

The impact of food matrices on egg allergenicity

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ABSTRACT

Background: Although many studies show the impact of high and prolonged heating on allergenicity, scarce research exists that examined the impact of the food matrix effect. We presented a case that demonstrates the need for further investigation into this field.

Case: An 8-month-old breast-fed girl with a history of moderate eczema presented with concern for food allergy. At 7 months old, she seemed to have difficulty with nursing after consumption of peanut butter, and her pediatrician recommended further avoidance. On presentation to allergy, she had not yet consumed eggs; therefore, skin testing was obtained for both peanut and egg. Her skin testing result to peanut was negative, whereas to egg was elevated at 5/20 mm. To further support clinical decision-making, blood work was obtained, and the egg white specific immunoglobulin E (IgE) value was elevated to 1.33 kU/L. It was recommended to the family to pursue home introduction of peanut and return for oral challenge to baked egg. At 14 months old, the patient returned for oral challenge and successfully tolerated one-half of a muffin. She was discharged with instructions to continue consumption of one-half of a muffin ideally three or more times a week, which the parents reported she continued to tolerate.

Conclusion: When the patient was 24 months old, the mother decided, without consultation, to introduce banana-chocolate chip muffins. With the first two ingestions, she developed immediate urticaria. On the third consumption, she developed anaphylaxis, which required epinephrine, with rapid improvement. The patient subsequently returned to regular consumption of standard egg muffins (as well as bananas and chocolate individually), which she continued to tolerate. Based on our patient's ability to tolerate baked egg muffins without banana but significant reaction to baked egg muffins with banana, a potential explanation is that the addition of banana disrupted the egg-wheat matrix. This report points toward a continued need to investigate the role food matrices play on the allergenicity of foods. Furthermore, this case demonstrated the importance of adhering to allergist-prescribed recipes to prevent allergic reactions.

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INTRODUCTION

With the increasing incidence of food allergy, there is a drive to better understand the dynamics of food allergenicity. For example, studies have shown¹ that with high and prolonged heating, conformational epitopes of food proteins are destroyed,

which results in decreased immunoglobulin E (IgE) binding capacity.¹ However, scarce research exists that examined the impact of the matrix effect on allergenicity. The matrix effect has been described as the interplay among proteins, fats, and sugars, and the impact that this may have on the allergenicity of specific foods. In this report, we describe an interesting case of a child with egg allergy who passed an oral food challenge and tolerated standard baked egg muffins but who had a significant reaction that required epinephrine when her mother altered the prescribed muffin matrix.

One of the first published studies to examine the effect of food matrices was in 2013. Libbers *et al.*² randomized 59 children with egg allergy to undergo oral challenge with either vanilla pudding, pancake, or minced meat, each with a different fat composition, of 22.8, 31.9, and 52.7%, respectively. They found that there was no significant difference in the severity of reactions among the groups. Unfortunately, the population studied included children who had improved atopic dermatitis with removal of egg from the diet,

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Table 1 Pitfalls of baking egg at home

Modification	Examples
Baking parameters	Altering temperature or time for baking may change the degree of protein denaturation
Serving size	Baking a whole bread or cake rather than individual muffins or cupcakes, may result in undercooked middle section
Recipe dose	Modifying the proportion of ingredients in recipes may increase the amount of egg protein per serving
Matrix vehicle	Substituting wheat flour with alternative flours, such as rice or corn, may alter the dynamics of binding; incorporating additives, such as fruit or chocolate, may also alter the dynamics of binding

and this may not represent what we now define as a true IgE-mediated egg allergy.²

In 2016, Miceli Sopo *et al.*³ randomized 48 children with milk allergy to get either a baked liquid form of milk or a baked form of milk in a wheat matrix (cake). They found that 81% tolerated cake, whereas only 56% tolerated baked liquid milk. Subsequently, this same group randomized 54-egg-allergic children to an oral challenge with either a baked form of egg in a wheat matrix (cake), frittata, or boiled hen's egg. They found that 88% tolerated cake, whereas only 74% tolerated the frittata challenge.⁴ In a 2018 study by Pettersson *et al.*,⁵ 69 children with peanut allergy underwent a challenge with peanut gingerbread that contained 5.9% fat and 141 children underwent oral challenge with peanut cookies that contained 23.9% fat. They found that the two groups had similar rates of tolerance; however, more severe reactions occurred in the peanut cookie group. They proposed that the matrix effect varies based not only on the type of matrix used but also the matrix and perhaps fat of the individual food itself.⁵

