

ment, appeared to be nonprogressive. The identification of the EAST syndrome and careful clinical observations now allow us to study the role of *KCNJ10* in brain and human physiology.²

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Antivenom for Children with Neurotoxicity from Scorpion Stings

TO THE EDITOR: Boyer et al. (May 14 issue)¹ report that among children with neurotoxic effects of scorpion envenomation, scorpion-specific F(ab')₂ antivenom resolved the clinical syndrome within 4 hours. In 1999, we published the results of a negative randomized, controlled trial of antivenom in patients with scorpion envenomation in southern Tunisia.² Although neurotoxic effects are reported in up to 78% of patients with venomous scorpion stings in North Africa, we assessed the efficacy of scorpion antivenom on objective end points such as a change in severity grade.³ The 100% rate of resolution of neurotoxic symptoms with scorpion-specific antivenom in the study by Boyer et al. is ascribed to rapid neutralization of circulating scorpion venom; this finding has been previously reported, and its clinical relevance largely debated.^{4,5} The distribution range and the standard deviation around the mean of baseline plasma venom levels in the control group suggest that some patients had no detectable levels of venom. Was the outcome for those patients the same as that of the active group or that of the control group? Midazolam infusion, which affected both the primary and secondary end points, was not standardized according to a validated grading system. Therefore, it is difficult to identify the precise moment that resolution of the neurotoxic syndrome occurred, and the decision to stop the midazolam infusion might have been delayed, since it was based on the observation of the patient's condition by the physician-investigator.

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TO THE EDITOR: Although Boyer et al. report that F(ab')₂ antivenom reversed neurotoxic signs and symptoms, one should keep in mind that *Centruroides sculpturatus* does not belong to the most toxic species, which include several Mexican, Brazilian, and “old world” scorpions, whose stings may cause, in addition to neurotoxic effects, cardiac arrhythmias, cardiogenic shock, pulmonary edema, and death. These life-threatening consequences have been shown in studies of humans and of laboratory animals.^{1,2}

It is questionable whether the antivenom can reverse the cardiac pathophysiological effects. Several authors have shown that antivenom, including F(ab')₂, does not alleviate hemodynamic changes or cardiogenic pulmonary edema, or prevent death,^{2,3} and the outcome was the same for patients treated with antivenom and those treated without antivenom.^{3,4}

De Rezende et al.⁵ found that although venom antigen in plasma from persons who had been stung by scorpions was not detected 1 hour after antivenom therapy, and pain and agitation disappeared within a few hours, patients with pulmonary edema recovered only 48 hours after serotherapy.

Antivenom may be given to patients with venomous scorpion stings to reverse neurotoxic effects, but patients should be closely observed and treated appropriately when secondary (cardiorespiratory) complications occur.

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THE AUTHORS REPLY: Sofer et al. rightly point out that differences in the venom from scorpions in various parts of the world place inherent limitations on the generalizability of results from studies that involve a single geographic location. This problem is compounded by differences in medical care and in the quality and safety of the antivenom. Envenomation by North American neurotoxic scorpions can, in fact, involve pulmonary edema and cardiac effects¹; however, we specifically avoided including these effects as end points for our small clinical trial, because they are less consistently observed than the more florid neuromotor effects and because slow resolution of pulmonary edema might obscure signs of toxin reversal, a possibility that is consistent with the

observation by Sofer et al. More commonly, in our sickest patients, neuromotor toxic effects themselves cause ventilatory failure, and this phenomenon is amenable to reversal with antivenom.

Differences in outcome between our study and the one by Abroug et al.² reflect some combination of the same issues — differences in venom, in clinical study design, and in antivenom potency. Our binary primary end point was selected to show a difference between very small groups, and our decision to study children who were sick enough to require intensive care (corresponding approximately to grade 3 on the severity scale used in Tunisia) ensured that reversal of the syndrome would be unambiguous. A standardized protocol, in which midazolam was used because of its short duration of action, allowed adjustment of the dose at 15-minute intervals. This allowed dosing to reflect the rising or diminishing severity of the syndrome, irrespective of the actual last moment of toxicity. Our findings that intravenous antivenom shortens the plasma half-life of venom are consistent with findings of Krifi et al.³ and of Ghalim et al.,⁴ and our primary and secondary end points show the clinical correlation between the administration of sufficient neutralizing doses of antivenom and the resolution of toxic effects. A direct comparison of our study of venom neutralization with the study by Abroug et al. cannot be made because their study design did not incorporate venom levels.

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