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CONCEPT

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

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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

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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