

31. Piper PJ, Samhoun MN: Stimulation of arachidonic acid metabolism and generation of thromboxane A_2 by leukotrienes B_4 , C_4 , and D_4 in guinea pig lung in vitro. *Br J Pharmacol* 77:267, 1982
32. Sirois P, Chagnon M, Borgeat P, Vallerand P: Role of cyclooxygenase products in the lung action of leukotrienes A_4 , B_4 , C_4 , D_4 , and E_4 . *Pharmacology* (in press)
33. Robinson C, Hoult JRS, Waddell KA, Blair IA, Dollery CT: Total profiling by GC/NICIMS of the major cyclooxygenase products from antigen and leukotriene-challenged guinea pig lung. *Biochem Pharmacol* 33:395, 1984
34. Piper PJ, Seale JP: Nonimmunological release of slow-reacting substance from guinea pig lungs. *Br J Pharmacol* 67:67, 1979
35. Borgeat P, Samuelsson B: Metabolism of arachidonic acid in polymorphonuclear leukocytes: effects of the ionophore A23187. *Proc Natl Acad Sci USA* 76:2148, 1979
36. Jubiz W, Radmark O, Malmsten C, Hansson G, Lindgren JA, Palmblad J, Udén AM, Samuelsson B: A novel leukotriene produced by stimulation of leukocytes with formylmethionylleucylphenylalanine. *J Biol Chem* 257:6106, 1982

Guidelines for venom immunotherapy

David B. K. Golden, M.D., and Howard J. Schwartz, M.D.

for The Committee on Insects, American Academy of Allergy and Immunology

The following guidelines for venom immunotherapy were agreed on at the annual meeting of the Committee on Insects of the American Academy of Allergy and Immunology in 1985. These guidelines are intended as an aid to the clinician in his delivery of the best possible patient care. They should be viewed as flexible guides that must allow for proper clinical judgment and application in each individual case. These guidelines were approved unanimously by the members of the Committee on Insects at the annual meeting in 1985 after considerable discussion of a preliminary draft in 1984.

1. The efficacy of Hymenoptera venom extract in the diagnosis and treatment of stinging insect allergy is established beyond doubt. Whole body extract should no longer be used for diagnosis or therapy of any patients complaining of allergic reactions to the stings of bees, wasps, hornets, or yellow jackets. Patients receiving whole body extract therapy should be reevaluated without regard to their previous treatment.^{1, 2}
2. All persons who have had systemic allergic reactions to insect stings should be skin tested with Hymenoptera venom extracts at concentrations up to and including 1.0 $\mu\text{g/ml}$. Starting dilutions will be dictated by the clinical history and the clinician's establishment of their own criteria for safety in diagnosis and treatment of such patients.

False positive skin tests are quite unusual at concentrations up to and including 1.0 $\mu\text{g/ml}$.

Venom-specific IgE antibodies have been found in the serum of persons with positive skin tests to these venom concentrations. Truly false positive, irritative skin reactions occur only rarely at concentrations of 1 $\mu\text{g/ml}$ and only somewhat more commonly at 10 $\mu\text{g/ml}$.³⁻⁵

3. All persons who have had systemic allergic sting reactions and have positive venom skin tests or venom RASTs are candidates for venom immunotherapy. Up to 60% of such patients have a risk of anaphylaxis when they are resting. There are no currently available, practical methods to improve prediction of future anaphylaxis on resting. Thus, clinical history and demonstration of venom-specific IgE by skin test or RAST constitute the only useful method for evaluating patients for venom immunotherapy.
4. The venom IgE RAST assay is helpful but is less sensitive than venom skin testing. It can be useful when skin tests cannot be performed for particular reasons or when skin test results are difficult to interpret.^{6, 7}
5. Venom immunotherapy is usually not indicated for children less than 16 years of age who have had strictly cutaneous sting reactions. This therapeutic decision is a matter of clinical judgment based on the specific situation, the preference of the patient and family, and the impression of the physician, although the available data suggest these individuals are at minimal risk for future serious reactions on re-sting.

Received for publication June 3, 1985.

Accepted for publication Oct. 16, 1985.

Reprint requests: Howard J. Schwartz, M.D., 1611 So. Green Rd., Suite 265, So. Euclid, OH 44121.

