



Guest Editorial

Does the amount of egg protein and type of preparation influence tolerability of baked egg products and potential development of regular egg tolerance in egg-allergic children?



In the current issue of the *Annals*, Saifi et al¹ report tolerability of 3.8 g of baked egg protein in a sponge cake by egg-allergic children in a retrospective study. This amount is higher than the 2.2 g of baked egg protein used in several other studies, the amount a serving of a baked product is thought to typically contain. Data on baked egg tolerance in different populations are important and add to our understanding of the potential forms of baked egg that might be added to the diets of egg-allergic children. The authors suggest that there are 2 potential benefits of challenging patients to a higher amount of baked egg protein. One is a greater assurance that patients will tolerate most baked egg products even if the products contain a higher than typical amount of egg protein. The other is the possibility that adding baked products with higher egg protein content to the diet may be more likely to lead to tolerance of regular egg.

Previous baked egg studies have used a range of 1 to 3 g of egg protein per serving of muffin or cupcake baked at 350°F to 375°F (180°C–190°C) for 20 to 30 minutes. In the study by Leonard et al,² 1 to 3 servings of baked egg products were recommended per day to individuals who tolerated a baked egg challenge. This equaled 2.2 to 6.6 g of baked egg protein per day, which was reported to be well tolerated. Tolerance of baked egg is not simply due to a smaller amount of egg protein in baked products but rather due to changes during the baking process that make the egg protein less allergenic. In several studies, egg-allergic individuals continued to have reactivity to amounts of regular egg protein that were lower than the amount of baked egg protein that they tolerated.³

In the study by Saifi et al,¹ 63% of the cohort tolerated challenges with 3.8 g of baked egg protein, similar to studies challenging with 1 to 3 g. To understand whether challenging to 3.8 g vs 2.2 g of baked egg protein makes a difference, one needs to consider the issue of tolerance thresholds. If egg-allergic patients were to be challenged to successively larger amounts of baked egg protein, would they all eventually react, or is there a threshold at which if patients tolerate a certain amount they are not likely to react to additional exposures no matter how much is given? For example, when egg-allergic patients tolerate one scrambled egg during a challenge, they are deemed egg tolerant and advised to liberalize egg in the diet, not to limit ingestion to only 1 egg at a time as was done during the challenge.⁴

Another factor that may play a role in tolerance of a larger amount of baked egg protein is how the baked product is

processed. Use of whole eggs vs processing egg whites and yolks separately affects egg proteins differently and transforms the final structure of the baked product. Whipping egg whites increases volume and forms a stable foam that gives products such as angel food and sponge cakes their light textures. Food science studies reveal that the whipping process introduces air, which leads to partial unfolding (surface denaturation) of proteins as the hydrophobic groups arrange in the direction of the air phase and the hydrophilic groups arrange in the direction of the water phase.⁵ Even a small amount of egg yolk may disrupt this process. It is possible that a higher content of egg protein tolerated in sponge cake is related to whipping the egg whites separately and thus partially denaturing egg white proteins even before mixing them with wheat and baking. If patients tolerate 3.8 g of egg protein in sponge cake, will they also tolerate 3.8 g of egg protein in products in which the egg whites have not been whipped separately?

The type of food matrix in a baked product may also affect tolerability of baked egg protein. Kato et al⁵ reported decreased antigenicity of ovomucoid when mixed with wheat flour in bread and suggested that this was a result of disulfide reactions between egg and wheat proteins, leading to insolubility. The authors further suggest that gluten was the main candidate for such reactions with egg because gluten has many free sulfhydryl groups. The sponge cake recipe used by Saifi et al¹ calls for cake flour vs all-purpose flour. Cake flour contains a lower percentage of gluten (8%–9%) compared with all-purpose flour (10%–13%). Kato et al⁶ found differences in allergenicity of ovomucoid when mixed with different types of flours in pasta, but it is not known whether cake flour vs all purpose flour makes a significant difference in sponge cake.⁵ This would be even more of a consideration if gluten-free substitute flours, such rice, almond, tapioca, teff, sorghum, or buckwheat flours, were to be used.

If the ingredients used and how they are used matter in baked egg tolerance, this is likely one of the reasons why predictability of serum specific IgE levels and skin prick test wheals vary among baked egg studies using different baked egg recipes. Many studies, including Saifi et al¹, also do not challenge to regular egg after a successful baked egg challenge, thus data may include those who have already outgrown their egg allergy. Lastly, variation may come from a difference in populations, selection criteria, and retrospective vs prospective nature. In a systematic review of cutoffs for raw, heated (lightly cooked or scrambled), and baked egg allergy, cutoffs for baked egg were not proposed because of the broad range of suggested cutoffs

Disclosures: Author has nothing to disclose.

<http://dx.doi.org/10.1016/j.anai.2016.03.019>

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among studies, the low quality of some of the studies, and the differences in baked egg preparation.⁷ Future prospective studies that use a standardized baked egg protocol would help to elucidate whether diagnostic testing can be used to predict baked egg tolerance.

Ingestion of baked egg has been associated with decreased time to tolerance of regular egg.² It is possible that baked egg acts as a form of oral immunotherapy (OIT).³ Alternatively, baked egg tolerance may be a natural progression of outgrowing egg allergy or a marker of a mild or transient phenotype.⁸ If a patient does not tolerate 3.8 g of baked egg protein, would it benefit them to repeat the challenge with a smaller amount? Or does it make sense to do successive challenges starting with very small amounts of baked egg protein and increasing over time, as in OIT? The only published study⁹ to use baked egg in an increasing fashion started patients at 0.63 g of baked egg protein per serving per day and gradually increased to 1.5 g, with 95% of individuals passing a regular egg challenge after 6 months. This study likely had some selection bias, with some participants experiencing only eczema to egg or only having positive testing without a history of egg ingestion. Additionally, the baked egg recipe was not described. A recent study¹⁰ attempted baked milk OIT in patients in whom regular milk OIT failed, starting with at least 25 mg of baked milk protein per serving per day and increasing monthly by 50% to 1.3 g; however, only 21% reached the target goal by 1 year. Additional studies to address the potential benefit of baked egg OIT and whether increased amounts of baked egg protein should be pursued could change management of egg allergy. In conclusion, although Saifi et al¹ report tolerance of a higher content of egg protein in a form of baked egg, one must consider several factors, including baked egg procedures, study methods, and population before deciding what these results mean for egg-allergic patients.

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