

Table 10. Insect Hypersensitivity

Referral Guideline	Rationale	Evidence Type
<p>Consider referral of patients with systemic reactions suspected or possibly due to insect stings for accurate identification of specific allergen and consideration for venom immunotherapy (or whole body extract in case of fire ant).</p>	<ul style="list-style-type: none"> • Up to 3% of the population are at risk for anaphylaxis to insect stings with approximately 40 documented deaths annually.¹⁻⁸ • Patient identification of the correct specific insect species causing an allergic reaction is frequently incorrect. • Allergy testing and history-test correlation can more accurately identify specific insects responsible for an allergic reaction and may be helpful in diagnosis, treatment and avoidance recommendations.^{7, 9-18} • Skin testing is generally preferred over in vitro testing for the initial evaluation of venom-specific IgE antibodies.^{4, 5, 13, 15, 17-21} • Venom immunotherapy (or fire ant whole body extract) greatly reduces the risk of systemic reactions in stinging insect-sensitive patients.^{2, 3, 5, 8, 15, 22-24} • Venom immunotherapy may prevent death due to subsequent stings in hypersensitive patients.^{3, 5, 15, 25} 	<p>Diagnostic</p> <p>Indirect outcome evidence (avoidance, early pharmacologic treatment of reaction, immunotherapy)</p>
<p>Consider referral of patients with systemic reactions suspected or possibly due to biting insects for accurate identification of specific allergen.</p>	<ul style="list-style-type: none"> • Biting insects such as <i>Triatoma</i> species and mosquitoes have been identified as a cause of systemic reactions.²⁶⁻³⁰ • RAST and skin testing to <i>Triatoma</i> salivary gland extracts and whole body extracts of other biting insects have been used to identify antigen specific IgE in sera of hypersensitive patients.³¹⁻⁴¹ • Patient education by an allergist/immunologist, including the etiology of their allergy, specific avoidance measures, recognition and treatment of anaphylaxis, and management of local side effects may reduce patient anxiety and potentially reduce morbidity from future bites.²⁶⁻³⁰ 	<p>Diagnostic</p> <p>Indirect outcome (avoidance, appropriate pharmacologic therapy)</p>
<p>Consider referral of patients on venom (or fire ant whole body extract) immunotherapy annually for review of interval history, tolerance of immunotherapy, need for repeat testing, and need for continued therapy.</p>	<ul style="list-style-type: none"> • Regular review of interval history immunotherapy dosing, schedule, and adverse events may contribute to reduced complications of treatment.¹⁷⁻¹⁸ • Regular review may identify new co-morbidities or medications that increase the risk of poor outcomes from natural stings or insect immunotherapy reactions.^{17-18, 42-45} 	<p>Indirect outcome evidence (avoidance, early pharmacologic therapy, immunotherapy)</p>

Referral Guideline	Rationale	Evidence Type
	<ul style="list-style-type: none"> • Assessment of reactions to interval stings can be used to monitor effectiveness of immunotherapy and may be cause for consideration of changes in dose and schedule.^{17-18, 46-49} • The interval between maintenance dose injections can be increased to 4-week intervals during the first year of immunotherapy and eventually to every 6-12 weeks in some patients.^{17-18, 49-50} • Many patients may safely discontinue venom immunotherapy after at least 3-5 years of treatment, although some patients may need to continue immunotherapy indefinitely. An allergist/immunologist with experience in treating insect allergic patients is best suited to facilitate individualized patient decisions.^{17-18, 50-63} 	

References:

