

Table 1
Summary of investigations

Blood tests	First episode August 28, 2012	Second episode October 10, 2012	After ID of diluent	After ID of human albumin	Before immunotherapy November 2009
MCT ($\mu\text{g/L}$)					
1 h	24.3	91.7	26.3	31.2	
2h	10.3	25.7			
12 h	8.5	8.9	8.1	8.8	
Baseline	8.2	8.3			8.6
IgE (kUA/L)					
Total	150	140			120
Specific honey bee venom	4.3	4.6			59
Specific r Api m 1	0.87	0.99			
Specific wasp venom	0.49	0.47			2.3
Specific r Ves v 1	<0.10	<0.10			
Specific r Ves v 5	<0.10	<0.10			
Skin tests	Skin prick tests		Intradermal tests		
	Concentrations	Results	Concentrations	Results	
Diluent (human albumin 0.3 mg/mL, phenol 4 mg/mL)	HSA 0.003 mg/mL, phenol 0.04 mg/mL	negative	HSA 0.0003 mg/mL, phenol 0.004 mg/mL	negative	
	HSA 0.03 mg/mL, phenol 0.4 mg/mL	negative	HSA 0.003 mg/mL, phenol 0.04 mg/mL	systemic, not local, reaction (Muller II)	
Human albumin (50 mg/mL)	undiluted	negative	0.05 mg/mL	negative	
	0.5 mg/mL	negative	0.5 mg/mL	negative	
	5 mg/mL	negative	5 mg/mL	10- × 12-mm wheal and 18- × 22-mm erythema + systemic reaction (Mueller II criteria)	
	undiluted	negative			
Phenol (50 mg/mL)	0.05, 0.5, 5 mg/mL	negative	0.005, 0.05, 0.5, 5 mg/mL	negative	
Mannitol (100 mg/mL)	1, 10 mg/mL, undiluted	negative	0.1, 1, 10 mg/mL, undiluted	negative	

Abbreviations: HSA, human serum albumin; ID, intradermal injection; MCT, mast cell tryptase.

Other possible mechanisms include IgG immune complexes forming in the circulation, causing direct activation of mast cells.

An important implication of this patient's allergy to albumin is the potential risk of developing severe reactions to vaccines.^{4–7} Furthermore, nonhuman proteins in vaccines that are known to induce IgE-mediated reactions include gelatin (bovine and porcine) and nonprotein constituents, such as polyethylene glycol, should be considered a risk factor for patients with allergy to HSA. It is currently recommended that a history of allergic or anaphylactic reaction to any vaccine component contraindicates vaccination with the same vaccine. There are 3 main sources of human protein in vaccines, including fetal cell lines, human blood, and human albumin, that is genetically engineered from yeast.⁸ Vaccines with albumin obtained from yeast might be the safest and should be considered in this patient's case. In summary, this report describes the first case of an immediate hypersensitivity reaction to human albumin during VIT with bee venom. Although an anaphylactic reaction during VIT can occur at any stage, the possibility of albumin allergy should be considered and investigated in stable patients with unexplained severe reactions during the maintenance phase of immunotherapy.

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Epinephrine preparedness in pediatric patients with food allergy: an ideal time for change

The recent publication of the Center for Disease Control and Prevention's *Voluntary Guidelines for Managing Food Allergies in Schools and Early Care and Education Programs* presents a unique

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References

- [1] Pharmalgen (lyophilized allergenic venom extracts) package insert. Hørsholm, Denmark: ALK-Abello.
- [2] Müller U, Mosbech H. Immunotherapy with Hymenoptera venoms. Position paper. *Allergy*. 1993;48(suppl 14):37–46.
- [3] Bonifazi F, Jutel M, Bilò BM, Birnbaum J, Müller U. Prevention and treatment of Hymenoptera venom allergy: guidelines for clinical practice. *Allergy*. 2005;60:1459–1470.
- [4] Quinlan GJ, Martin GS, Evans TW. Albumin: biochemical properties and therapeutic potential. *Hepatology*. 2005;41:1211–1219.
- [5] Stafford CT, Lobel SA, Fruge BC, Moffitt JE, Hoff RG, Fadel HE. Anaphylaxis to human serum albumin. *Ann Allergy*. 1988;61:85–88.
- [6] Ring J, Messmer K. Incidence and severity of anaphylactoid reactions to colloid volume substitutes. *Lancet*. 1977;1:466–469.
- [7] Fishbein DB, Yenne KN, Dreesen DW, Teplis CF, Mehta N, Briggs DJ. Risk factors for systemic hypersensitivity reactions after booster vaccinations with human diploid cell rabies vaccine: a nationwide prospective study. *Vaccine*. 1993;11:1390–1394.
- [8] Salisbury D, Ramsey M, Noakes K. *Immunisation Against Infectious Disease*. Green Book. London: Department of Health; 2013.



