Letters to the Editor

Hymenoptera Allergy

Dear *Cutis*®:
I read the article by Bacelieri and Elston, "What's Eating You? Vespids" (*Cutis*. 2004;73:157-160), and offer the following comments. Currently, the preferred route of administering epinephrine is intramuscularly (0.3–0.5 mL of the 1:1000 concentration).[1] This is believed to be more effective than subcutaneous administration.

Regarding prophylaxis, every patient that has had an anaphylactic reaction to a Hymenoptera insect should be evaluated further to consider immunotherapy with the venom that caused the reaction. Patients judged to be at significant risk of another anaphylactic reaction from a Hymenoptera sting and patients with demonstrable antibodies to the Hymenoptera insects should be given immunotherapy with the appropriate insect venoms to reduce the risk of anaphylaxis from the 30% to 60% range to about 2%.[2]

Sincerely,
Macy I. Levine, MD
Pittsburgh, Pennsylvania

The author reports no conflict of interest.

REFERENCES

1. Valentine MD. Treatment of insect sting reactions. In: Levine MI, Lockey RF, eds. *Monograph on Insect Allergy*. 4th ed. Pittsburgh, Pa: American Academy of Allergy Asthma & Immunology; 2003:97-102.
2. Graft GF. Venom immunotherapy: indications, selections of venoms, techniques and efficacy. In: Levine MI, Lockey RF, eds. *Monograph on Insect Allergy*. 4th ed. Pittsburgh, Pa: American Academy of Allergy Asthma & Immunology; 2003:103-112.

Dear *Cutis:*
I read the Bacelieri and Elston article (What's eating you? vespids. *Cutis*. 2004;73:157-160) on stinging insects with interest. I would like to make 2 brief comments.

Epinephrine given intramuscularly, preferably in the vastus lateralis (the muscle of the upper leg), is recommended now for the treatment of a severe systemic allergic reaction or anaphylaxis. Epinephrine is absorbed more rapidly and distributed throughout the cardiovascular system when given intramuscularly. A preloaded auto-injector device (ie, EpiPen®) delivering 0.3 mg and 0.15 mg of epinephrine to adults and children, respectively, is available.

Bacelieri and Elston stated: "Symptoms of anaphylaxis generally start within 10 to 20 minutes after the sting." In patients with a severe immunoglobulin E (IgE)–mediated allergy, the symptoms of a systemic reaction/anaphylaxis actually may start within a few minutes or seconds! Measurable IgE levels may take a couple of weeks or more to develop after an insect sting. Therefore, allergy skin tests with insect venom or radioallergosorbent tests should not be conducted for at least 3 to 4 weeks following an allergic reaction.

Sincerely,
Roswitha Moehring, MD
Denver, Colorado

The author reports no conflict of interest.

Dear *Cutis:*
I read the article on vespids (Bacelieri RE, Elston DM. What's eating you? vespids. *Cutis*. 2004;73:157-160) with interest. The article was well written, but there was a major omission regarding treatment.

Hymenoptera venom immunotherapy has been used for decades. The initial treatment with whole-body extract proved to be nontherapeutic more than 25 years ago.[1,2] Since then, according to extensive scientific data, specific venom immunotherapy has been shown to decrease the repeat reaction rate from more than 50% to less than 5%, consistent with that of the general population.[3,4] That is, venom immunotherapy can cure a patient of venom anaphylaxis.

Unfortunately, it is not uncharacteristic for non–allergy trained physicians to diagnose and treat venom anaphylaxis with recommendations that

include avoidance measures and EpiPen use only. Like the Bacelieri and Elston review on the subject, immunotherapy is not even mentioned.

Many physicians in the United States do not know that venom immunotherapy can be curative. The Bacelieri and Elston article is another review of the subject that incredulously omits the most definitive treatment available today, one that is considered standard of care by the American Academy of Allergy Asthma & Immunology and the American College of Allergy, Asthma & Immunology.[5-7]

Sincerely,
Paul Detjen, MD
Kenilworth, Illinois

The author reports no conflict of interest.

