically significant species, as a guide to manufacturers, is ineffective.[6,10] Purchasing authorities in specific countries purchase ASVs, and it is important that each specific country can identify which ASV it requires and that the venom mix is appropriate to their country. A primary consideration is access to venom for inoculation of the animals (usually horses) and obtaining venom from as wide a geographic area as possible in order to overcome the regionality of species venom variation.[4] Potential producers who may be considering entering the market require clear guidance on species and venom sources. In addition, confirmation of likely levels of ASV volume is vital if the economics of production are to be accurately calculated, which is essential for sustainability.

This paper now enables those current manufacturers who produce ASVs close to the recommended configurations to be able to adjust their mix to fully capture medically significant species in the defined zones. Manufacturers such as those in India, who have significant capacity to supply ASVs to Africa, can now, with this paper, produce effective and relevant ASVs using venoms pooled from a widely reliable and *appropriate* source.

References

1. Chippaux JP. Snakebites: appraisal of the global situation. *Bull World Health Org*. 1998;76:515–524.
2. Chippaux JP. *Snake Venoms and Envenomations*. Malabar, FL: Krieger Publishing Company; 2006:211–246.
3. Theakston RDG, Warrell DA. Crisis in snake antivenom supply for Africa. *Lancet*. 2000;356:2104.
4. Theakston RDG, Warrell DA, Griffiths E. Report of a WHO workshop on the standardization and control of antivenoms. *Toxicon*. 2003;41:541–557.
5. Stock RP, Massougbodji A, Alagon A, Chippaux JP. Bringing antivenoms to Sub-Saharan Africa. *Nature*. 2007; 25:173–177.
6. World Health Organisation. *Rabies and Envenomings: A Neglected Public Health Issue*. Geneva, Switzerland: World Health Organisation; 2007.
7. Serum Institute of India. *Polyvalent Anti-Snake Venom Serum (Lyophilised) Central Africa* [package insert]. Pune, India: Serum Institute of India Ltd; 2007. Available at: http://www.seruminstitute.com/content/products/product_antisera2.htm. Accessed September 7, 2008.
8. Vacsera. ASV description. Available at: http://www.egyvac.com/egyproducts/SNAKE%20VENOM-Sub-Saharan%20.htm. Accessed September 7, 2008.

9. Bharat Serums and Vaccine. *Anti Venom ASNA Antivenom* [product insert]. Available at: http://www.bharatserums.com/pdf/ASVS_africa.pdf. Accessed September 7, 2008.
10. World Health Organisation. Progress in the characterization of venoms and standardization of antivenoms *WHO Offset Publ*. 1981;58:1–44.
11. Warrell DA. Bites by venomous snakes outside the Americas. In: Auerbach PS, ed. *Wilderness Medicine*. St Louis, MO: Mosby; 2007:1086–1123.
12. 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;102:397–399.
13. Sutherland SK. Antivenom use in Australia. *Med J Aust*. 1992;157:734–739.
14. Coetzer PW, Tilbury CR. The epidemiology of snakebite in northern Natal. *S Afr Med J*. 1982;62:206–212.
15. Blaylock R. Epidemiology of snakebite in Eshowe, KwaZulu-Natal, South Africa. *Toxicon*. 2004;43:159–166.
16. Aventis Pasteur. Lyon, France. *Anti Venom FAV-AFRIQUE Antivenom* [product insert]. 2000.
17. South African Vaccine Producers. SAVP products: equine antivenoms. Available at: http://www.savp.co.za/Products.htm. Accessed October 13, 2008.
18. Blaylock RS, Lichtman AR, Potgieter PD. Clinical manifestations of Cape cobra (*Naja nivea*) bites. Two cases. *S Afr Med J*. 1985;68:342–344.
19. Simpson ID. Time for an alternative perspective: the eternal problem of supply and quality of anti snake venom in the developing world—'It's the Economy Stupid.' *Wilderness Environ Med*. 2008;19:186–194.
20. Blaylock R. Snake bites. *Trop Surg*. 2002;20:25–29.
21. Blaylock R. Suggested management of snakebites in South Africa. *Dermatol Rev*. 2003;3:33–38.
22. Blaylock RSM. The identification and syndromic management of snakebite in South Africa. *S Afr Fam Pract*. 2005;47:48–53.
23. Sano-Martins IS, Fan HW, Castro SCB, et al. Reliability of the simple whole blood clotting test (WBCT20) as an indicator of low plasma fibrinogen concentration in patients envenomed by *Bothrops* snakes. *Toxicon*. 1994;32:1045–1050.
24. Christensen PA. The scope of South African anti-snakebite sera. *S Afr Med J*. 1960;34:684.
25. Blaylock RS. The treatment of snakebite in Zimbabwe. *Cent Afr J Med*. 1982;28:237–246.
26. Hoffmann LAC, De Wetpotgieter S. *Naja mossambica* Mozambique spitting cobra or M'fezi envenomation. *J Herpetol Assoc Afr*. 1988;35:41–42.
27. Muguti GI, Maramba A, Washaya CT. Snake bites in Zimbabwe: a clinical study with emphasis on the need for antivenom. *Cent Afr J Med*. 1994;40:83–88.
28. Snow RW, Bronzan R, Roques T, Nyamawi C, Murphy S, Marsh K. The prevalence and morbidity of snake bite and treatment-seeking behaviour among a rural Kenyan population. *Ann Trop Med Parasitol*. 1994;88:665–671.
29. Coombs MD, Dunachie SJ, Brooker S, Haynes J, Church J, Warrell DA. Snake bites in Kenya: a preliminary survey of four areas. *Trans R Soc Trop Med Hyg*. 1997;91:319–321.
30. Wuster W, Broadley D. Get an eyeful of this: a new species of giant spitting cobra from eastern and north-eastern Africa (Squamata: Serpentes: Elapidae: *Naja*). *Zootaxa*. 2007;1532:51–68.
31. South African Venom Suppliers. Available at: http://www.venomsa.com/venoms.html. Accessed August 17, 2008.
32. Bio-Ken. Available at: http://www.bio-ken.com/milking.htm. Accessed August 17, 2008.
33. Latoxan. Available at: http://www.latoxan.com/VENOM/SNAKE/index.html. Accessed August 17, 2008.
34. Swaroop S, Grabb B. Snakebite mortality in the world. *Bull World Health Organization*. 1954;10:35–76.
35. Odio W, Musama E, Engo Biongo G, Malukisa J, Biezakala E. Epidemiology of snakebites in sugar cane plantations of Kwilu Ngongo in Democratic Republic of Congo. *Bull Soc Pathol Exot*. 2005;98:312–315.
36. Blaylock RSM. Snake bites at Triangle Hospital January 1975 to June 1981. *Cent Afr J Med*. 1982;28:1–11.
37. McNally SL, Reitz CJ. Victims of snakebite. A 5-year study at Shongwe Hospital, Kangwane, 1978–1982. *S Afr Med J*. 1987;72:855–860.
38. Onuaguluchi GO. Clinical observations on snakebite in Wukari, Nigeria. *Trans R Soc Trop Med Hyg*. 1960;54:265–269.
39. Pitman CRS. The saw-scaled viper or carpet viper (*Echis carinatus*) in Africa and its bite. *J Herpetol Assoc Afr*. 1973;9:6–34.
40. Warrell DA, Davidson NMcD, Ormerod LD, et al. Bites by the saw-scaled or carpet viper (*Echis carinatus*): trial of two specific antivenoms. *BMJ*. 1974;277:437–440.
41. Warrell DA, Ormerod LD, Davidson NMcD. Bites by puff adder (*Bitis arietans*) in Nigeria and value of antivenom. *BMJ*. 1975;4:697–700.
42. Warrell DA, Ormerod LD. Snake venom ophthalmia and blindness caused by the spitting cobra (*Naja nigricollis*) in Nigeria. *Am J Trop Med Hyg*. 1976;25:525–529.
43. Warrell DA, Arnett C. The importance of bites by the saw-scaled or carpet viper (*Echis carinatus*). Epidemiological studies in Nigeria and a review of the world literature. *Acta Trop (Basel)*. 1976;33:307–341.
44. Pugh RNH, Bourdillon CCN, Theakston RDG, Reid HA. Bites by the carpet viper in the Niger valley. *Lancet*. 1979;2:625–627.
45. Warrell DA, Davidson NM, Greenwood BM, et al. Poisoning by bites of the saw-scaled viper (*Echis carinatus*) in Nigeria. *QJM*. 1977;181:33–62.
46. Tilbury CR. Observations on the bite of the Mozambique spitting cobra (*Naja mossambica mossambica*). *S Afr Med J*. 1982;61:308–313.
47. Laing GD, Lee L, Smith DC, Landon J, Theakston RD. Experimental assessment of a new, low-cost antivenom for treatment of carpet viper (*Echis ocellatus*) envenoming. *Toxicon*. 1995;33:307–313.

