## Letters to the Editor

Online-Only Letters to the Editor

The Role of Nonpharmacologic Therapies for Back Pain Benjamin Kligler, MD, MPH, with reply by Brian A. Casazza, MD (http://www.aafp.org/ afp/2012/1101/ol1. html)

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### Does an Isolated Allergic Reaction Increase the Risk of Anaphylaxis?

**Original Article:** Anaphylaxis: Recognition and Management

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TO THE EDITOR: I enjoyed and appreciated this article, but there was one question I had that was not addressed. Is there any evidence to suggest that an allergic reaction, such as isolated urticaria, can "get worse" and pose a risk of future anaphylaxis?

Scenarios that I often encounter in my practice involve patients who were seen in an emergency department or urgent care setting who were either stung by a bee and had a large local reaction (but no systemic symptoms to suggest anaphylaxis) or had urticaria after exposure to an unknown allergen that was presumed to be food (again without cardiovascular or gastrointestinal symptoms suggesting anaphylaxis). These patients are often sent home with an epinephrine autoinjector and told that a future reaction is typically more severe. However, I wonder if there is evidence to support this assertion, or if this is simply a perpetuated medical myth?

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IN REPLY: Knowing what to do for a patient with a previous significant allergic reaction to an insect or food that does not meet the criteria for anaphylaxis (i.e., involvement of at least two organ systems<sup>1</sup>) is a clinical challenge. Trials on how to approach these patients are lacking; therefore, guidance is based on retrospective data and consensus opinion from allergy and immunology experts.<sup>2-5</sup> Unlike allergies to medication,

allergies to food and insects are particularly problematic because avoidance is difficult.<sup>2-5</sup>

In the United States, patients with allergies to insect stings are predominantly allergic to the Hymenoptera species, which includes bees, wasps, yellow jackets, and hornets.<sup>1-3</sup> Systemic allergic reaction to an insect sting is the best understood pathophysiologic model for anaphylaxis.<sup>2,3</sup> It is also the most predictable with regard to what is expected in future reactions.<sup>2,3</sup> Large, local insect sting reactions are defined as skin reactions (e.g., erythema, pain, swelling) greater than 10 cm contiguous to the bite site.2,3 Persons who have large local reactions may actually have a decreased likelihood of anaphylaxis with future stings of 5 to 10 percent, compared with 17 percent in persons with asymptomatic sensitization to venom.<sup>3</sup> Skin and serum venom-specific immunoglobulin E (IgE) testing and venom immunotherapy are not recommended in patients with large local reactions.<sup>2,3</sup> Prescribing an epinephrine autoinjector is also not recommended.<sup>2,3</sup>

For patients with mild, single organ systemic reactions (e.g., urticaria, flushing, angioedema) not contiguous with the bite site, recommendations vary based on age. In patients younger than 17 years, the exposure may be protective.<sup>2,3</sup> Therefore, IgE testing, immunotherapy, and epinephrine autoinjector prescription are not required.<sup>2,3</sup> In patients 17 years and older, risk of future anaphylaxis is thought to be increased.<sup>2,3</sup> In addition to an epinephrine autoinjector prescription, referral to an allergist for IgE testing, guidance on avoiding the specific insect species, and immunotherapy, when indicated, are recommended.<sup>2,3</sup>

In contrast to allergies to insect stings, food allergies are highly unpredictable.<sup>1,4,5</sup> Epinephrine autoinjectors are currently recommended for all patients with a history of any IgE-type reaction (e.g., urticaria, upper airway restriction, angioedema) to food, even if it is a single organ reaction and does not meet anaphylaxis criteria.<sup>4,5</sup> These persons should also be referred to an allergist for testing.<sup>4,5</sup> Avoidance cannot always be ensured because food labels may be misleading and because restaurants do not always advertise all the ingredients in the food served.<sup>4,5</sup> Although a positive result on IgE food allergy testing is not predictive of severity of the reaction, it may assist with food avoidance.<sup>4,5</sup>

It is important to remember that the greatest contributor to preventing mortality from anaphylaxis is timely administration of intramuscular epinephrine.<sup>1</sup> Although anaphylaxis-related death is rare—with 150 cases annually in the United States related to food and fewer than 50 cases annually related to insect stings—level of risk is impossible to determine based on current data.<sup>1-5</sup> Physicians should "inform, not alarm"<sup>5</sup> patients at risk, and educate them in anaphylaxis symptom recognition, proper use of the epinephrine autoinjector, and allergen avoidance.<sup>1-5</sup>

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### Case Report: Treatment of Male Subfertility with Dietary Supplements

TO THE EDITOR: A 40-year-old man with cryptorchidism that was corrected at 12 years of age presented in November 2010 with a four-year history of infertility. In November 2008, his sperm concentration was 3 million per mL, and motility was 30 percent. Microscopy revealed 2 percent normal morphology with a round cell count of 2 million per mL. Testicular ultrasonography and hormone levels were normal.

