

A new approach to epinephrine deficiency and fatal food anaphylaxis



Until a disease-modifying approach for food anaphylaxis becomes standard of care, the mainstays of therapy will likely remain allergen recognition, avoidance, and the prompt administration of epinephrine in medical facilities or via epinephrine autoinjectors for acute anaphylactic reactions.¹ Not receiving epinephrine or the delayed administration of epinephrine for anaphylaxis is associated with fatal outcomes, and for more than a decade this has been recognized as a critical issue, even in patients with known food allergy.² Although one might reasonably conclude that the threat of fatal food anaphylaxis might be incentive enough to encourage a patient to carry self-injectable epinephrine, a plethora of studies suggest otherwise. The practicing allergist may recommend that at-risk individuals carry their epinephrine autoinjector at all times, but survey studies^{3,4} suggest that the actual carriage rate may range from as low as 6% to as high as 61% of the time. Adolescents or young adults may be particularly at risk because patients in this age group may be more likely to engage in risky behaviors, such as eating foods that they know they are allergic to so as not to stand out among their peers.^{3,5} Approaches to improve adherence to self-injectable epinephrine carriage remain focused on patient education or other clinician-centric didactic techniques, with the efficacy of such efforts difficult to prove and likely largely ineffective.⁶

Clearly, new and innovative approaches to encourage epinephrine autoinjector carriage are required, and in this issue of the *Annals*, Cannuscio et al⁷ report the results of a randomized clinical pilot trial of a behavioral economics approach toward tackling this problem. During a 2-year period from 2012 to 2014, 33 individuals 18 to 30 years old with known food allergy, with most individuals having had an emergency department visit for anaphylaxis and having been prescribed epinephrine autoinjectors, and access to a cell phone capable of text messaging were recruited. A total of 15 individuals were assigned to a control group and 18 to an intervention group. All participants received text messages containing epinephrine autoinjector reminders and informational briefs on food allergy management. The intervention group also received financial incentives and feedback on their performance, with an update on the incentives accrued to date. During the study period, the participants were prompted with 10 text message queries that asked them to send a photograph of their epinephrine autoinjector along with a handwritten code-word of the day within 30 minutes. For each successful check-in, a \$10 reward was given, for a maximum of \$100 earned at the end of the study. The primary study end point was the proportion of check-ins at which the participants could demonstrate that they were carrying their autoinjector. The authors found that 54% of those in the intervention group carried their epinephrine autoinjectors at more than half of their check-ins compared with 27% of the those in the control group ($P = .02$), a statistically significant improvement.

The use of incentives, particularly financial incentives, to encourage medication adherence has been attempted in a number of chronic medical conditions, including hypertension, human immunodeficiency virus infection, anticoagulation therapy, and smoking cessation.⁸ Incentives can include fixed amounts awarded with proof of adherence, such as in this study, and can also include vouchers for no-cost medications, progressively escalating payments for continued adherence, and lottery-structure rewards. By and large, incentive programs that include at least a moderate value

financial incentive (such as >\$100 per month) have been suggested to improve adherence by 20 to 30 percentage points.⁸ The improvement in adherence is even seen in conditions in which the individuals have a significant negative incentive to take the drug, such as with naltrexone therapy for opioid addiction or disulfiram therapy for alcohol addiction.⁹

Problems with incentive-based adherence strategies include criticisms that financial incentives may be coercive, especially with lower-income patients, and that financial incentives may be difficult to apply fairly in socioeconomically heterogeneous populations. Most pilot studies also properly focus on the efficacy of the incentives but do not then explore the scalability (and ultimate cost) of such programs because high-cost pilot programs may not be of much value if they cannot be scaled and applied to larger patient populations. Food allergic patients 18 to 30 years old likely would not be incentivized to alter their behavior based on a reward of stickers or pencils. However, the most compelling criticism of incentive-based medication adherence programs is that the effect of the intervention seems to disappear after the incentive program is discontinued, thus leading to no long-term change in behavior, no learning of a beneficial behavior, and no successful operant conditioning.⁸ This seems to suggest that research participants may be motivated to earn the reward only and that they could be equally motivated to wear the colors of an opposing city's sports team. It would be of interest if the authors of this study were to follow up to see whether epinephrine carriage rates were sustained in the intervention group.

Although the sample size is small and the study population was mostly female (73%), this study makes an important contribution in suggesting that the behavior of food allergic patients can be changed in a positive way—with improved epinephrine autoinjector carriage rates. The authors also point out that the positive outcomes may be also influenced by the text-message reminders, social supports, and a sense of autonomy developed as a result of involvement in a group program—all considerations worthy of future study. The study highlights that autoinjector carriage rates in a highly educated population (91% of individuals with college education or above) remain depressingly low, and one wonders why even with the financial incentives the outcome was not better; in the intervention group, the carriage rate was not even close to 100%. It remains abundantly clear that food allergic patients continue to make what appear to be irrational, systematic errors (ie, persist in risky behavior with regard to epinephrine carriage) that seem contrary to the assumptions of rational market participants, and we will need further help from behavioral economists to help us decrease adverse outcomes in this high-risk patient population.

Fred H. Hsieh, MD
Allergy and Immunology
Respiratory Institute
Department of Pathobiology
Lerner Research Institute
Cleveland Clinic
Cleveland, Ohio
hshief@ccf.org

Disclosures: Author has nothing to disclose.

Funding: This work was supported by an Early Career Grant from the Howard Hughes Medical Institute.

References

- [1] Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update-2014. *J Allergy Clin Immunol*. 2014;134:1016–1025.

- [2] Bock SA, Munoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol*. 2001;107:191–193.
- [3] Greenhawt MJ, Singer AM, Baptist AP. Food allergy and food allergy attitudes among college students. *J Allergy Clin Immunol*. 2009;124:323–327.
- [4] Sampson MA, Munoz-Furlong A, Sicherer SH. Risk-taking and coping strategies of adolescents and young adults with food allergy. *J Allergy Clin Immunol*. 2006;117:1440–1445.
- [5] Macadam C, Barnett J, Roberts G, et al. What factors affect the carriage of epinephrine auto-injectors by teenagers? *Clin Transl Allergy*. 2012;2:3.
- [6] Spina JL, McIntyre CL, Pulcini JA. An intervention to increase high school students' compliance with carrying auto-injectable epinephrine: a MASNRN study. *J Sch Nurs*. 2012;28:230–237.
- [7] Cannuscio C, Dupuis R, Graves A, et al. A behavioral economics intervention to encourage epinephrine-carrying among food allergic adults: a randomized controlled trial. *Ann Allergy Asthma Immunol*. 2015;115:234–240.
- [8] Defulio A, Silverman K. The use of incentives to reinforce medication adherence. *Prev Med*. 2012;55(suppl):S86–S94.
- [9] Carroll KM, Sinha R, Nich C, Babuscio T, Rounsaville BJ. Contingency management to enhance naltrexone treatment of opioid dependence: a randomized clinical trial of reinforcement magnitude. *Exp Clin Psychopharmacol*. 2002;10:54–63.