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Editorial

Clinical and Laboratory Predictors of Egg Allergy Resolution in Children

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▸ See the article "Reduction Rate of Specific IgE Level as a Predictor of Persistent Egg Allergy in Children" in volume 11 on page 498.

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The prevalence of immunoglobulin E (IgE)-mediated egg allergy is one of the most common food allergies in infants and young children; the estimating rate is about 0.1% to 8.9%, with the lowest rate in Greece (0.07%) and the highest rate in the population-based Health Nuts study (8.9%).[1-4] The prevalence of egg allergy in infants is 2.8% in Korea.[5]

According to a study of meta-analysis, egg allergy is the second most common food allergy (FA) in children and adults.[1] Egg allergy is the second most common immediate-type FA (cow's milk, 37%; egg, 34%) in Korean children less than 2 years of age.[6] Egg allergy can cause life-threatening anaphylactic reactions that lead to significant morbidity and impaired quality of life, and also can develop other allergic diseases, such as atopic dermatitis and/or asthma, simultaneously or later in life.

Hen's egg contains high-quality proteins and nutrients, and is widely consumed worldwide in various ways. Thus, the patients with egg allergy can hardly avoid eating foods that are containing eggs, so that allergic reactions from accidental consumption are common. Among the cases with food-induced anaphylaxis, the egg is the second most common cause, followed by cow's milk in Korean young children.[6] A nationwide multi-institutional survey in the US reported that hen's eggs, fruit, peanuts and tree nuts are frequently observed in anaphylactic cases of children under 5 years of age.[7] Hen's egg and cow's milk are the most frequent causes of anaphylaxis among children under 3 years of age in a European study.[8]

It is difficult to know the exact natural course of specific FA, since various factors, including food culture, are involved therein. Nevertheless, it is important to evaluate and predict the natural course of specific FA for assisting in the personalized care of individual patients. Prognostic factors should also be investigated to understand the natural course of FA.

Fortunately, egg allergy is expected to resolve in the majority of children by school age.[9] However, some studies on the natural history of egg allergy have reported different findings in terms of the average age at which allergy resolves. The population-based cohort HealthNuts study followed up infants who had a detectable wheal to egg allergen and positive oral egg challenges, and reported that 47% of infants with egg allergy developed tolerance by the age of 2 years.[10] A retrospective study using chart review of children with egg allergy

(median age at initial visit, 14 months; median initial egg specific IgE [sIgE], 7.3 kU/L; and the median peak egg sIgE, 9.4 kU/L) in a tertiary referral center reported that only 11% of children developed tolerance by the age of 4 years, 26% by the age of 6 years, and 82% by the age of 16 years when tolerance was defined as tolerating concentrated egg or having a last recorded egg sIgE level of less than 2 kUA/L and no history of clinical reactivity in the previous 12 months.[11] A cohort in the Consortium of Food Allergy Research followed up children aged from 3 to 15 months with clinical egg allergy and found that about half of children with egg allergy resolved at a median age of 6 years when tolerance was defined as tolerating concentrated egg products.[12]

In the current issue of the *AAIR*, Kim *et al.*[13] reported that about 82% of children with egg allergy (mean age at diagnosis, 14 months) resolved at a median age of 3 years. Of infants with egg allergy in another study in Korea, 90% without atopic dermatitis developed tolerance at the age of 3 years, while 60% with atopic dermatitis.[14] Tolerance developed in 30% of children with egg allergy by the age of 3 years, 59% by the age of 5 years, and 73% by the age of 6 years in Japan.[15] In previous studies, there are big differences in the natural course of egg allergy, which may be attributed to differences in study subjects and methods as well as cultural differences in the way foods are consumed.

Although inconsistent findings for predicting egg allergy resolution have been reported, indicators known to be related with developing tolerance or persisting allergy are severity of clinical reaction, skin prick test (SPT) reactivity, age at diagnosis, comorbid atopic dermatitis, serum sIgE levels, and rate of change in sIgE levels or SPT reactivity.[16] In addition, component-resolved diagnoses and laboratory-based cellular assays[17,18] have been investigated to predict the natural course of egg allergy. Among them, careful history taking for clinical characteristics and blood tests for sIgE to egg and component protein are readily available. Characteristics of initially presenting reactions, which only manifest skin symptoms, are associated with resolution.[12] Infants who were tolerant to baked egg were more likely to develop tolerance to regular egg compared to those allergic to baked egg (56% vs. 13% by the age of 2 years); however, the consumption of baked egg was more effective in developing tolerance compared to the initial baked egg reactivity.[19] The baseline egg sIgE level has been considered a predictor of tolerance development. Many studies showed a favorable response in children with low sIgE levels,[4,9,12,19] although some reported no association between sIgE level and prognosis.[20,21]

Kim *et al.*[13] in the current issue also attempted to identify the clinical factors predicting tolerance in children with IgE-mediated egg allergy. The authors showed that comorbidities (wheat allergy, peanut allergy and atopic dermatitis) and the egg sIgE level of ≥ 16 kU/L at diagnosis were less likely to resolve egg allergy. In addition, they reported that about 50% of children with peak egg sIgE level of ≥ 50 kU/L resolved, a higher remission rate than 11% of those who developed tolerance by the age of 4 years in a patient-based study of a tertiary referral center.[11] In this current retrospective study, 226 out of 430 children with egg allergy were excluded because they could not be confirmed whether they developed tolerance at the last visit based on medical records, which may overestimate the resolution rate of egg allergy.[13] Although this inconsistency of resolution rate in children with the same sIgE value between the 2 studies may be due in part to discrepancies in the study designs and methods including characteristics of study subjects, there may be more important reasons, which need to be clarified by well-designed prospective studies. They proposed a 30% change in egg sIgE level during a period of 12 months as a useful indicator of tolerance acquisition with

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area under the curve 0.835.[13] This findings with decrease in egg sIgE levels are consistent with those of a study in which a 50% decrease in egg sIgE level over a period of 12 months resulted in a negative probability of 52% in the next challenge test[22] and a Danish study which showed the association between tolerance development and decreases in IgE levels to the egg white and ovomucoid.[21]

In conclusion, the majority of young children with egg allergy develop tolerance over time, so that repeated egg challenge tests are required to determine the tolerance acquisition. The scheduling a challenge test should not be too early or too late to avoid unnecessary testing or unjustified restriction diet, which may impair growth and development. Integration of careful history of clinical characteristics and serologic markers can provide insights into the natural history as well as information for planning an appropriate time to perform the tests (blood and/or challenge).

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