The patient was prescribed clomiphene (Clomid), 25 mg per day. Four months later, sperm concentration was 5 to 7 million per mL. Thirteen months after discontinuing clomiphene, bilateral varicoceles were diagnosed. At that time, sperm concentration was 4 million per mL, and motility was 63 percent.

Varicocelectomy and in vitro fertilization/intracytoplasmic sperm injection (IVF/ ICSI) were recommended. The patient and his 27-year-old wife consulted a physician who recommended dietary supplements. In November 2010, the patient began taking a formulation containing vitamin C, 1,000 mg; vitamin E, 400 IU; vitamin D, 800 IU; L-carnitine, 2,000 mg; L-arginine, 1,500 mg; vitamin B complex (containing folic acid, 1,600 mcg; vitamin B<sub>12</sub>, 1,000 mcg; niacin, 200 mg; biotin, 400 mcg; vitamin  $B_6$ , 160 mg; and 100 mg each of thiamin, riboflavin, pantothenic acid, and para-aminobenzoic acid), and ginseng, 1,000 mg (Panax quinquefolius, dried root, Hsu Ginseng Enterprises, United States). All supplements were taken in divided doses twice daily.

After three months of treatment, sperm concentration normalized to 47 million per mL, and motility was 45 percent. In March 2011, co-enzyme Q10, 60 mg per day; zinc, 30 mg per day; and selenium, 100 mcg per day, were added to the regimen.

Pregnancy was confirmed in May 2011 and resulted in a successful cesarean delivery.

Subfertility affects one in every 20 men.<sup>1</sup> One-half (51.2 percent) of infertility cases are associated with male factor infertility.<sup>2</sup> A recent Cochrane systematic review of eight randomized controlled trials including 607 patients found no benefit to surgical varicocele treatment for subfertility.<sup>3</sup> Conversely, a ►

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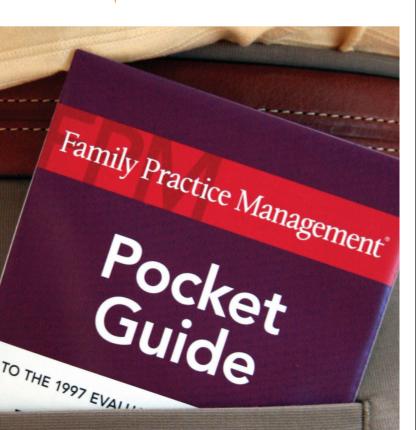
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### Letters

Cochrane review of 34 randomized controlled trials found that oral antioxidants were associated with a statistically significant increase in pregnancy rate (pooled odds ratio = 4.18; 95% confidence interval, 2.65 to 6.59).<sup>4</sup>

This case illustrates a couple who were advised to undergo surgical procedures but successfully achieved pregnancy with a mixture of benign, inexpensive supplements. Based on the existing evidence, perhaps other infertile couples should be offered a trial of dietary supplements before considering expensive and invasive procedures.

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Author disclosure: Dr. Fugh-Berman is the author of a textbook on herbal and dietary supplements.

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### **Correction: CME Quiz Error**

In the CME Quiz (September 15, 2012, page 509), question 6 (page 510) pertaining to the article "Transient Ischemic Attack: Part II. Risk Factor Modification and Treatment" (page 527) was ambiguous and listed incorrect answers in the answer box (page 576). The case scenario described in the question should have more clearly indicated that the patient was at low risk of stroke, which would make answer C (hospitalization) an incorrect answer. The question should have read: "A 78-year-old man presents to the emergency department with recent symptoms suggestive of transient ischemic attack. His lipid levels are normal, and brain magnetic resonance imaging shows no ischemia. Which of the following interventions are recommended for this patient?" The answers should have been: A (aspirin) and B (statin therapy). The online version of the quiz has been corrected.