

Letter to the Editor

The predictive relationship of food-specific serum IgE concentrations to challenge outcomes for egg and milk varies by patient age

To the Editor:

It is complicated to interpret food-allergy symptoms in children because of the dynamic nature of the allergic response that changes with time: the acquisition of food tolerance and amelioration of symptoms is reported in children with all types of food allergy.¹ The various diagnostic errors and pitfalls in the management of food allergy suggest that we should utilize all available tests more fully in the best interests of the patient. Sampson and Ho² and Sampson³ were first to publish studies on utilization of serum specific IgE in order to predict which food-allergic patients were likely to fail in oral food challenge. They suggested threshold values for egg 7 kilounits of specific IgE antibodies per liter (kU_A/L) and for milk 15 kU_A/L, respectively, ie, food-specific serum IgE concentrations in which approximately 95% of the patients are predicted to have clinical reaction.³ These diagnostic values were helpful to the physician in deciding if food challenge was necessary or potentially harmful to the patients and also led to an interest among other researchers to investigate these relationships. Boyano-Martinez et al⁴ and Garcia-Ara et al⁵ found that the 90% diagnostic value for egg was >0.35 kU_A/L and for milk 1.5, 6, and 14 kU_A/L in the age range 13-18 months, 19-24 months, and in the third year, respectively. Osterballe and Bindslev-Jensen⁶ showed the 95% diagnostic value was 1.5 kU_A/L for egg. Celik-Bilgili et al⁷ found diagnostic values for 95% probability of allergy to hen's egg was 10 kU_A/L and to cow's milk 46 kU_A/L, values showing substantial difference from those published previously.

These differences in diagnostic values may be explained by the fact that their study populations differed. We hypothesized that the age of the child additionally influences the specific IgE diagnostic values when predicting the outcome of food challenge for egg and milk.

The objective of this study was to relate the specific IgE antibody concentration to egg and milk to the outcome of food challenge for children of various ages suspected of suffering from egg and milk allergy.

Eight hundred sixty-one oral challenges were performed for cow's milk and 764 oral challenges for hen's egg among 969 children (median age 1.3 years, range: 0.2-14.6). Of a total 1625 oral food challenges, 1606 were open challenges according to recommendations of European Academy of Asthma and Clinical Immunology and the American Academy of Asthma, Allergy & Immunology. Seventy-four percent of patients had atopic dermatitis and 18% had asthma; allergic rhinitis and allergic conjunctivitis were present in 8% and 5% of the patients, respectively. Allergen-specific IgE antibody levels were measured using the Pharmacia CAP System (Phadia AB,

TABLE I. Symptoms provoked by oral food challenge

	Total (n = 589) No. (%)	Egg white (n = 374) No. (%)	Cow's milk (n = 215) No. (%)
Cutaneous	581 (99)	368 (98)	213 (99)
Mucous membrane	16 (3)	7 (2)	9 (4)
Lower respiratory	36 (6)	21 (6)	15 (7)
Gastrointestinal	48 (8)	34 (9)	14 (7)
Anaphylaxis	16 (3)	8 (2)	8 (4)
Other	3 (1)	1 (0)	2 (1)

Uppsala, Sweden) towards hen's egg and cow's milk. The detection limit of the assay was 0.35 kU_A/L.

Oral food challenge was used as the gold standard by which the sensitivity, specificity, and receiver operator characteristic curve analysis were calculated. The relationship between sensitization status and outcome measure was analyzed using logistic regression. Fitted predicted probability curves were plotted using the results from the logistic regression.

Forty-nine percent of the performed egg challenges and 25% of the performed cow's milk challenges were assessed as positive. Symptoms provoked by the oral food challenge are listed in Table I.

Comparing the specific IgE antibody levels for those children who failed and those who passed the oral challenge, a significant difference was found both for egg and milk ($P < .001$). A dichotomous evaluation gave the sensitivity for hen's egg and cow's milk as 0.92 and 0.84, respectively, whereas the specificity showed lower results, 0.48 and 0.70. The relationship between sensitivity and specificity were further explored by receiver operator characteristic curves, yielding acceptable areas under the curve, 0.91 for hen's egg and 0.85 for cow's milk. The food-specific IgE concentration indicating a 95% risk of reaction was 25.5 kU_A/L for hen's egg and 50.9 kU_A/L for cow's milk.