48. Chippaux JP, Lang J, Amadi-Eddine S, Fagot P, Le Mener V. Short report: treatment of snake envenomations by a new polyvalent antivenom composed of highly purified F(ab)2: results of a clinical trial in northern Cameroon. *Am J Trop Med Hyg*. 1999;61:1017–1018.
49. Einterz EM, Bates ME. Snakebite in northern Cameroon: 134 victims of bites by the saw-scaled or carpet viper, *Echis ocellatus*. *Trans R Soc Trop Med Hyg*. 2003;97:693–696.
50. Hantson P, Verhelst D, Wittebole X, El Gariani AW, Goossens E, Hermans C. Defibrination and systemic bleeding caused by an imported African snakebite. *Eur J Emerg Med*. 2003;10:349–352.
51. Visser LE, Kyei-Faried S, Belcher DW, Geelhoed DW, van Leeuwen JS, van Roosmalen J. 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*. 2008;102:445–450.
52. Drewes RC, Sacherer JM. A new population of carpet vipers *Echis carinatus* from northern Kenya. *J E Afr Nat Hist Soc*. 1974;145:1–7.
53. Mahaba HM. Snakebite: epidemiology, prevention, clinical presentation and management. *Ann Saudi Med*. 2000;20: 66–68.
54. Hanssens Y, Deleu D, Taqi A. Etiologic and demographic characteristics of poisoning: a prospective hospital-based study in Oman. *J Toxicol Clin Toxicol*. 2001;39:371–380.
55. Rippey JJ, Rippey E, Branch WR. A survey of snakebite in the Johannesburg area. *S Afr Med J*. 1976;50:1872–1876.
56. Warrell DA, Barnes HJ, Piburn MF. Neurotoxic effects of bites by the Egyptian cobra (*Naja haje*) in Nigeria. *Trans R Soc Trop Med Hyg*. 1976;70:78–79.
57. Gear JHS. Non-polio causes of polio-like paralytic syndrome. *Rev Inf Dis*. 1984;6:S379–S384.
58. Nhachi CF, Kasilo OM. Snake poisoning in rural Zimbabwe—a prospective study. *J Appl Toxicol*. 1994; 14:191–193.
59. Simpson ID, Jacobsen IM. Anti snake venom production crisis—who told us it was uneconomic and unsustainable? *Wilderness Environ Med*. 2009:144–155.