opportunity for improvement in the care of pediatric patients with food allergy.¹ The suggestions made for education and management are practical and broadly applicable. Implementation of such measures has the potential to raise community awareness of food allergy in addition to appropriate prevention

and management of allergic reactions. This increased attention to food allergy provides the medical community with additional educational opportunities and avenues for dialog. Further, the recommendations made in the guidelines for emergency management of anaphylactic reactions show recognition of some existing barriers to rapid, effective epinephrine administration. With the current environment of increased public focus on this problem, it is an ideal time for medical professionals to reassess what measures can be taken to help improve epinephrine availability to food-allergic children.

Food allergy is one of the leading causes of anaphylactic reactions in the community setting, with a prevalence of disease that is increasing in school-age children.^{2–6} Epinephrine is the treatment of choice for anaphylactic episodes, with delayed administration leading to poorer outcomes, including death.³ Previous studies have indicated that many food-allergic children might not have immediate access to their epinephrine auto-injectors, potentially leading to a delay in medication administration in emergency situations.^{3–7} Some impediments to timely epinephrine administration include inability to recognize symptoms of anaphylaxis, lack of an emergency action plan, fear of medication side effects, and misperception of risks, particularly in teenage patients.^{5–7}

We conducted a pilot study with a goal of assessing access to self-injectable epinephrine in our food-allergic pediatric patient population cared for at a tertiary care academic medical center. A questionnaire was provided to patients or families of patients with a documented history of food allergy presenting for follow-up evaluation to the Nationwide Children's Hospital outpatient allergy clinic over a 30-day period. Patients' ages ranged from infancy to 18 years. Patient information collected included age, previously diagnosed food allergies, method of food allergy diagnosis, symptoms associated with previous reactions to food, and comorbid atopic conditions. Additional information was collected regarding carriage of an epinephrine auto-injector, including appropriate dose for weight, expiration date on available auto-injectors, and whether epinephrine was available at the time of the visit. If the

injector was not currently available, patients provided responses as to why this was the case.

All patients agreeing to take the survey completed it during a clinic visit. Thirty-five surveys were returned at the end of the collection period. Twenty percent of respondents reported a prior allergic reaction to food requiring treatment with self-administered epinephrine. Of these patients, 29% had self-injectable epinephrine present when the survey was administered. Sixty percent of patients endorsed carrying self-injectable epinephrine at all times, but only 40% could produce the medication at the time of the survey. Of those with self-injectable epinephrine available at the time of survey, almost 90% had an appropriate dose for their weight, but nearly 50% of auto-injectors were expired. Peanut allergy was reported in close to 90% of respondents, with only 43% of these patients having self-injectable epinephrine available. Of the 60% of patients diagnosed with asthma, merely 38% had self-injectable epinephrine available (Fig 1). Thirty percent of patients reported accidental exposure to a food allergen in the past year, but only one third of those patients had epinephrine available at the time of the survey. Reasons given for a lack of available self-injectable epinephrine included availability in other places such as the home, car, or school, expiration of the previous prescription, cost, and lack of awareness that it was supposed to be carried at all times.

This survey has some limitations, including availability of an epinephrine auto-injector during a follow-up allergy visit used as a proxy for availability at other times and a small sample size. However, our findings reinforce those of previous studies that showed a lack of immediate access to epinephrine in a high-risk patient population.^{3–7} Despite being a potentially life-saving treatment and first-line therapy for anaphylaxis, there is a lack of access to epinephrine auto-injectors in food-allergic pediatric patients. Unfortunately, improper use is not limited to lack of availability, because other studies have indicated that even when available, epinephrine auto-injectors are often not used appropriately.^{5–7} Our findings indicate that even food-