1. Chafee FH. The prevalence of bee sting allergy in an allergic population. *Acta Allergol* 1970; 25:292-3. Evidence grade: III
2. Settignano GA, Boyd GK. Prevalence of bee sting allergy in 4,992 Boy Scouts. *Acta Allergol.* 1970; 25:286-7. Evidence grade: II
3. Antonicelli L, Beatrice Bilo M, Bonifazi F. Epidemiology of Hymenoptera allergy. *Curr Opin Allergy Clin Immunol.* 2002; 2:341-46. Evidence grade: IV
4. Golden DBK. Epidemiology of allergy to insect venoms and stings. *Allergy Proc.* 1989; 16:103-7. Evidence grade: IV
5. Charpin D, Birnbaum J, Vervloet D. Epidemiology of Hymenoptera allergy. *Clin Exp Allergy* 1994; 24:1010-5. Evidence grade: IV
6. Barnard JH. Studies of 400 Hymneoptera sting deaths in the United States. *J Allergy Clin Immunol* 1973; 52:259-64. Evidence grade: III.
7. DeShazo R, Butcher B, Barber W. Reactions to stings of the imported fire ant. *N Engl J Med* 1990; 323:463-6. Evidence grade: III
8. Freeman T, Hylander R, Ortiz A, Martin M. Imported fire ant immunotherapy: effectiveness of whole body extracts. *J Allergy Clin Immunol* 1992; 90:210-5. Evidence grade: II
9. Hunt K, Valentine M, Sobotka A, Liechtenstein L. Diagnosis of allergy stinging insects by skin testing with Hymenoptera venoms. *Ann Intern Med* 1976; 85:56-9. Evidence grade: II
10. Rueff F, Pryzbilla B, Muller U, Mosbech H. The sting challenge test in hymenoptera venom allergy. Position paper of the Subcommittee on Insect Venom Allergy of the European Academy of Allergology and Clinical Immunology. *Allergy.* 1996; 51:216-25. Evidence grade: IV
11. Georgitis J, Reisman R. Venom skin tests in insect-allergic and insect-nonallergic populations. *J Allergy Clin Immunol* 1985; 76:803-7. Evidence grade: II

12. Golden DBK, Marsh DG, Friedhoff LR, et al. Natural History of Hymenoptera Venom Sensitivity in adults. *J Allergy Clin Immunol* 1997; 100:760-6. Evidence grade: III
13. Golden DBK, Kagey-Sobotka A, Norman PS, et al. Insect sting allergy with negative venom skin test responses. *J Allergy Clin Immunol* 2001; 107:897-901. Evidence grade: III
14. Moffitt J, Barker J, Stafford C. Management of imported fire ant allergy: results of a survey. *Ann Allergy* 1997; 79:125-30. Evidence grade: III
15. Oude Elberink JNG, Dubois AEJ. Quality of life in insect venom allergic patients. *Curr Opin Allergy Clin Immunol* 2003; 3:287-93. Evidence grade: IV
16. Reisman R. Insect stings. *N Engl J Med* 1994; 331:523-7. Evidence grade: IV
17. Stinging Insect Hypersensitivity: A Practice Parameter. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council on Allergy, Asthma and Immunology. *J Allergy Clin Immunol*. 1999; 103(5 pt 1):963-980. Evidence grade: IV
18. Stinging Insect Hypersensitivity: A Practice Parameter Update. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council on Allergy, Asthma and Immunology. *J Allergy Clin Immunol*. 2004; 114(4):869-8. Evidence grade: IV
19. Valentine M. Allergy to the stinging insects. *Ann Allergy* 1993; 70:427-32. Evidence grade: IV
20. Valentine M. Insect venom allergy: diagnosis and treatment. *J Allergy Clin Immunol* 1984; 73:299-304. Evidence grade: IV
21. 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. *JACI* 1981; 67:81-85. Evidence grade: II
22. Hunt K, Valentine M, Sobotka A. A controlled trial of immunotherapy in insect hypersensitivity. *N Engl J Med* 1978; 299: 156-61. Evidence grade: II
23. Triplett R. Sensitivity to the imported fire ant: successful treatment with immunotherapy. *South Med J* 1973; 66:477-80. Evidence grade: III
24. Valentine M, Schuberth K, Kagey-Sobotka A. The value of immunotherapy with venom in children with allergy to insect stings. *N Engl J Med* 1991; 323:1601-3. Evidence grade: Ib
25. Sasvary T, Muller U. Fatalities from insect stings in Switzerland 1978 to 1987 *Schweiz Med Wochenschr*. 1994; 29; 124(43):1887-94. Evidence grade: III
26. Feingold BF, Benjamin E. Allergy to flea bites. *Ann Allergy* 1961; 19:1275-1289. Evidence grade: III.