REFERENCES

1. Lichtenstein LM, Valentine MD, Sobotka AK. A case for venom treatment in anaphylactic sensitivity to Hymenoptera sting. *N Eng J Med.* 1974;290:1223-1227.
2. Busse WW, Reed CE, Lichtenstein LM, et al. Immunotherapy in bee-sting anaphylaxis: use of honey bee venom. *JAMA.* 1975;231:1154-1156.
3. Hunt KJ, Valentine MD, Sobotka AK, et al. A controlled trial of immunotherapy in insect hypersensitivity. *N Engl J Med.* 1978;299:157-161.
4. Golden DBK, Valentine MD, Kagey-Sobotka A, et al. Regimens of Hymenoptera venom immunotherapy. *Ann Intern Med.* 1980;92:620-624.
5. Portnoy JM, Moffitt JE, Golden DB, et al, for the Joint Task Force for Practice Parameters in Allergy and Immunology. Stinging insect hypersensitivity: a practice parameter. *J Allergy Clin Immunol.* 1999;103:963-980.
6. Freeman TM. Hypersensitivity to Hymenoptera stings. *N Engl J Med.* 2004;351:1978-1984.
7. Moffit JE, Golden DBK, Reisman RE, et al. Stinging insect hypersensitivity: a practice parameter update. *J Allergy Clin Immunol.* 2004;114:869-886.

Dear *Cutis:*
I am writing regarding the article "What's Eating You? Vespids" by Bacelieri and Elston (*Cutis.* 2004;73:157-160). I would like to commend the authors on their timely article and the beautiful photographs contained therein. I think it is very important to continue to raise awareness on this potentially life-threatening problem.

However, I am concerned that there is some information in this article that is not current. The authors stated: "Anaphylaxis is treated initially with 0.3 cc of subcutaneous epinephrine." I would like to call their attention to published articles stating that epinephrine injections for the treatment of anaphylaxis should be given intramuscularly.[1,2] Given that epinephrine is the most essential element in the management of anaphylaxis, it is most important to include the current recommendations for the optimal route of administration.

My other major concern with this article is that there is no mention of desensitization with specific venom immunotherapy for Hymenoptera insect stings. This form of treatment is highly successful in preventing anaphylaxis upon re-sting and should be offered to any patient who has documented IgE-mediated hypersensitivity to Hymenoptera insects and a history of anaphylaxis following a Hymenoptera insect sting. When a patient presents with a history of systemic reaction to a stinging insect, it is not the current standard of care for the physician simply to encourage the patient to avoid being stung and carry an epinephrine injection for self-administration. The patient should be made aware of the availability of specific venom immunotherapy and should be referred to a board-certified allergy and immunology specialist for evaluation and treatment of this potentially life-threatening but manageable condition.

Respectfully,
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Tampa, Florida

The author reports no conflict of interest.

REFERENCES

1. Simons FE, Roberts JR, Gu X, et al. Epinephrine absorption in children with a history of anaphylaxis. *J Allergy Clin Immunol.* 1998;101:33-37.
2. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injections. *J Allergy Clin Immunol.* 2001;108:871-873.

Dear *Cutis:*
We enjoyed the fine article by Bacelieri and Elston, "What's Eating You? Vespids" (*Cutis.* 2004;73:157-160), and their assertion of the serious nature of anaphylaxis risk with vespid stings. We agree with their recommendation to refer all patients with a history of vespid-sting systemic reactions to an allergist. Formal allergy evaluation of these patients includes venom skin tests to determine the presence of specific IgE to venom proteins. Although venom skin tests have a 90% to 95% sensitivity, in some clinical

situations, the allergist may complement skin tests with in vitro measurement of venom-specific IgE antibodies. Individuals with recent severe systemic reactions and positive venom skin tests have a 40% to 70% risk of repeat anaphylactic reaction with the next sting.[1] Venom immunotherapy is considered the standard of care therapy for these individuals because it will decrease the risk of subsequent systemic reaction to 5%.[2] It should be continued for at least 3 to 5 years.[3] In addition to vespid allergy, this is also true for other insects within the order Hymenoptera (eg, honey bees, imported fire ants [IFAs]). Of interest in endemic areas, IFAs are the most frequent causes of Hymenoptera hypersensitivity.[4] Whole-body IFA immunotherapy has been shown to decrease the risk of anaphylaxis in sensitized patients with a prior history of systemic reaction to less than 2%.[5] Working together to educate and treat our patients with Hymenoptera hypersensitivity is the best way to diminish the morbidity and mortality associated with this growing health threat.

