Many antidotes to snake venom do not work as well as they might

Venom varies from place to place. Antivenoms must take account of this

NO GENUS of snakes kills more people and causes more economic damage than *Echis*. Saw-scaled vipers, to give the group's common name, are found in Africa, the Middle East and Asia. Their venom makes blood clot, bringing agonising death. Victims are often farm workers who support entire households, so an attack can plunge a family into poverty.

Antivenoms—chemicals that reverse or blunt the effects of a snake's toxin—are standard medicines in areas where bites are common. But a study led by Bryan Fry of the University of Queensland, in Australia, which has just been published in *Toxicology Letters*, has found a problem: against many snake populations, these medicines do not work.

Antivenom production, which was pioneered in the 19th century by Albert Calmette, a student of Louis Pasteur, involves extracting venom from snakes and injecting it into animals, such as horses, that can, thanks to their size, survive large doses of the stuff. The injected animals' immune systems produce antibodies that neutralise the venom. These can be extracted and stored for later use on human victims. Nowadays, rather than producing a single antivenom for each type of snake, the animals employed to make the stuff are injected with several different toxins, in the hope of creating an antivenom effective against them all. This makes sense. Most victims of snake bites will not know exactly what bit them. But the underlying principle is the same as Calmette's.

The antivenom approach does, though, depend on the venom injected into a victim being among those used to make the treatment. Dr Fry, observing the huge ranges of some of the species involved, and the tendency of evolution to result in local adaptations even within such species, wondered whether that was always true for existing snake-bite remedies.

To find out, he obtained venom from saw-scaled vipers in Ghana, India, Kenya, two regions of Mali, Nigeria, Pakistan, Senegal, Saudi Arabia and the United Arab Emirates. He and his colleagues measured the rate at which venom from each of

these caused human blood to clot. They then re-ran the experiment in the presence of each of four different commercial antivenoms, to see if these slowed the process down. Two of the antivenoms in question, EchiTab-Plus-ICP and SAIMR Echis, were made using venom from African snakes. The other two, Sii Polyvalent Anti-snake Venom Serum and Snake Venom Antiserum I.P., were from Indian snake venoms.

The best of the antivenoms, EchiTab-Plus-ICP, did well against toxins used by the vipers of Ghana, Nigeria, one of the Malian regions and Senegal. But it did little against all other saw-scaled vipers, despite being listed as a treatment in Kenya and in the region of Mali for which the experiment suggested it did not work. SAIMR Echis was similar. It performed well against snakes from Saudi Arabia, Kenya and one region of Mali, moderately against snakes from Ghana, Nigeria and the other part of Mali, and poorly elsewhere. This antivenom is listed as effective against a species called *Echis carinatus* (pictured overleaf). But Dr Fry's results suggest that protection does not extend to populations of this species living in India.

The makers of both of these antivenoms have been receptive to the findings. Megan Saffer of SAVP, in Johannesburg, the firm responsible for the SAIMR Echis antivenom, says that an effort is now under way to re-label this antivenom so that it will be used only in regions where it is truly effective. Alberto Alape-Girón, the head of Instituto Clodomiro Picado, in Costa Rica, where EchiTab-Plus-ICP is made, noted that his team was responding to the situation by "developing a new antivenom of wider neutralisation efficacy".

The results were worse for Sii Polyvalent Anti-snake Venom Serum, which worked well only against venom from populations of *E. carinatus* in Pakistan, and for Snake Venom Antiserum I.P., which had only a mild effect against even that venom. Both are listed as being effective against Indian populations of *E. carinatus*, but Dr Fry's results call this into question.

Rajendra Prabhu, chief scientist at VinsBio, in Hyderabad, the firm that makes Snake Venom Antiserum I.P., says that the "antiserum is geospecific to neutralise our Indian region species only", yet the new findings do not support this claim. Dr Prabhu also argues that "it is not appropriate to compare potency against other venoms of African or Asian countries". But Dr Fry says that both it and Sii Polyvalent Anti-snake Venom Serum are routinely found on the shelves of African clinics, even though they grant no benefit against native vipers.

What seems clear from Dr Fry's work is that makers of antivenoms—including, presumably, antivenoms against snakes other than saw-scaled vipers—need to look

more closely at how snake venom varies from place to place, even within what appear to be single species. Antivenoms are wonderful things, and have saved many lives. But this study suggests they could, with a little effort, be made better still.

Source: The Economist