6. Persons who have had only large local sting reactions do not require venom immunotherapy. The risk of subsequent systemic sting reactions is estimated to be <10%.^{8,9} Venom testing is not truly necessary but may be performed as a matter of interest in some patients. Prophylactic venom immunotherapy may be considered in special situations that may be present.
7. Persons who have never had an abnormal sting reaction should not be tested or treated with venoms. Venom skin tests and/or venom RAST assays can be positive in up to 20% of the population.^{10,11} The clinical significance or the prognostic value of these positive results is not yet known. The sensitivity may be transient, and thus, there is no clinical value to these test findings. As in other fields of medicine, patients should not be treated based on an isolated laboratory finding alone.
8. Maintenance venom immunotherapy should be administered at 4- to 6-week intervals.¹² Criteria have not yet been established that define at what point venom immunotherapy can be stopped.^{13,14} One supposes that the loss of venom skin test or RAST reactivity would be one such criterion. However, we do not yet know how low the sensitivity must become before one can safely stop treatment; therefore, we cannot recommend any cessation of therapy if positive skin tests or venom RAST reactivity persists. Similarly, there are no guidelines for cessation of immunotherapy that are based on the level of antivenom IgG.
9. Patients with sting anaphylaxis and negative tests for antivenom IgE are not candidates for immunotherapy, unless the culprit is venom can be identified. Therapy would have no scientific basis and would be of unproven "benefit."
10. There are no absolute contraindications to venom immunotherapy that are generally agreed on.
11. Many questions yet remain open for study that

cannot be properly addressed in this consensus statement.

REFERENCES

1. Lichtenstein LM, Valentine MD, Sobotka AK: Insect allergy: the state of the art. *J ALLERGY CLIN IMMUNOL* 64:5, 1979
2. Golden DBK, Langlois J, Valentine MD, et al: Treatment failures with whole body extract therapy of insect sting allergy. *JAMA* 246:2460, 1981
3. Hunt KJ, Valentine MD, Sobotka AK, Lichtenstein LM: Diagnosis of allergy to stinging insects by skin testing with Hymenoptera venoms. *Ann Intern Med* 85:56, 1976
4. Schwartz HJ, Lockey RF, Sheffer AL, et al: A multicenter study on skin test reactivity of human volunteers to venom as compared with whole body Hymenoptera antigens. *J ALLERGY CLIN IMMUNOL* 67:81, 1981
5. Reisman RE, Dvorin DJ, Randolph CC, Georgitis JW: Stinging insect allergy: national history and modification with venom immunotherapy. *J ALLERGY CLIN IMMUNOL* 75:735, 1985
6. Sobotka AK, Adkinson NF Jr, Valentine MD, et al: Allergy to insect stings. IV. Diagnosis by radioallergosorbent test (RAST). *J Immunol* 121:2477, 1978
7. Santrach PJ, Peterson LG, Yunginger JW: Comparison of diagnostic tests for Hymenoptera sting allergy. *Ann Allergy* 45:130, 1980
8. Graft DF, Schuberth KC, Kagey-Sobotka A, et al: A prospective study of the natural history of large local reactions following Hymenoptera stings in children. *J Pediatr* 104:664, 1984
9. Mauriello PM, Barde SH, Georgitis JW, Reisman RE: National history of large local reactions from stinging insects. *J ALLERGY CLIN IMMUNOL* 74:494, 1984
10. Golden DBK, Valentine MD, Kagey-Sobotka A, et al: Prevalence of Hymenoptera venom allergy. *J ALLERGY CLIN IMMUNOL* 69:124, 1982 (abst)
11. Stuckey M, Cobain T, Sears M, et al: Bee venom hypersensitivity in Busselton. *Lancet* 2:41, 1982
12. Golden DBK, Valentine MD, Kagey-Sobotka A, Lichtenstein LM: Prolonged maintenance interval in Hymenoptera venom immunotherapy. *J ALLERGY CLIN IMMUNOL* 67:482, 1981
13. Golden DBK, Johnson K, Addison BI, et al: Evolution of Hymenoptera venom allergy (HVA). *J ALLERGY CLIN IMMUNOL* 73:189, 1984 (abst)
14. Dvorin DD, Georgitis JW, Reisman RE: Natural history of insect sting anaphylaxis: evaluation of untreated and incompletely treated PTS. *J ALLERGY CLIN IMMUNOL* 73:188, 1984 (abst)