

Clinical Communications

Food allergen component proteins are not detected in early-childhood vaccines

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Clinical Implications

- Limited studies have explored the potential impact of vaccines on food allergy development. This study investigates and does not support the theory that early-childhood vaccines contain specific food allergens that induce sensitization.

TO THE EDITOR:

Since the 1990s, a substantial increase has occurred in the incidence of food allergy, particularly in early childhood.¹ Although some vaccines contain potential allergens,^{2,3} social media and Internet Web sites have promulgated the concern that vaccines contain food proteins, which then induce sensitization. Parental unease regarding the immunologic impact of vaccines appears to be quite common as 72.5% of pediatricians report that parents are concerned that the number of vaccines recommended stress their child's immune system and may be the cause of various diseases.⁴ Studies that address a potential association between vaccines and T_H2 immunity are limited. The likelihood is low that early-childhood vaccines would contain food allergens. However, casein derivatives are used in the manufacture of many vaccines, egg protein can be found in influenza and yellow fever vaccines, and parents may not understand that only these 2 vaccines are made with chicken eggs, and there is always the worry of contamination or cross-reactivity with allergen components. This study sought to address parental—and physician—concern that early-childhood vaccines given within the first 6 to 18 months contain food allergens.

The immune response that underlies allergic disease is thought to begin during a critical window in early childhood.⁵ Given that some children already have manifestations of allergic disease as early as age 2 months, this investigation initially targeted the earliest vaccine administered to children: the hepatitis B (HepB) vaccine. The Centers for Disease Control and Prevention recommends that the HepB vaccine be administered within 24 hours of birth and 2 to 3 subsequent times in the first year of life.⁶ Because vitamin K (VitK) is also administered to newborns at birth (to prevent hemorrhagic disease of the newborn), it too may be considered a candidate for early-life induction of sensitization and was included in the study. As early as age 6 weeks, children may receive Pediarix, which protects against HepB; diphtheria, tetanus, acellular pertussis; and poliovirus. Given that Pediarix contains HepB and may be administered within the potential critical window, we also included it in our investigation. Because the time frame for early sensitization is not known,

we included 2 other first-year vaccines in our analysis: Prevnar 13 and ActHIB. The aim was to determine whether component proteins of the common food allergens peanut, egg, and cow's milk were detectable in these early-life injections. These 3 allergens were selected on the basis of the prevalence of these allergies in children.

To investigate the possibility that early-childhood vaccines and injectable VitK contain food proteins, we used ELISA to detect specific food allergens. Engerix-B (1 of 2 brands of HepB-only containing vaccines administered at birth), Pediarix (which contains HepB; diphtheria, tetanus, acellular pertussis; and poliovirus), Prevnar 13, ActHIB, and VitK were purchased through the University of Virginia Pharmacy. Vaccine samples were analyzed using highly sensitive allergen-specific ELISA methods for 5 peanut allergens, 3 milk allergens, and 1 egg allergen (Indoor Biotechnologies, Inc., Charlottesville, Va). The antibody pairs used in each assay are specified in brackets as follows:

- Peanut—Ara h 1 [2C12/2F7], Ara h 2 [1C4/pAb], Ara h 3 [1E8/4G9], Ara h 6 [3B8/3E12], and Ara h 8 [4G6/pAb];
- Milk—beta-lactoglobulin, as native Bos d 5 [NBD5-1/NBD5-2]; as denatured Bos d 5 [DBD5-1/DBD5-2]; and as beta casein Bos d 11 [CC11/VB1C];
- Egg—Gal d 1 [CB-1/CB-2].

The limits of detection of the ELISA were as follows: Ara h 1, 156.25 ng/mL; Ara h 2, 2.44 ng/mL; Ara h 3, 4.88 ng/mL; Ara h 6, 0.98 ng/mL; Ara h 8, 4.88 ng/mL; nBos d 5, 0.78 ng/mL; dBos d 5, 7.81 ng/mL; Bos d 11, 31.25 ng/mL; and Gal d 1, 13.28 ng/mL. Samples from 2 lots of Engerix-B, 4 lots of Pediarix, 2 lots of ActHIB, 1 lot of Prevnar 13, and 1 lot of injectable VitK were tested.

