significant increase in airway inflammation as determined by BAL fluid cytologic evaluation with total white blood cells 11.4 ± 3 cells/ml × 10^4 at baseline versus 14 ± 4 cells/ml × 10^4 after treatment (p = 0.45). Cell differential showed no significant changes in percentage of alveolar macrophages (p = 0.3), lymphocytes (p = 0.5) or neutrophils (p = 0.15). Furthermore, gene transcripts of the proinflammatory molecules interleukin (IL)-1β (p = 0.46) and IL-8 (p = 0.26) showed no evidence for upregulation after rIFN-γ therapy (Table II). Thus treatment with rIFN-γ did not enhance T_{H1} cell-mediated inflammation.

Of potentially greatest interest, we observed that four of the five patients had a decrease in the percent of BAL eosinophils (Table I). Robinson et al.[7] have recently shown that improvement in asthma after treatment with a course of prednisolone may be related to the observed decrease in BAL cells expressing mRNA for IL-4 and IL-5 (a T_{H2} pattern) and an increase in cells expressing mRNA for IFN-γ, with decreased number of BAL eosinophils. Because IFN-γ has been shown to inhibit T_{H2} cell function, immunomodulation of IL-4 and IL-5 cytokine production could lead to decreased eosinophil infiltration and activation with a decrease in T_{H2} cell-mediated inflammation. Future studies are needed to examine the potential role of nebulized rIFN-γ in asthma and other pulmonary diseases.

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REFERENCES

1. Gajewski TF, Fitch FW. Antiproliferative effect of IFN-γ in immune regulation. I. IFN-γ inhibits the proliferation of Th2 but not Th1 murine helper T lymphocyte clones. J Immunol 1988;140:4245-52.
2. Hanifin J, Schneider LC, Leung DYM, et al. Recombinant interferon-gamma therapy for atopic dermatitis. J Am Acad Dermatol 1993;28:189-97.
3. Boguniewicz M, Schneider LC, Milgrom H, et al. Treatment of steroid-dependent asthma with recombinant interferon-gamma. Clin Exp Allergy 1993;23:785-90.
4. Jaffe HA, Buhl R, Mastrangeli A, et al. Organ specific cytokine therapy: local activation of mononuclear phagocytes by delivery of an aerosol of recombinant interferon-γ to the human lung. J Clin Invest 1991;88:297-302.
5. Martin RJ, Boguniewicz M, Henson JE, et al. The effects of inhaled interferon gamma in normal human airways. Am Rev Respir Dis 1993;148:1677-82.
6. Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. Am Rev Respir Dis 1986;136:225-44.
7. Robinson D, Hamid Q, Ying S, et al. Prednisolone treatment in asthma is associated with modulation of bronchoalveolar lavage cell interleukin-4, interleukin-5, and interferon-γ cytokine gene expression. Am Rev Respir Dis 1993;148:401-6.

Immediate, late, and delayed skin test responses to *Centruroides vittatus* scorpion venom

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As one of 40 species inhabiting the United States, the common Texas striped scorpion, *Centruroides vittatus*, produces a low toxicity venom,[1] which usually causes immediate sharp pain and local swelling after a sting. Venom neurotoxins may also produce skeletal muscle spasms and paresthesias, particularly of the sting site, face, and tongue.[2] Immunologic reactions to envenomation have not been well documented.