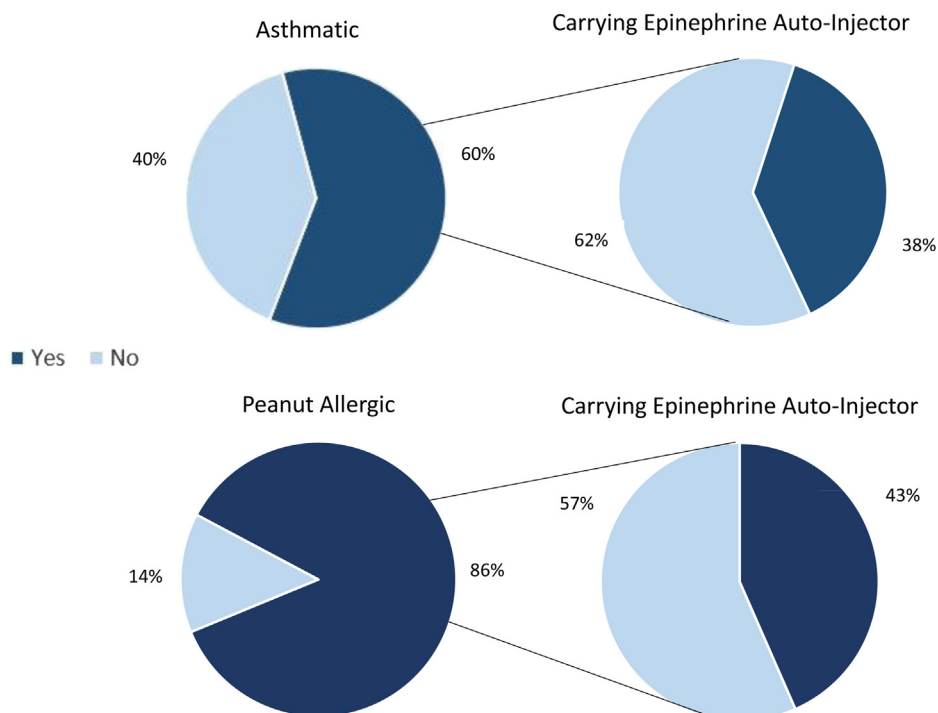


Figure 1. Survey responses from food-allergic patients regarding availability of auto-injectable epinephrine.

allergic patients with known accidental food allergen exposure in the past year, placing them at higher risk for allergic reactions, had poor auto-injector carriage rates. In addition, patients who are at higher risk for fatal anaphylaxis, such as patients with asthma and those with peanut allergy,² were found to have limited compliance. Currently, an expanded version of this survey is being used within our allergy clinic to assess a larger number of patients. Additional questions will explore which demographic factors could affect compliance with self-injectable epinephrine carriage, and follow-up surveys have been prepared to evaluate the efficacy of additional patient and family education measures.

Recently, the US Senate passed the School Access to Emergency Epinephrine Act in hopes of helping to formalize access to epinephrine auto-injectors in US schools.⁸ As public recognition of the need for the presence of epinephrine auto-injectors increases and programs are established to improve medication availability, it is a worthwhile venture as a specialty to focus on our role in this process. Our experience and input as specialists will be vital in ongoing legislation and implementation of food-allergy management programs in schools. It will be necessary to continue to foster relationships with patients and their families, teachers, school administrators and staff, and community leaders to provide comprehensive food allergy care. Moreover, we must routinely evaluate our educational methods with respect to epinephrine efficacy and access; if these methods are ineffective, it will be necessary to improve them. Through these avenues, we can be more effective agents of change and help provide potentially life-saving interventions for our food-allergic pediatric patients.

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References

- [1] Centers for Disease Control and Prevention. *Voluntary Guidelines for Managing Food Allergies in Schools and Early Care and Education Programs*. Washington, DC: US Department of Health and Human Services; 2013.
- [2] Sampson HA. Update on food allergy. *J Allergy Clin Immunol*. 2004;113:805–819.
- [3] Sicherer SH, Simons FE. Section on Allergy and Immunology, American Academy of Pediatrics. Self-injectable epinephrine for first-aid management of anaphylaxis. *Pediatrics*. 2007;119:638–646.
- [4] Ben-Shoshan M, Kagan R, Primeau MN. Availability of the epinephrine auto-injector at school in children with peanut allergy. *Ann Allergy Asthma Immunol*. 2008;100:570–575.
- [5] DeMuth KA, Fitzpatrick AM. Epinephrine autoinjector availability among children with food allergy. *Allergy Asthma Proc*. 2011;32:295–300.
- [6] Young MC, Munoz-Furlong BA, Sicherer SH. Management of food allergies in schools: a perspective for allergists. *J Allergy Clin Immunol*. 2009;124:175–182.
- [7] Gallagher M, Worth A, Cunningham-Burley S, Sheikh A. Epinephrine auto-injector use in adolescents at risk of anaphylaxis: a qualitative study in Scotland, UK. *Clin Exp Allergy*. 2011;41:869–877.
- [8] School Access to Emergency Epinephrine Act, S 1503, 113th Cong (2013).