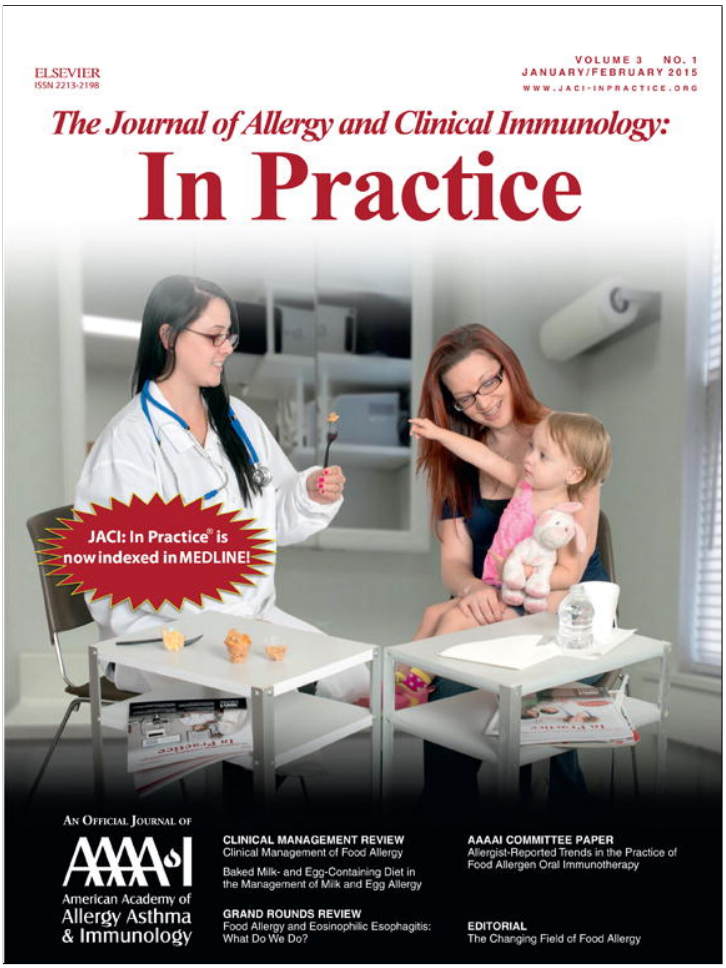

Clinical Communications

The predictive relationship between peanut- and Ara h 2–specific serum IgE concentrations and peanut allergy

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Clinical Implications

- Increasing levels of IgE antibodies to peanut and Ara h 2 correlate with increasing risk of peanut allergy and are useful in predicting outcomes.

TO THE EDITOR:

The prevalence of peanut allergy has increased during recent decades.[1] However, many patients sensitized to peanut might be tolerant, and overdiagnosis of peanut allergy is a problem in society. Sampson and Ho were the first to study the relationship between specific IgE levels to predict failure in an oral food challenge (OFC).[2] These diagnostic values were informative for the physician in deciding if a food challenge was necessary for patients. It also led to an interest among other researchers in investigating similar relationships. Later, differences in predictive values between studies were found, explained by the dependence on disease prevalence for these values as well as patient age, differences in exposure, consumption habits, and other factors.[3]

Studies of food allergy now emphasize the utility of component testing for specific IgE analysis as a possibility for an improved diagnosis.[1] Specific IgE to Ara h 2 has been shown to be a superior marker in differentiating peanut-allergic and -tolerant adults and children, but the inclusion of other components such as Ara h 1, 3, 6, 8, and 9 could also improve testing.[4-7] The inclusion criterion has often been sensitization to peanut, and many studies are limited with regard to the number of peanut challenges. Knowledge of the value of quantitative analysis of Ara h 2–specific IgE antibodies in relation to clinically relevant peanut allergy is therefore limited.

The present objective was to study the association between the serum concentration of specific IgE antibodies against peanut and Ara h 2 and clinical peanut allergy defined as a positive diagnosis based on OFC or a convincing positive case history for children suspected of suffering from peanut allergy.