There have also been few studies that tried to detect the allergenicity of food matrices *in vitro*. In an article by Villa *et al.*,⁶ the investigators discuss the modalities of testing for food allergenicity. They advocate that real-time polymerase chain reaction (PCR) allows for identification of allergen given the stable and ubiquitous expression of DNA throughout all cells. They used PCR to assess the allergenicity of lupine in different food matrices. They found that detection was 20-fold lower in wheat flour as opposed to rice flour, and proposed that fat, carbohydrates, and other plant metabolites may affect the PCR efficiency and possibly the allergenicity. Although these studies portray the controversial role of food matrices, we presented a case that demonstrated the impact food matrices can play on allergenicity.

CASE REPORT

At the time of the first encounter, our patient was an 8-month-old breast-fed female with a history of moderate

eczema and concern for food allergy. Per her parents, on her first exposure to peanut butter at 7 months of age, she seemed to have unusual difficulty with nursing for a few hours after consumption. Subsequently, her pediatrician recommended peanut avoidance and referral to allergy. At the time of our visit, the patient had been successfully introduced to milk (yogurt) but had not yet been exposed to eggs. Results of skin testing performed at that time were negative to peanut and positive to egg 5/20 mm; with negative saline solution, and histamine measuring 4/10 mm. To further support clinical decision-making, egg white ImmunoCAP (Thermo Fisher Scientific/Phadia, Uppsala, Sweden) assessment was obtained, and the egg white specific IgE value was 1.33 kU/L. Based on these results, the family was advised to continue consumption of peanuts, and they were offered an oral challenge to baked egg.

At 14 months old, the patient returned for an oral challenge to baked egg, which was performed with the Jaffe Food Allergy Institute at Mount Sinai recipe for baked muffins (~2 g of egg white protein per serving) (see Supplemental Appendix A).⁷ The patient successfully tolerated one-half of a muffin (typical dose for a toddler), and she was discharged with instructions to the parents to continue consumption of one-half of a muffin, ideally \geq three times a week. Per the parent's report, at a subsequent follow up, the patient tolerated baked egg muffin at home in the months after oral food challenge.

Outcome and Follow-Up

At 24 months old, given the patient's consistent tolerance of muffins, the mother introduced banana-chocolate chip muffins without consultation. With the first two separate ingestions of banana-chocolate chip muffin at previously tolerated portions, she developed urticaria immediately after consumption. On the third consumption, she developed urticaria on her face and buttocks. She was given diphenhydramine, but the mother noted progression of urticaria and perceived

difficulty swallowing. Her mother administered epinephrine, and the patient clinically quickly improved. The patient was at her healthy baseline during all three episodes. Per the mother, the muffins were prepared identically to the original challenge muffin recipe but with the addition of banana and chocolate chips. The patient subsequently returned to regular consumption of standard egg muffins (as well as bananas and chocolate individually), which she continued to tolerate.

DISCUSSION

Based on our patient's ability to tolerate baked egg muffins without banana but a significant reaction to baked egg muffins with banana, a potential explanation is that the addition of banana disrupted the egg-wheat matrix. The banana may have served to protect the egg protein from denaturation during heating, which, therefore, resulted in increased allergenicity. Alternatively, when banana was added, it could have displaced the egg from being "hidden" by the wheat matrix. This may have resulted in more egg allergen exposure, which allowed further opportunity for IgE recognition.

This case represents a previously unreported outcome during home manipulation of a baked egg recipe, potentially due to matrix disruption. Previous publications^{3,4} focused on the matrix effect as it relates to the flour type in baked egg recipes rather than additives such as fruit or chocolate. This case contributes to the well documented pitfalls of baking egg products at home after a successful baked egg oral food challenge

(Table 1) and introduces an additional and novel concept to consider when advising families.

CONCLUSION

Although this was a single case report, the clinical scenario was striking and represents an unexpected and severe reaction to baked egg with deviation from a prescribed recipe. This report introduces the importance of adherence to established baked egg muffin recipes for home administration but also points toward a continued need to question and investigate the role that food matrices play on the allergenicity of foods.

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