

You Can't Unscramble an Egg. Or Can You?

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Although reliable figures are still largely unavailable, IgE-mediated food hypersensitivity (hereafter referred to as food allergy) is thought to affect around 1–2% of adults and 4–8% of children, i.e. roughly around 10 million EU inhabitants (reviewed in [1, 2]). The golden standard to diagnose food allergy is still the double-blind placebo-controlled food challenge. However, this is an elaborate and expensive test, only available in specialized centers. Therefore, the diagnosis of food allergy is often based on the patient's history and (level of) sensitization alone. The diagnostic methods available to test for sensitization [skin prick test or in vitro testing for sIgE (RAST, (Immuno)CAP) are not always clinically relevant and, in addition, they are dependent on the quality of the extract or the allergens used. Food extracts used in diagnostics are generally made from unprocessed foods. However, it becomes more and more apparent now that preparation [e.g. heating (roasting, boiling, frying), and fermentation] and storage of the food can reduce/increase allergenicity or even induce the formation of new allergenic epitopes [3, 4]. Over the past decades, major allergens have been identified, purified, cloned and produced as recombinant proteins, first inhalant allergens and also more recently, many major food allergens (reviewed in [5]). The use of recombinant allergens offers the possibility to replace biological extracts with highly purified active in-

gredients. This will enhance the efficacy of diagnostics and eliminate the major source of variability in product quality that is inherent to biological extracts. In addition, the ability to measure specific IgE (sIgE) to individual allergens may help to understand the different clinical symptoms that are found in food allergic patients. Therefore, nowadays, there are many advocates for the use of component-resolved diagnostics (CRD) and also specific allergen immunotherapy using purified allergen components as opposed to allergen extracts.

The importance of using highly purified allergens in CRD studies, as well as the weakness of commercially available allergen preparations which can be contaminated and thus diffuse the diagnosis, emerges clearly in the article from Everberg and colleagues in the present issue [6]. In this article the authors focused on egg-white allergens.

Egg allergy is one of the most frequent food allergies in children below the age of three. Egg allergy has been reported to vary from 1.3–1.7% (challenge confirmed [7–9]) to 7% (self-reported [1]) but is outgrown in the vast majority of children before the age of five. Four major allergens have been shown to be of importance: ovomucoid (Gal d 1), ovalbumin (Gal d 2), ovotransferrin (Gal d 3) and lysozyme (Gal d 4). Eggs can be eaten pickled, hard-boiled, soft-boiled, scrambled, fried, refrigerated and

even raw. Egg yolks are an important emulsifier in the kitchen and the proteins in egg white (e.g. albumin) allow it to form foams and are used in desserts such as meringues and mousse. Furthermore, egg lysozyme is commonly used as a food preservative. Allergic reactions against egg white are more common than reactions against egg yolks. Additionally, it has been shown that the level of sIgE to ovomucoid is either associated with allergy (high) or tolerance (low) to heated egg and egg in baked foods, and it has been suggested as a prognostic marker for persistent egg allergy [10].

Everberg and colleagues [6] characterized four commercial preparations of the major egg allergens with ImmunoCAP and three crude extracts contained one or more contaminations (only the lysozyme preparation contained none). These preparations were further purified

using monoclonal antibody-based affinity chromatography and extensively monitored by size exclusion chromatography, SDS-PAGE, Western blotting and ImmunoCAP. Subsequently IgE reactivity of a panel of 83 egg-white-sensitized individuals was measured in both the purified and commercial preparations. The results indicated that a considerable number of subjects who were IgE reactive to crude ovomucoid and conalbumin turned out to be false positives ($n = 15$ and 16 , respectively). Therefore this study clearly emphasizes the need to use highly purified allergen preparations when aiming for specific and sensitive CRD studies. However, it is now necessary to take this one step further and use these extensively purified allergens to link specific sensitizations to the clinical symptoms and/or try to establish cut-off points to be used in the treatment of egg allergy.

References

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