The retrospective study included 165 consecutive Japanese patients (median age: 6 years, range: 1-16 years, 56 girls and 109 boys) referred to pediatric specialists at the Sagamihara National Hospital or Aichi Children's Health and Medical Center between 2005 and 2010 for the investigation of suspected peanut allergy. An open OFC was performed in 121 children (73%) following Japanese guidelines.[8] Only objective symptoms were considered for challenge failure. Thirty-five (29%) of the peanut challenges performed were assessed as positive. In 44 children (27%), the diagnosis was based on a detailed anamnesis and other clinical findings. Of them, 36 (82%) had a convincing positive history defined as generalized urticaria, respiratory symptoms, and anaphylaxis in close conjunction with the intake of peanut. The other 8 (18%) were diagnosed as peanut tolerant after the anamnesis (Table E1 in this article's Online Repository at www.jaci-inpractice.org). In total 71 children (43%) were diagnosed as peanut allergic and 94 (57%) were considered tolerant (see the summary in Table E2 available in this article's Online Repository at www.jaci-inpractice.org). Serum samples were collected and stored at −20 °C until analysis. Naturally, all allergic patients diagnosed by case history had the blood sampling sometime after the reaction, which resulted in a difference for the allergic group when the sampling was done in relation to the reaction and/or challenge (median: −1.7 months, range: −17.6 to 9.5 months) compared with the tolerant group (median: 2.4 months, range: −16.1 to 12.7 months). Ethical approval was obtained through the Institutional Review Boards at Sagamihara National Hospital. Informed consent was obtained from all participants and/or their parents before the study.

Levels of serum IgE antibodies to peanut and Ara h 2 were measured using ImmunoCAP (Phadia AB, Uppsala, Sweden). The measuring range of the assay is 0.10-100 kU_A/L. The children with a diagnosed peanut allergy had significantly higher peanut- and Ara h 2-specific IgE antibody levels than did the peanut-tolerant children (Table E3 in this article's Online Repository at www.jaci-inpractice.org). No association was found between the age of the children and the levels of specific IgE to peanut or Ara h 2 in the peanut-allergic group ($r_S = -0.08$, $P = .53$ and $r_S = -0.05$, $P = .69$, respectively) or the peanut-tolerant group ($r_S = -0.19$, $P = .07$ and $r_S = -0.04$, $P = .66$, respectively).

The relationship between peanut- and Ara h 2–specific IgE antibody levels and peanut allergy was analyzed with logistic regression (using $\log_2$-transformed concentrations). Fitted predicted probability curves were plotted using the results from the logistic regression (Figure 1). Significant associations between the probability of peanut allergy and the concentration of IgE antibodies to peanut and Ara h 2 were found. For peanut, the odds of a peanut allergy diagnosis increased 1.68-fold per doubling of the IgE antibody concentration (95% CI 1.39-2.03), whereas for Ara h 2 the odds increased 1.74-fold per doubling (95% CI 1.49-2.03). This means that the odds of having peanut allergy were nearly twice greater for children having a peanut- or Ara h 2–specific IgE level of 2 kU_A/L than for those having a level of 1 kU_A/L. Specific IgE levels associated with peanut allergy were lower for Ara h 2 than for peanut, as shown in Figure 1.

Clinical specificities of at least 90% and 95% were obtained at 1.2 kU_A/L and 4.0 kU_A/L of Ara h 2–specific IgE, respectively (Table I). The higher cutoff level gave a positive predictive value (PPV) of 91.3% for this Japanese study population. Both probability curves and PPVs for specific IgE test results are dependent on the allergy disease prevalence and the age of the patients, so it is important that clinicians who interpret results from clinical studies know these facts.

Previous studies have shown a relationship between the probability of reacting to peanut and the concentration of peanut-specific IgE.[2] We set out to determine the relationship between the levels of specific IgE to Ara h 2 and the outcome of a peanut allergy diagnosis in children. Our retrospective study