Sincerely,
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Lt Col Michael S. Tankersley, MD
3rd Medical Group
Elmendorf AFB, Alaska

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REFERENCES

1. Golden DBK, Tracy JM, Freeman TM, et al. Negative venom skin test results in patients with histories of systemic reaction to a sting. *J Allergy Clin Immunol.* 2003;112:495-498.
2. Hunt KJ, Valentine MD, Sobotka AK, et al. A controlled trial of immunotherapy in insect hypersensitivity. *N Engl J Med.* 1978;299:157-161.
3. Portnoy JM, Moffitt JE, Golden DBK, et al. Stinging insect hypersensitivity: a practice parameter. *J Allergy Clin Immunol.* 1999;103:963-980.
4. Freeman TM. Hymenoptera hypersensitivity in an imported fire ant endemic area. *Ann Allergy Asthma Immunol.* 1997;78:369-372.
5. Tankersley MS, Walker RL, Butler WK, et al. Safety and efficacy of an imported fire ant rush immunotherapy protocol with and without prophylactic treatment. *J Allergy Clin Immunol.* 2002;109:556-562.

Author Response

I appreciate the comments from Drs. Levine, Moehring, Detjen, Stewart, Messier, and Tankersley, as well as their interest in our article. They are absolutely correct to state that some data favor intramuscular injection of epinephrine, though it should be noted that recommendations for the acute treatment of anaphylaxis are based largely on animal data and limited controlled human data. Additional controlled data are needed regarding dosage and administration mode for epinephrine, as well as the amount and kind of intravenous fluids that may be beneficial.[1]

Epinephrine remains the most important acute intervention for the treatment of anaphylaxis, and the patient with an increased risk of allergic reactions should have an auto-injector kit on hand at all times. EpiPens deliver an intramuscular injection. Some evidence suggests that the absorption of intramuscular epinephrine is faster and the plasma levels are higher compared with subcutaneous injection.[2,3] Recent data also suggest that carefully titrated intravenous adrenaline combined with volume resuscitation can be an effective strategy for treating sting anaphylaxis, and patients with severe bradycardia may benefit from treatment with atropine.[4] Such treatment is obviously not easily self-administered.

The American Academy of Allergy Asthma & Immunology noted[5]: "Although intravenous infusion of epinephrine may be more dangerous, the standard subcutaneous dose of epinephrine, 1:1000, 0.3 mL, has far greater benefit than risk in the management of acute anaphylaxis." The advocacy statement also notes: "Frequent or higher doses of subcutaneous epinephrine should be avoided if possible; but repeated doses may be necessary for severe anaphylaxis, and simultaneous efforts to obtain emergency medical help should always be made when the initial dose is given."[5] However, because subcutaneous kits are no longer readily available, the EpiPen injector is usually prescribed.

The respondents are absolutely correct that patients with documented anaphylaxis to a hymenopterid should be evaluated further to consider immunotherapy. Immunotherapy has been shown to improve quality of life for patients with severe hymenopterid allergy. I regret this was not emphasized in the article. I also thank Dr. Moehring for the comments on the timing of radioallergosorbent testing.

In addition, I appreciate the comments made by Drs. Messier and Tankersley. IFA stings are an important cause of allergic reactions in the southern

United States. Their thoughtful comments are worth heeding because patients may benefit from consulting an allergist.

Sincerely,
Dirk M. Elston, MD
Geisinger Medical Center
Danville, Pennsylvania

The author reports no conflict of interest.

REFERENCES

1. Ranft A, Kochs EF. Treatment of anaphylactic reactions: a review of guidelines and recommendations [in German]. *Anasthesiol Intensivmed Notfallmed Schmerzther*. 2004;39:2-9.
2. Simons FE, Roberts JR, Gu X, et al. Epinephrine absorption in children with a history of anaphylaxis. *J Allergy Clin Immunol*. 1998;101:33-37.
3. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. *J Allergy Clin Immunol*. 2001;108:871-873.
4. Brown SG, Blackman KE, Stenlake V, et al. Insect sting anaphylaxis; prospective evaluation of treatment with intravenous adrenaline and volume resuscitation. *Emerg Med J*. 2004;21:149-154.
5. American Academy of Allergy Asthma & Immunology. The use of epinephrine in the treatment of anaphylaxis. Available at: www.aaaai.org/media/resources/academy_statements/advocacy_statements/ps26.asp. Accessed May 10, 2004.