Abbreviations used
LLR: Large local reaction of greater than 24 hours' duration
LPR: Late-phase response

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TABLE I. Skin test responses

Subject	Historical reaction	Years since last sting	Intradermal immediate				Intradermal late/delayed			
			1:1M	1:100K	1:10K	1:1000	8 hr	12 hr	24 hr	48 hr
P1	Systemic	1	−	+, Sym	ND	ND	37 × 45/ 50 × 65*	25 × 39/ 42 × 62	21 × 32/ 33 × 57	−
P2	Sys + LLR	7	−	−	−	−	−	19 × 22	55 × 60	120 × 125†
P3	Sys + LLR	5	−	−	−	+	−	−	24 × 25	30 × 38†
P4	LLR	3	−	−	−	+	−	−	23 × 28	25 × 36† 10 × 10‡
P5	LLR	2	−	−	−	+	−	−	−	−
P6	Minor	30	−	−	−	+	−	−	−	−
P7	Minor	2	−	−	−	+	−	−	−	−
C1	NA	NA	−	−	−	+	−	19 × 24§	−	−
C2	NA	NA	−	−	−	+	−	−	−	−
C3	NA	NA	+	+	+	+	−	−	−	−
C4	NA	NA	−	−	−	−	−	−	−	−
C5	NA	NA	−	−	−	+	−	−	−	−
C6	NA	NA	−	−	−	+	−	−	−	−

Patients (P1 to P7) have a history of a scorpion sting. C1 to C6 are unstung control subjects. Historical reactions included toxic symptoms alone (minor) or toxic symptoms in addition to an LLR or systemic (i.e., anaphylactic) symptoms. Immediate intradermal test results were positive (+) if wheal was greater than 5 mm and erythema was greater than 10 mm in diameter. For P1, systemic symptoms were temporally related to the 11 × 10/26 × 37 (wheal/flare) positive skin test. Late and delayed responses were positive if swelling or induration, as well as associated erythema, was equal to or greater than 10 mm in each orthogonal diameter.

Sys, Systemic; *ND,* not done; *NA,* not applicable.

*Maximal subcutaneous swelling erythema after skin test with 1:100,000 diluted venom.

†Maximal erythematous induration after skin test with 1:1000 diluted venom.

‡Maximal erythematous induration after skin test with 1:10,000 diluted venom.

§Erythema after skin test with 1:1000 diluted venom.

CASE REPORTS

Seven patients with a history of *C. vittatus* envenomation and six control subjects were evaluated by prick and intradermal skin testing with *C. vittatus* venom. Three subjects had a history of immediate anaphylactic reactions to envenomation.

Case 1

The patient was a 38-year-old woman with a history of five episodes of scorpion envenomation. Each of the three most recent episodes, which occurred within a single 30-day period, resulted in immediate local pain, which was followed in minutes by regional paresthesias, chest tightness, wheezing, nausea, vomiting, dizziness, and light-headedness.

Case 2

The patient was a 53-year-old woman with a history of two episodes of scorpion envenomation. The first sting resulted in a large local reaction (LLR), and the second sting, within the same year, resulted in large local swelling, wheezing, and chest tightness within 1 to 2 minutes.

Case 3

The patient was a 57-year-old woman with a history of two episodes of scorpion envenomation. Her initial sting resulted in an LLR, and the subsequent sting 2 years later resulted in an LLR and shortness of breath, abdominal cramps, light-headedness, and a sense of impending doom within 1 hour.

Four additional cases included three women and one man, 35 to 48 years old, with histories of LLR (two subjects) and/or neurotoxic symptoms after 1 to 12 scorpion stings each.

The group of six control subjects included one woman and five men, 33 to 45 years old, with no history of scorpion stings.

METHODS

Venom was collected from dissected venom sacs of *C. vittatus* scorpions captured within Bexar County, Texas. Three microliters of venom was diluted 1:1000 in sterile diluent before filtering (0.22 μm), resulting in approximately 100 μg of venom protein/ml.[3]

Subjects underwent skin prick tests with this 1:1000 diluted venom before titrated intradermal tests (0.02 ml

of a 1:1,000,000; advancing by serial 10-fold dilutions to 1:1000) were performed. Orthogonal wheal and flare diameters were recorded at 15 minutes; and late and delayed tissue induration were measured at 6, 12, 24, and 48 hours. Histamine and diluent controls were used.