The results demonstrate that none of the 9 specific food allergens from peanut, cow's milk, and hen's egg was detected in Engerix-B, Pediarix, Prevnar 13, ActHIB, or injectable VitK (Table I). These findings do not support the concept that early-childhood vaccines or VitK injections contain allergy-causing food allergens. Without evidence of significant food allergen within the vaccines, the aforementioned hypothesis of vaccine-associated sensitization is unsupported. These findings also suggest that there are no cross-reacting components in the ingredients listed on the packaging (Table II) with any of the food allergens tested. Although the ELISA detection limits are quite low, the amount of allergen required to cause sensitization is poorly understood. Theoretically, it could be argued that the ELISA limits of detection may not be low enough, though this seems unlikely because these are the most sensitive assays available with detection limits in the nanogram range and have been used before to detect these antigens.⁸ What is reassuring is that children with peanut, cow's milk, and egg allergy continue to receive these vaccines in the first year of life without having allergic reactions. This implies that even if allergen was present (in subpicogram amounts), the quantities are too low for the immune system to mount an IgE-mediated allergic response.

This study does not negate the concept that other components of the vaccine, such as aluminum adjuvant, could alter the immune response in a developing child. It is well known that

TABLE I. Absence of food allergens in early-childhood vaccines and in VitK injection

Medication	Lot no.	Value (ng/mL)								
		Ara h 1	Ara h 2	Ara h 3	Ara h 6	Ara h 8	nBos d 5	dBos d 5	Bos d 11	Gal d 1
Engerix-B	EG9Y2	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Engerix-B	EG9Y2	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Engerix-B	P7XF7	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
ActHIB	UI787AAA	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
ActHIB	UI735AAA	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Pediarix	3J9R3	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Pediarix	437M5	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Pediarix	529PP	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Pediarix	FY7FK	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
Prevna 13	S31255	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3
VitK	58-272-EV	<156	<2.44	<4.88	<0.98	<4.88	<0.78	<7.81	<31.3	<13.3

Engerix-B contains HepB virus surface antigen (recombinant). *Pediarix* contains HepB virus surface antigen (recombinant); diphtheria and tetanus toxoids and acellular pertussis (DTaP); and inactivated poliovirus vaccine. *Prevna 13* contains pneumococcal 13-valent conjugate. VitK contains phytonadione. Complete list of product ingredients can be found in [Table II](#). ELISA limits of detection is based on testing vaccines at 1/5 dilution.

TABLE II. Ingredients in early-childhood vaccines⁷ and in VitK injection

Medication	Vaccine antigens	Ingredients
Engerix-B	HepB	Aluminum hydroxide, yeast protein, sodium chloride, disodium phosphate dihydrate, sodium dihydrogen phosphate dihydrate
ActHIB	Hemophilus b	Sodium chloride, modified Mueller and Miller medium (the culture medium contains milk-derived raw materials [casein derivatives]), formaldehyde, sucrose
Pediarix	HepB Diphtheria, tetanus, acellular pertussis (DTaP) Poliovirus	Fenton medium containing a bovine extract, modified Latham medium derived from bovine casein, formaldehyde, modified Stainer-Scholte liquid medium, VERO cells, a continuous line of monkey kidney cells, calf serum and lactalbumin hydrolysate, aluminum hydroxide, aluminum phosphate, aluminum salts, sodium chloride, polysorbate 80 (Tween 80), neomycin sulfate, polymyxin B, yeast protein
Prevna 13	Pneumococcal 13-valent	Soy peptone broth, casamino acids and yeast extract-based medium, CRM197 carrier protein, polysorbate 80, succinate buffer, aluminum phosphate
VitK	NA	Phytonadione, polyoxyethylated fatty acid derivative, hydrous dextrose, benzyl alcohol; may contain hydrochloric acid

NA, Not applicable.

aluminum adjuvant induces a robust immune response that results in great protection by many vaccines. Although the effect on IgE production in animal models is somewhat understood, the effect of aluminum adjuvant in humans is uncertain. The impact on IgE production is particularly unclear during early childhood, when the immune system is developing away from the tolerant, fetal phenotype and into a more mature, adult immune system. It has been suggested that allergen exposure at the time of vaccination may direct the immune response toward a T_H2 bias, leading to allergen sensitization. This is unlikely for the HepB vaccine and VitK because they are given at the time of birth before allergen exposure would occur. What is highly unlikely—and refuted in our study—is that early-life vaccines and injectable VitK contain food allergens and thereby contribute to the increase in food allergy. Some vaccines do contain food proteins, such as gelatin, and people with gelatin allergy, including patients with the galactose- α -1,3-galactose allergy, should consult with their allergy-immunology specialist regarding questions about vaccines.⁹ In most cases, the benefits of the vaccine outweigh the risk of a reaction, and the vaccine can be administered in the specialist's office. Overall, the concept

that food proteins in early-life vaccines are the cause of food allergy is unlikely and unsupported and, thus, should not be a concern when considering vaccination.

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