27. Hoffman DR. Allergic reactions to biting insects. In: Monograph on Insect Allergy, 4th edition. Levin MI & Lockey RF eds. Dave Lambert Associates, Pittsburgh. 2003:161-203. Evidence grade: IV
28. McCormack DR, Salata KF, Hershey JN, Carpenter GB, Engler RJ. Mosquito bite anaphylaxis: Immunotherapy with whole body extracts. *Ann Allergy Asthma Immunol* 1995; 74:39-44. Evidence grade: IV
29. Rohr AS, Marshall NA, Saxon A. Successful immunotherapy for *Triatoma protracta*-induced anaphylaxis. *J Allergy Clin Immunol* 1984; 73:369-75. Evidence grade: II
30. Simons FER, Peng Z. Mosquito Allergy. In: Monograph on Insect Allergy, 4th edition. Levin MI & Lockey RF eds. Dave Lambert Associates, Pittsburgh. 2003:161-203. Evidence grade: IV
31. Gauci M, Lob RKS, Stone BF, Thong YH. Evaluation of partially purified salivary gland allergens from the Australian paralysis tick, *Ixodes holocyclus*, in diagnosis of allergy by RIA and skin prick test. *Ann Allergy* 1990; 64:297-299. Evidence grade: III
32. Hoffman DR. Biting-insect allergens. *Clin Allergy Immunol*. 2004; 18:355-68. Evidence grade: IV
33. Peng Z, Lam H, Cheng XW, Cheen YL, Simons FER. Characterization and clinical relevance of two recombinant mosquito *Aedes aegypti* salivary allergens rAED a 1 and rAed a 2. *J Allergy Clin Immunol* 1998; 101:S32. Evidence grade: III
34. Peng Z, Yang M, Simons FER. Measurement of mosquito *Aedes vexans* salivary gland-specific IgE and IgG antibodies and the distribution of these antibodies in human sera. *Ann Allergy Asthma Immunol* 1995; 74:259-64. Evidence grade: III
35. Pinnas JL, Chen TMW, Hoffman DR. Evidence of IgE mediation of human sensitivity to Reduviid bug bites. *Fed Proc* 1978; 37:1555. Evidence grade: III
36. Renula T, Brummer-Korvenkontio H, Palosuo K, et al. Frequent occurrence of IgE and IgG4 antibodies against saliva of *Aedes communis* and *Aedes aegypti* mosquitoes in children. *Int Arch Allergy Immunol* 1994; 104:366-371. Evidence grade: III
37. Renula T, Brummer-Korvenkontio H, Rasanen L, Francois G, Palosuo T. Passive transfer of cutaneous mosquito-bite hypersensitivity by IgE anti-saliva antibodies. *J Allergy Clin Immunol* 1994; 94:902-6. Evidence grade: III
38. Shan EZ, Taniguchi Y, Shimizu M, et al. Immunoglobulins specific to mosquito salivary gland proteins in the sera of persons with common or hypersensitive reactions to mosquito bites. *J Dermatol* 1995; 22:411-18. Evidence grade: III
39. Trudeau WL, Fernandez-Caldas E, Fox RW, Brenner R, Lockey RF. Allergenicity of the cat flea (*Ctenocephalides felis felis*). *Clin Exp Allergy* 1993; 23:377-383. Evidence grade: III
40. Van Wye JE, Hsu Y—P, Lane RS, et al. IgE antibodies in tick bite induced anaphylaxis. *J Allergy Clin Immunol* 1991; 88:968-970.
41. Wilbur RD, Evans R. An immunologic evaluation of deerfly hypersensitivity. *J Allergy Clin Immunol* 1975; 55:72.
42. Hepner M, Ownby D, Anderson J. Risk of severe reactions in patients taking beta blocker drugs receiving allergen immunotherapy injections. *J Allergy Clin Immunol* 1990; 86:407-11. Evidence grade: II

