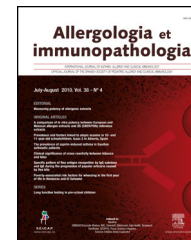




# Allergologia et immunopathologia

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## EDITORIAL

### Could slightly cooked egg be a suitable medium for oral immunotherapy in persistent hen's egg allergy?

Hen's egg, together with milk and peanut, is one of the foods most frequently incriminated in IgE-mediated food allergy in the paediatric population.<sup>1</sup> Egg allergy usually develops in the first years of life with an estimated prevalence of 1.8–2% in children younger than five years<sup>2</sup> and following resolution rates from 12% by age six years to 68% by age 16.<sup>3</sup>

Egg white, the major source of allergens in egg, contains 23 different glycoproteins, most of which have been purified. Ovomuroid (Gal d 1) and ovalbumin (Gal d 2) are considered the main allergens; the former is considered the dominant allergen in accordance with its stability against heat and digestion, the latter is the most abundant protein in egg white although its allergenicity is strongly reduced by thermal treatments.<sup>4,5</sup> Even though heating renders ovomucoid more susceptible to enterocytic intracellular enzyme generating non-allergenic peptides.<sup>5</sup> Furthermore, allergenicity of ovomucoid could be additionally decreased by blocking epitope access through interactions with a complex food matrix. For this reason, patients with egg allergy may differ in the immune response against egg proteins and children who acquire tolerance to cooked egg, may not necessarily reach tolerance to raw egg.

A study by Kato et al.<sup>6</sup> demonstrated a marked decrease in the solubility of ovomucoid when egg white was mixed with wheat flour and wheat gluten and then heated at 180 °C for 10 min, mimicking the process of bread-making. As a matter of fact it has been reported that approximately 70% of children with a previous diagnosis of egg allergy tolerated baked egg ingestion (e.g. muffin, cookies).<sup>7</sup> Starting from this evidence, some authors have suggested that tolerance to baked egg could develop spontaneously earlier than tolerance to uncooked egg<sup>8</sup> and that continued ingestion of baked egg could accelerate resolution of allergy to regular (slightly cooked) egg<sup>9</sup> (e.g. scramble egg, French toast, omelette). In both these studies many subjects were baked-egg tolerant at enrolment and the authors did not specify if they had already been baked-egg tolerant at diagnosis or not. In the study by Leonard et al.<sup>9</sup> there were also other limitations. First of all, the subjects enrolled had a mild allergy, with a good chance of outgrowing their allergy without any intervention. In effect the median value of their egg-white IgE

was 2.1 kU/L while it is well known that children with higher egg IgE levels at all ages and egg IgE greater than 50 kU/L are at risk of persistent egg allergy.<sup>3</sup> Another bias of Leonard's study was to have a retrospective comparison group, so that, as stated by the same authors, the shorter time to tolerance might reflect close follow-up of subjects within the active group and a more proactive pursuit of diagnostic challenges to regular egg.

From a theoretical point of view it is difficult to think that an allergen altered in its structure might lose its capacity to trigger an allergic reaction while maintaining its tolerogenic power. In their mice model Peng et al.<sup>10</sup> demonstrated that the boiling of egg white proteins abrogated the induction of oral tolerance. It is more likely that baked egg is simply better tolerated than raw egg. A recent study from Australia reported that 83.3% of the infants younger than 12 months with challenge-proven raw egg allergy tolerated a baked egg challenge.<sup>11</sup> Similarly, in 24 children with severe hen's egg allergy (egg white IgE > 50 kU/L and/or positive challenge at a dose < 1 ml of raw egg emulsion) that underwent a desensitisation treatment in our Institution during the last two years, baked egg was tolerated at the baseline in 75% of cases, and, after a few months of desensitisation, in almost 100% (unpublished data). Maybe we should change our minds about hen's egg allergy considering baked and raw eggs as two different antigens, with the latter associated with persistent egg allergy, separated by a continuum represented by foods prepared with egg at intermediate levels of cooking.

As was the case for milk and peanut allergy, several experiences and some randomised clinical trials about the efficacy of desensitisation to hen's egg allergy have been published.<sup>12–14</sup> These studies demonstrated that egg desensitisation can be safely and feasibly performed and has immunomodulatory properties, but differed mostly for protocol, including the substrate used for immunotherapy (raw egg emulsion, liquid raw egg extract, egg white powder).

In the current issue of *Allergologia et Immunopathologia*, Fuentes-Aparicio et al.<sup>15</sup> present the results of their open-label trial in which 72 patients were randomised to perform an oral desensitisation to egg or an elimination diet. They used powder pasteurised egg for tolerance induction with

92.5% of children in the active group able to ingest a quantity of powder egg equivalent to one whole egg in about 13 weeks and obtained tolerance also to raw egg in about 50% of patients in the active group versus 22% of patients in the control group who developed tolerance spontaneously. Unfortunately the authors do not specify what type of thermal treatment was used for pasteurising powder egg, but it is probably similar to a slightly cooked egg. This issue is relevant in order to properly counsel patients about foodstuffs that they could consume after completing the desensitisation protocol. Indeed regular intake of allergen is pivotal, at least in the early phases of oral immunotherapy, for maintaining the acquired tolerance.<sup>13,16</sup>

Finally, it should be highlighted that in this context some authors may reject the definition of specific oral tolerance induction (SOTI) used by Fuentes-Alparico et al., because it should imply that the achievement of a sustained unresponsiveness to allergen has been proven by means of egg challenge after a new period of avoidance of egg starting at the end of the desensitisation phase. On a pragmatic base, considering the extraordinary commitment that a protocol of oral immunotherapy requires for children and their families, we find this choice, outside a highly specific research setting, inconvenient and of very little use, at least in common foods such as milk and egg.

A normal diet is sufficient to ensure continuous exposure to these allergens, assuming that it is well known to patients what kind of food they have been desensitised to: baked (e.g. muffin), slightly cooked (e.g. scrambled egg) or uncooked (e.g. homemade ice cream).

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