

exempts highly refined oils derived from the 8 major food allergens, including peanut and tree nuts. Nut oils that are not highly refined require a FALCPA food allergen label. The absence of a FALCPA label is evidence that the oil is highly refined and therefore safe.

As clinicians, we must be ever mindful that although anecdotal experience cannot overrule carefully collected and tested data, each patient and family is unique. Experienced physicians know that some parents will act on their physician's recommendation and others will not be reassured without a test result. Allergists and immunologists who perform in vivo or in vitro IgE food testing must provide appropriate, evidence-based guidance regarding food allergy management including the meaning of test results, application of the results to the individual patient, and a discussion of the risks and benefits of avoidance and introduction. In addition, they must be prepared to perform food challenges, when appropriate, to confirm or refute the diagnosis of food allergy. Our patients deserve no less.

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Allergists' use of epinephrine for food-induced anaphylaxis Time to practice what we preach



The current food allergy epidemic and recent focus on early introduction of peanut has led many allergists to perform more oral food challenges (OFCs).¹ Foods are the most common trigger of anaphylaxis in children, and as such, we are seeing an increase in severe reactions.² It is not controversial that epinephrine is the treatment of choice for anaphylaxis.³ Since the term was first used in 1901, the definition of *anaphylaxis* has been controversial and only more recently well-defined as “a severe, potentially fatal, systemic allergic reaction that occurs suddenly after contact with an allergy-causing substance.”⁴ This definition, however, does nothing to help the physician diagnose anaphylaxis and initiate proper treatment. Tables listing signs and symptoms of anaphylaxis in practice parameters and other publications also fall short in helping a physician or parent determine exactly when epinephrine should be administered.

A variety of grading systems for anaphylaxis have also been proposed from worldwide allergy societies, symposia, and individual authors. Although each has intended to help the practicing allergist and create a definitive grading scale, the variety among these scales and number that exist have not added clarity to this situation. The use of epinephrine when lower respiratory tract signs (eg, cough and wheeze) are present is not controversial. Two common yet controversial signs of an allergic reaction, hives and vomiting, are frequently debated. Some argue that any combination of 2

systems should be treated with epinephrine (eg, hives/skin and vomiting/gastrointestinal symptoms), whereas others suggest that some assessment of severity of these signs of an allergic reaction should be made.^{3–5} Ultimately, the truth likely lies between these 2 positions, and the answer may remain elusive because randomized clinical trials for the treatment of anaphylaxis cannot be undertaken for ethical and safety concerns.⁵ The management of anaphylaxis in the field and the emergency department (ED) setting has received a lot of attention over the years, and allergists are frequently critical of how allergic reactions and anaphylaxis are treated by parents, first responders, and ED practitioners.^{6,7}

In this issue of the *Annals*, the findings by van der Valk et al⁸ suggest that we as allergists should be criticizing ourselves for the underuse of epinephrine, just as we have been critical of other groups. This retrospective study examined 900 failed OFCs performed between 2005 and 2015 at 3 centers in the Netherlands. The OFCs included a mix of clinical and research, as well as open and double-blind, placebo-controlled, challenges. Among the failures, the authors identified 83 cases of anaphylaxis (26.6% of all failed OFCs) that were retrospectively graded using the European Academy of Allergy and Clinical Immunology (EAACI) clinical criteria for diagnosing anaphylaxis.⁹ Of these 83 cases, only 39% were treated with epinephrine. Interestingly, the individuals who underwent clinical OFCs were more likely to be treated with epinephrine compared with the research group, which had a higher rate of anaphylaxis. There was also a significant difference in treatment with epinephrine based on symptoms. Children who had anaphylaxis based on a combination of skin and gastrointestinal symptoms were significantly less likely to receive epinephrine (22%)

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compared with those who had skin and respiratory symptoms (70%). These sobering results are similar to a review of research OFCs conducted before entry into immunotherapy trials in which 39.2% of failed OFCs were treated with epinephrine.¹⁰ However, this descriptive study by Noone et al¹⁰ did not specifically assess the use of epinephrine by any grading scale.