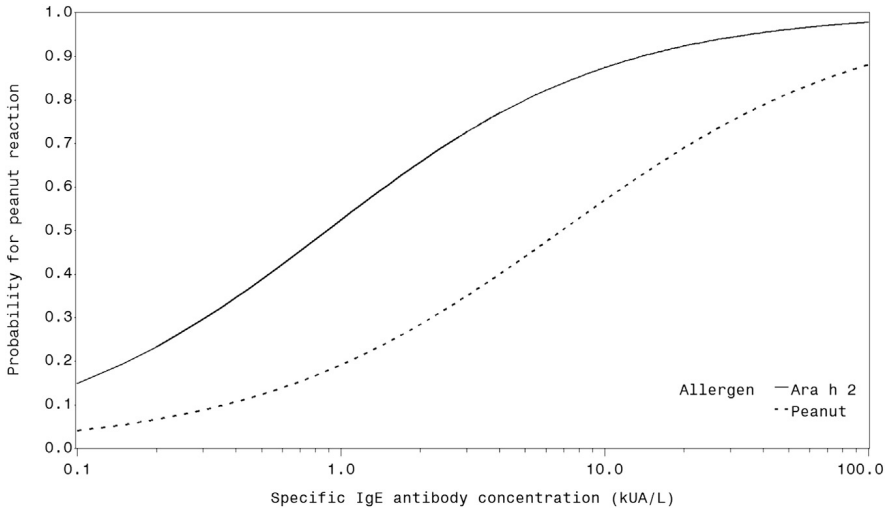

FIGURE 1. Fitted predicted probability curves, plotted using the results from logistic regression, showing the relationship between levels of IgE antibodies to peanut (broken line) and Ara h 2 (solid line) and clinical peanut allergy.

TABLE I. Diagnostic parameters of the Ara h 2 ImmunoCAP test for specific IgE measurement defined at cutoff levels specified by >90% and >95% clinical specificity

Cutoff (kU_A/L)	Specificity (%)	Sensitivity (%)	PPV (%)	NPV (%)
1.2	90.4	74.3	85.2	82.5
4.0	95.7	60.0	91.3	76.3

PPV, positive predictive value; *NPV*, negative predictive value.

shows that there is a relationship between the probability of having peanut allergy (including failure in OFC) and the concentration of Ara h 2–specific IgE. Higher levels of peanut-specific IgE than those of Ara h 2–specific IgE were needed to reach a comparable probability of having peanut allergy. Our study, together with many others, supports the concept that measuring Ara h 2–specific IgE is useful in the clinic when patients with suspected peanut allergy are evaluated.[9] However, this is the first time that a fitted predicted probability curve for Ara h 2–specific IgE has been published.

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Conflicts of interest: R. Movérare is employed by Thermo Fisher Scientific. M. P. Borres is employed by Thermo Fisher Scientific as well as Uppsala University, Sweden. The rest of the authors declare that they have no relevant conflicts.

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TABLE E1. Characteristics of the 8 patients who were diagnosed as tolerant to peanut based on detailed anamnesis

Patient ID	Sex	Age at blood sampling	Specific IgE (kU_A/L)		Latest known peanut consumption in relation to blood sampling time	Type of peanut consumption
			Peanut	Ara h 2		
439884	Male	4 y, 9 months	6.31	0.22	8 months before	Chocolate bar containing peanut
486744	Male	5 y, 8 months	16.3	1.15	7 months before	Peanut cream
572090	Male	3 y, 2 months	3.56	<0.10	1 month before	Peanut
609649	Male	6 y, 0 months	1.23	<0.10	4 months after	Peanut
637230	Male	2 y, 8 months	1.69	3.01	4 months after	Peanut
637267	Male	3 y, 0 months	3.19	<0.10	2 months after	Peanut butter
655581	Male	1 y, 5 months	33.4	<0.10	6 months after	Peanut (dislikes the taste)
679441	Male	1 y, 2 months	10.0	1.38	2 wk after	Peanut cream

TABLE E2. Diagnosis of peanut allergy in the studied children by oral food challenge (OFC, n = 121) or detailed anamnesis (n = 44)

	Number of patients	
Peanut-allergic children		
Failed OFC	35	71
Positive case history	36	
Peanut-tolerant children		
Passed OFC	86	94
Tolerant (anamnesis)	8	

TABLE E3. Specific IgE levels (kU_A/L)

Test	Peanut allergic	n	Min	5th perc.	Median	95th perc.	Max
Peanut*	Yes	71[1]	0.43	1.39	8.54	>100	>100
	No	94[2]	<0.10	0.12	2.18	25.4	58.8
Ara h 2*	Yes	70†[,3,4]	<0.10	<0.10	5.79	72.4	>100
	No	94[5]	<0.10	<0.10	<0.10	3.98	32.8

[1] >100 kU_A/L, n = 4 (6%); [2] <0.10 kU_A/L, n = 4 (4%); [3] <0.10 kU_A/L, n = 8 (11%); [4] >100 kU_A/L, n = 1 (1%); [5] <0.10 kU_A/L, n = 50 (53%).
*Comparison between peanut-allergic and -tolerant children: Mann-Whitney *U*-test $P < .0001$.
†Analysis of Ara h 2-specific IgE was missing for 1 peanut-allergic patient.