



# Allergologia et immunopathologia

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## EDITORIAL

### What to do with children who have never eaten egg and are egg-sensitised

Egg allergy is one of the most frequent food allergies in children below the age of three and constitutes the most common food allergy in children with atopic dermatitis.<sup>1</sup> Incidence of egg allergy in cohorts of infants allergic to milk is high. In a study carried out in the Danish municipality of Odense, 38% of 39 milk-allergic children recruited from a birth cohort and followed over the course of three years developed adverse reactions to other foods, with egg white being responsible for 29% of all reactions.<sup>2</sup> Bishop et al.<sup>3</sup> tracked 100 milk-allergic children over a five-year period and found that 58% had adverse reactions to egg.<sup>3</sup> Other studies have also confirmed the higher prevalence of egg allergy among milk-allergic children, with incidence ranging from 41% to 67%.<sup>4,5</sup> All these studies support the notion that milk-allergic children have a higher incidence of egg allergy. Indeed, Monti G et al.,<sup>6</sup> in a prospective study of 107 atopic dermatitis cases in children, concluded that children with atopic dermatitis may be sensitised to egg even if they have never eaten it and that clinical reactions are observed in 67.3% of children upon first exposure challenge.<sup>6</sup> Similarly, Lowe et al.<sup>7</sup> demonstrated infant eczema (before the age of 6 months) as being associated with increased risk of new sensitisations appearing at one year; most new sensitizations were due to food allergens (milk, eggs and/or peanuts).<sup>7</sup> In their study on the association between high levels of immunoglobulin E food sensitisation and eczema in infancy, Hill DJ et al.<sup>8</sup> conclude that IgE-food sensitisation is likely to have an important role in infants who develop eczema in the first 12 months and that infants with moderate or severe eczema should be routinely assessed for food allergy.<sup>8</sup>

Although egg allergy usually appears upon first exposure, it is not uncommon for clinicians to encounter children with egg-specific IgE before egg is introduced in their diet, especially in milk-allergic patients and infants with moderate or severe eczema. Sensitisation might occur in the intrauterine environment, by means of breastfeeding or by

unrecognised exposure. As in other cases of food allergy, it is rather difficult to determine whether the child has a true allergy or is just egg-sensitised. It is generally accepted that controlled food challenges constitute the gold standard for diagnosing food allergy.<sup>9</sup> However, food challenge is time-consuming, expensive and troublesome for the patient, involving risk of severe systemic reactions. In recent years, research efforts have sought to discover a simple in vivo or in vitro test which can accurately diagnose food allergy and thereby render oral food challenges unnecessary. Several studies have been performed to establish diagnostic decision points for skin prick tests and specific serum IgE to predict symptomatic egg allergy.<sup>10–12</sup> However, predicted probabilities vary remarkably among authors and populations studied. Sources of variability of studies were the inclusion of children with a clinical history of reactions following egg intake, a wide range of ages, variations in prevalence of atopic dermatitis, immediate and delayed reactions, and different methods for establishing cut-off point. In the current issue of *Allergologia et Immunopathologia*, in a study by Fadeeva T et al. the authors used cut-off values of 1.5 kU/L to egg white for the oral challenge to egg they performed; however, the authors point out that for children with no previous allergic reaction to egg, the cut-off point could be decreased to 0.5 kU/L without significantly increasing the risk of the provocation being positive.

New diagnostic tools for egg allergy are currently being developed. Recent findings show a relationship between the decrease in food-specific IgE levels over a specific period between two challenges and the development of tolerance.<sup>13</sup> This is consistent with the study by Fadeeva T et al. A greater decrease in specific IgE levels over a shorter period of time was indicative of a greater likelihood of developing tolerance in the two groups of egg-sensitised children (with and without prior egg intake). In addition, quantification of OVM antibodies, IgE/IgG4 and peptide-specific IgE could be useful in guiding clinical decision-making on whether to

perform a challenge or not.<sup>12–15</sup> However, additional studies on larger patient populations may be necessary to further elucidate these aspects.

In the current issue of *Allergologia et Immunopathologia*, Fadeeva T et al. present the results of oral egg-challenge tests performed on two different groups of children: one group with a history suggestive of allergic reaction to egg and the other group being IgE-sensitized to egg without previous egg intake. After a period of egg-avoidance, both groups revealed a similar proportion of positive open oral challenges to egg, with 31.8% of the children without previous egg intake producing positive results vs. 38% of those with a history suggestive of allergic reaction upon egg intake. Using open challenge testing, Diéguez et al.<sup>10</sup> confirmed egg allergy at the age of 14 months with no prior egg ingestion in 56.9% of the 104 children who were allergic to milk and IgE-sensitized to egg.<sup>10</sup> The inconsistency between the two studies can be attributed to the different age at which the challenges were carried out. In the study by Diéguez et al.,<sup>10</sup> challenge tests were performed in children with a mean age of 14 months at the time of diagnosis. In the study by Fadeeva T et al., challenge tests were performed after an exclusion diet and at a higher mean age (25 months). It is well known that age at egg challenge test constitutes a factor which influences the outcome, since the natural history of egg allergy shows that tolerance increases with age.<sup>16</sup>

It seems clear that patients with moderate or severe atopic dermatitis, and those diagnosed with milk allergy have a higher risk of sensitisation to egg and of clinical reaction to egg even when they have never eaten the food. Children with risk factors for egg allergy who have never eaten eggs should be evaluated for specific IgE to egg and, where necessary, should undergo a controlled food challenge in a hospital environment in order to receive a definitive diagnosis and thus avoid the risk of an allergic reaction upon first ingestion.

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