There are some important limitations that must be considered when reviewing the study by van der Valk et al.⁸ The OFCs were conducted during a period of 10 years, and the data were not analyzed to determine whether epinephrine use changed over time; it is possible that during this long period clinicians changed their practice style based on increased experience and greater attention paid to food allergy, anaphylaxis, and epinephrine use. There is also no comment regarding the occurrence of biphasic or delayed reactions observed in this cohort, something that all anaphylaxis studies should address. The time to administration of epinephrine was also not examined but is an important consideration given that delayed administration of epinephrine is a known risk factor for more severe or fatal anaphylaxis.¹¹ Perhaps the most important limitation of this study is that it relied solely on the EAACI anaphylaxis guidelines rather than analyzing the OFC failures using multiple different grading systems.⁸ The EAACI guidelines have a rather broad definition of anaphylaxis, which could lead to the apparent underuse of epinephrine when applied retrospectively for analysis. The different rates of epinephrine use seen in this study for those patients with respiratory symptoms compared with gastrointestinal symptoms, both with cutaneous symptoms, suggest the EAACI guidelines may not realistically reflect clinical practice among most clinicians. Indeed, the use of epinephrine for gastrointestinal symptoms is controversial, with many different recommendations existing for what severity of gastrointestinal symptoms warrant treatment with epinephrine.

The EAACI anaphylaxis guidelines identify several gaps in the evidence related to anaphylaxis. Among these gaps, in agreement with the study by van der Valk et al,⁸ is the need for a “clinical definition and diagnostic criteria for allergic anaphylaxis that are easy to use in practice by emergency room medical staff.”⁹ Guidelines should be developed for use by all clinicians not just ED practitioners. The treatment algorithm should err on the side of overuse of epinephrine, given that there are no absolute contraindications to the use of epinephrine for anaphylaxis.³ In other words, these guidelines should have a high sensitivity and lower specificity to ensure that no patient with potential anaphylaxis is missed and does not receive epinephrine, putting them at higher risk for a more severe, potentially fatal reaction.

The study by van der Valk et al⁸ retrospectively applied the EAACI guidelines, which were published in 2014 and thus not available to the clinicians during most of this study. Thus, it may not be an entirely fair assessment of adequate epinephrine use. Importantly, they also did not examine reasons why epinephrine was not administered. In fact, no published study has done so. Studies must be undertaken among allergists who perform OFCs to assess barriers to epinephrine administration so that targeted interventions can be developed to address these barriers; without such information, it would be imprudent to surmise what these barriers might be. An ED intervention found that the development of an anaphylaxis management order set, including a graphic representation of the anaphylaxis diagnostic criteria and medication dosing guides,

led to a significantly increased administration of epinephrine for anaphylaxis.¹² Before the intervention, 33% of patients with anaphylaxis were treated with epinephrine, whereas after the intervention, this number increased to 51%. The order set was also preceded by a 1-hour orientation on nursing education regarding the use of epinephrine autoinjectors and the availability of these devices from automated dispensing machines in the ED. This study suggests that similar interventions among allergists may be beneficial at increasing the use of epinephrine for anaphylaxis.

Despite these limitations, it is clear from this and other studies that epinephrine continues to be underused in almost all settings, even though it is the treatment of choice for anaphylaxis. We often tell our patients, “If you’re thinking about giving epi, you should give it.” We as allergists need to follow our own advice. Whatever the ultimate reasons for underuse, we must come together as a specialty to honestly assess our treatment practices, agree on a grading system and definition of anaphylaxis, develop an easy-to-follow treatment algorithm that can be used in multiple settings, and then consistently implement these tools in our offices. We must not wait for adverse events to drive quality improvement in food allergy and anaphylaxis.

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