Poststratification into age groups showed diagnostic values for 95% probabilities for failing oral challenge, for children less than 1 year old (13.0 kU_A/L), 1 year old (23.0 kU_A/L) and 2 years or older (30.0 kU_A/L) for egg (Fig 1, A). Corresponding numbers for cow's milk were for children less than 1 year old (5.8 kU_A/L), 1 year old (38.6 kU_A/L), and 2 years or older (57.3 kU_A/L) (Fig 1, B).

Our results confirm that increasing IgE levels to milk and egg correlate with increasing risks for reactions upon food challenge are useful to predict outcomes and are influenced by age. Of note, the specific IgE levels indicating a 95% risk of reaction were much higher in our patient population compared to those observed in previous studies.²⁻⁷ There are several possible explanations for these differences, including different selection criteria, the influence of age, and different criteria for determining a failed or passed food challenge. If very mild and transient symptoms are counted as positive, this has a definite influence on the diagnostic values. IgE levels have been

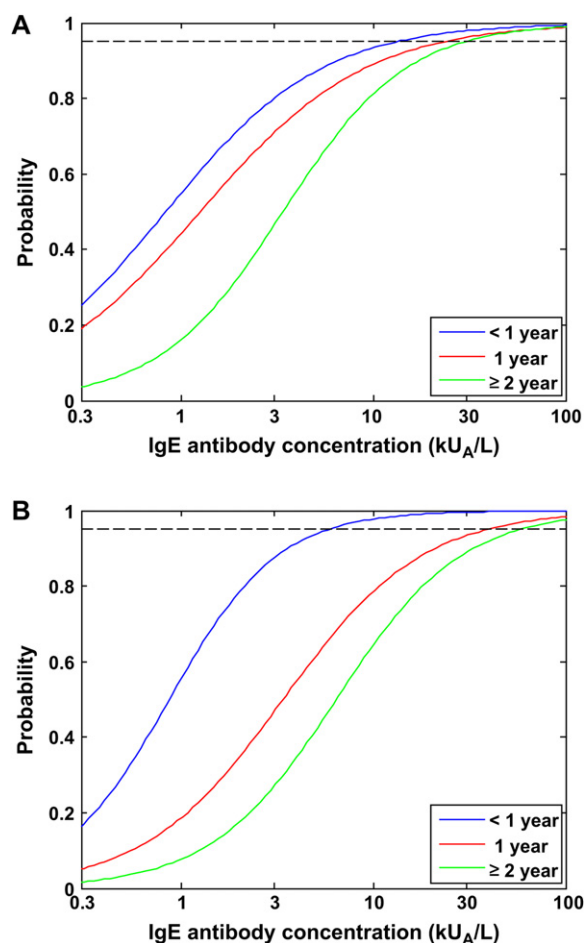


FIG 1. Fitted predicted probability curve for failing oral food challenge at a given allergen-specific IgE antibody level derived from logistic regression, egg challenge (**A**), and milk challenge (**B**) with indicated 95% probability.

regarded as a useful predictor of challenge outcome but as a less useful predictor for the degree of reaction severity during failed food challenge. Hourihane et al⁸ have also recently shown that peanut-specific IgE concentration can predict severity of reaction in double-blind, placebo-controlled food challenge if the dose of allergen is considered. Our data add to previous studies from other investigators showing that the specific predictive values may vary among studies. This variation should be explored in further studies and currently requires caution in applying results to distinct patient populations.

We conclude that there is a relationship between allergen-specific IgE levels to egg and milk and oral food challenge outcome and that this relationship is influenced by age. Younger children react on low levels of specific IgE antibody concentration to egg and milk compared to older children.

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Takatsugu Komata, MD^{a,b}
Lars Söderström, MSc^c
Magnus P. Borres, MD, PhD^{c,d}
Hiroshi Tachimoto, MD, PhD^a
Motohiro Ebisawa, MD, PhD^e

From ^athe Department of Pediatrics, Sagami National Hospital, Kanagawa, Japan; ^bthe Department of Pediatrics, Jikei University School of Medicine, Tokyo, Japan; ^cPhadia AB, Uppsala, Sweden; ^dthe Department of Pediatrics, Sahlgrenska Academy of Göteborg University, Göteborg, Sweden; and ^ethe Clinical Research Center for Allergy and Rheumatology, Sagami National Hospital, Sagami City, Japan. E-mail: m-ebisawa@sagami-hosp.gr.jp.

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