RESULTS

Table I lists responses to venom skin testing. The patient in case 1 had a significantly positive immediate reaction in response to an intradermal test with 1:100,000 diluted venom and a characteristic late-phase response (LPR) with warm, erythematous swelling and surrounding erythema, which were maximal at 8 hours. Concurrent with her positive immediate skin test response, she experienced light-headedness and chest tightness, which resolved spontaneously within approximately 5 minutes. She did not undergo further skin tests. Two remaining patients with systemic reaction and LLR histories and one patient with history of an LLR had firm erythematous indurations after intradermal skin tests with 1:1000 diluted venom. These delayed reactions were maximal at 48 hours and were characteristic of a delayed-type hypersensitivity skin reaction.

Nonspecific immediate reactivity was seen in five of six stung patients and five of six unstung control subjects in response to intradermal test with 1:1000 diluted venom. One control subject had a small positive intradermal skin test response to 1:1,000,000 diluted venom (6 × 6 mm wheal and erythema), which did not increase significantly in size with subsequent skin testing and had no associated late reactions.

No subject experienced toxic local or systemic symptoms of envenomation during skin testing.

DISCUSSION

In case 1, IgE-mediated hypersensitivity to *C. vittatus* envenomation was suggested by the patient's history of a systemic reaction, positive intradermal skin test response to 1:100,000 venom dilution, immediate systemic symptoms, and LPR 8 hours after skin testing. Despite a history of systemic reactions to field stings 7 and 5 years before, the patients in cases 2 and 3 demonstrated no immediate response to intradermal skin testing with venom. This lack of response may represent loss of IgE hypersensitivity with time, as has been suggested with other venoms.[4] The isolated delayed reactions manifested by the patients in cases 2 and 3 and one other stung subject suggest a second immunologic response to scorpion venom—a type IV delayed hypersensitivity reaction, with maximal skin test induration observed at 48 hours. Each of these three patients had reported an LLR with envenomation. Characterization of delayed reactions to scorpion venom will require skin biopsy and analysis of the cellular infiltration during delayed reactions.

Patient responses to skin testing with scorpion venom were similar to the clinical experience with skin testing to other venoms.[4, 5] Nonspecific skin test responses were seen in 10 (five stung and five unstung) of 12 subjects (83%) intradermally skin tested with scorpion venom diluted 1:1000 (an estimated 100 μg protein/ml). This threshold for nonspecific reactivity is slightly higher than that for Hymenoptera venom, for which a 25% nonspecific skin test rate is reported at 10 μg/ml.[4]

Our one control subject with immediate scorpion skin test reactivity but no sting history might have been stung unknowingly. Alternatively, because of this subject's extensive exposure to flying Hymenoptera and imported fire ant stings, we speculate that his positive skin test responses might represent cross-reactivity with other venoms. Further investigation is required to confirm this possibility.

In summary, scorpion venom contains antigenic and potentially allergenic proteins. In addition to well-known toxic responses to scorpion envenomation, some individuals may exhibit immunologically mediated responses to envenomation. Among the patients we have studied, immediate and delayed hypersensitivity to the sting of the *C. vittatus* scorpion may play an important role in the morbidity of scorpion envenomation.

REFERENCES

1. Keegan HL, Lockwood WR. Secretory epithelium in venom glands of two species of scorpions of the genus *Centruroides marx*. Am J Trop Med Hyg 1971;20:770-85.
2. Rochat H. Scorpion toxin and mode of action. Adv Cytopharmacol 1979;3:325-334.
3. Yahel-Niv A. Comparative studies in venom obtained from individual scorpions by natural stings. Toxicon 1979;17:435-46.
4. Georgitis JW, Reisman RE. Venom skin tests in insect-allergic and insect-nonallergic populations. J ALLERGY CLIN IMMUNOL 1985;76:803-7.
5. Hunt KJ, Valentine MD, Sobotka AK, Lichtenstein LM. Diagnosis of allergy to stinging insects by skin testing with hymenoptera venoms. Ann Intern Med 1976;85:56-7.