43. Hermann K, Ring J. The renin-angiotensin system in patients with repeated anaphylactic reactions during Hymenoptera venom hyposensitization and sting challenge. *Int Arch Allergy Immunol* 1997; 112:251-6. Evidence grade: III
44. Simon P, Potier J, Thebaud HE. Risk factors for acute hypersensitivity reactions in hemodialysis. *Nephrologie* 1996; 17: 163-70. Evidence grade: III
45. Toogood J. Risk of anaphylaxis in patients receiving beta-blocker drug. *J Allergy Clin Immunol* 1988; 81:1-5. Evidence grade: IV
46. Golden D, Kagey-Sobotka A, Valentine M. Dose dependence of Hymenoptera venom immunotherapy. *J Allergy Clin Immunol* 1981; 67:370-4. Evidence grade: II
47. Rueff F, Wenderoth A, Przybilla B. Patients still reacting to a sting challenge while receiving conventional Hymenoptera venom immunotherapy are protected by increased venom doses. *J Allergy Clin Immunol* 2001; 108:1027-32. Evidence grade: III
48. Tracy J, Demain J, Quinn J, Hoffman D, Goetz D, Freeman T. The natural history of exposure to the imported fire ant (*Solenopsis Invicta*). *J Allergy Clin Immunol* 1995; 95:824-28. Evidence grade: II
49. Reisman R, Livingston A. Venom immunotherapy: 10 years of experience with administration of single venoms and 50 micrograms maintenance dose. *J Allergy Clin Immunol* 1992; 89:1189-95. Evidence grade: III
50. Goldberg A, Confino-Cohen. Maintenance venom immunotherapy administered at 3 month intervals is both safe and efficacious. *J Allergy Clin Immunol* 2001; 107:902-6. Evidence grade: II
51. Golden D, Valentine M, Kagey-Sobotka A. Prolonged maintenance interval in Hymenoptera venom immunotherapy. *J Allergy Clin Immunol* 1981; 67:482-4. Evidence grade: II
52. Golden D, Kwiterovich K, Kagey-Sobotka A. Discontinuing venom immunotherapy, outcome after five years. *J Allergy Clin Immunol* 1996; 97:579-87. Evidence grade: II
53. Golden DBK, Kagey-Sobotka A, Lichtenstein LM. Survey of patients after discontinuing venom immunotherapy. *J Allergy Clin Immunol* 2000; 105:385-90. Evidence grade: III
54. Golden DBK, Kwiterovitch KA, Adisson BA, et al. Discontinuing venom immunotherapy: extended observations. *J Allergy Clin Immunol* 1998; 101:298-305. Evidence grade: II
55. Graft D, Golden D, Reisman R, Valentin M, Yunginger J. The discontinuation of Hymenoptera venom immunotherapy. *J Allergy Clin Immunol*. 1998;101:573-5. Evidence grade: IV
56. Hauguard L, Norregard O, Dahl R. In-hospital sting challenge in insect venom allergic patients after stopping venom immunotherapy. *J Allergy Clin Immunol*. 1991; 87(3):702-9. Evidence grade: III

57. Keating M, Kagey-Sobotka A, Hamilton R, Yunginger J. Clinical and immunological follow-up of patients who stop venom immunotherapy. *J Allergy Clin Immunol*. 1991; 88:339-48. Evidence grade: III
58. Lerch E, Muller U. Long-term protection after stopping immunotherapy. *J Allergy Clin Immunol* 1998; 101:606-12. Evidence grade: II
59. Light WC. Insect sting fatality 9 years after venom treatment (venom allergy, fatality). *J Allergy Clin Immunol* 2001; 107:925. Evidence grade: III
60. Muller U, Berchold E, Helbring A. Honeybee venom allergy: results of a sting challenge 1 year after stopping successful immunotherapy in 86 patients. *J Allergy Clin Immunol* 1991; 87:702-9. Evidence grade: II
61. The diagnosis and management of anaphylaxis. Joint Task Force on Practice Parameters representing the American Academy of Allergy, Asthma & Immunology, the American College of Allergy, Asthma and Immunology, and the Joint Council on Allergy, Asthma and Immunology. *J Allergy Clin Immunol* 1998; 101(Suppl):S465-528. Evidence grade: IV
62. Reisman R. Duration of venom immunotherapy: relationship to the severity of symptoms of initial insect sting anaphylaxis. *J Allergy Clin Immunol* 1993; 92:831-6. Evidence grade: II
63. Ross RN, Nelson HS, Finegold I. Effectiveness of specific immunotherapy in the treatment of hymenoptera venom insensitivity: a meta-analysis. *Clin Ther*. 2000;22(3):351-8. Evidence grade: II