

Letter to the Editor

Utility of peanut-specific IgE levels in predicting the outcome of double-blind, placebo-controlled food challenges

To the Editor:

Public awareness regarding peanut allergy is growing.¹ Double-blind, placebo-controlled food challenges (DBPCFCs) are the gold standard for diagnosing food allergy.² Although DBPCFCs are important to determine the clinical relevance of sensitization to allergens, this method is expensive and time-consuming and requires dedicated hospital facilities. Several studies have investigated the association between peanut-specific IgE levels and the outcome of DBPCFCs.^{1,3-7} Cutoff levels were formulated and have differed significantly, ranging from 5 to 57 KU/L to produce a 100% positive predictive value.⁵ These studies were not consistent with respect to the study population, nature of the provocation test (open or double blind), provocation protocol, and focus on early, late, or both types of reactions. In most studies DBPCFCs were not performed in case of a history of anaphylaxis.^{1,3,6,7} Frequently, confirmation of a food allergy was solely based on a positive skin test response, increased food-specific IgE levels, or an open provocation.^{1,3,4}

We conducted a study in which the peanut-specific IgE level was determined in all children suspected of having peanut allergy within 6 months before the challenge, and a DBPCFC was performed independently of a possible history of anaphylaxis. The purpose of this study was to determine the utility of peanut-specific IgE levels in a large, unselected pediatric population using the DBPCFC as a gold standard.

We studied 103 Dutch children referred to our tertiary hospital and suspected of peanut allergy (70 boys and 33 girls). The median age was 6.7 years (5.0-10.3 years). The study population was highly atopic, with 88.3% having atopic dermatitis, 57.3% having asthma, and 35.0% having allergic rhinitis. All participants underwent a DBPCFC between January 2004 and July 2008. DBPCFCs were performed as described previously.⁸ The DBPCFCs were performed in the day care unit. Every child remained under observation after the final dose for at least 2 hours depending on severity of the symptoms to minimize the risk associated with these challenges. DBPCFC results were considered positive after the occurrence of objective symptoms (urticaria, angioedema, vomiting, stridor, and hypotension) or after the occurrence of 3 subjective symptoms (nausea, oral allergy, and abdominal pain). Serum samples were obtained and analyzed for peanut-specific IgE by using the CAP system FEIA (Pharmacia Diagnostic, Uppsala, Sweden). Receiver operator characteristic curves were calculated. Two-by-two tables were used to estimate sensitivity, specificity, and positive and negative predictive value. Logistic regression analysis was used to determine the utility of specific IgE to predict the outcome of the DBPCFC (predicted probability).

Peanut allergy was confirmed in 56 (54.4%) of 103 patients. The receiver operator characteristic curve revealed an area under the curve of 0.91. This means that peanut-specific IgE levels are a useful tool in predicting the outcome of a DBPCFC. Table I shows the peanut-specific cutoff levels calculated by using 2 × 2 tables. Use of 2 × 2 tables revealed 90%, 95%, and 100% positive predictive values of 10.4, 24.8, and 26.5 KU/L, respectively. It should

TABLE I. Cutoff levels of peanut-specific IgE

	Cutoff level (kU/L)	Sensitivity	Specificity	Negative predictive value
Positive predictive value* using 2 × 2 table				
90	10.4	66%	92%	68%
95	24.1	48%	98%	61%
100	26.5	48%	100%	62%
Predicted probability† using logistic regression (ln IgE)				
50	2.79			
90	21.8			
95	43.8			
97	71.3			
99	‡			

*Probability of allergy among those who had specific IgE levels of greater than the cutoff level (the denominator is the number of subjects with levels greater than the cutoff value).

†Model-predicted probability of allergy at different levels of specific IgE (denominator is total sample size).

‡Specific IgE level greater than 100 KU/L, clinically not relevant.

be noted that these cutoff levels have poor sensitivity. Therefore physicians cannot assume that a patient with a peanut-specific IgE level of less than these levels will not have an allergic reaction. Logistic regression analysis led to a predicted probability of 90% and 95% at peanut-specific IgE cutoff levels of 24.8 and 43.8 KU/L, respectively. The association between specific IgE levels and the outcome of the food challenge (logistic regression model) is presented in Fig 1. The higher the concentration of peanut-specific IgE levels, the higher the predicted probability of a positive DBPCFC result.

Our results are in the range of those described by Roberts and Lack⁶ and Rance et al.⁵ Rance et al.⁵ found relatively high cutoff levels. They found a positive predictive value of 100% using a cutoff value of 57 KU/L. This is higher than our cutoff level of 26.5 KU/L and could probably be explained by a single child in their study having a negative provocation result with a peanut-specific IgE level of 57 KU/L, thereby increasing the 100% cutoff value. The area under the curve was 0.87 compared with 0.91 according to our data. The area under the curve classifies the accuracy of a diagnostic test. An area of 1 represents a perfect test, and an area of 0.5 represents a worthless test. A strength of the study⁵ is that all children underwent a DBPCFC independent of the anaphylactic history, as in our study.

A number of studies found significantly lower specific IgE cutoff levels.^{1,3,4,7} Sampson et al.^{1,7} found a 95% cutoff level of 15 KU/L. One explanation could be the difference in study populations. Another more important explanation could be that a substantial number of children (43%) were given diagnoses of peanut allergy by means of history without undergoing a DBPCFC. Our data clearly demonstrate that peanut allergy cannot be diagnosed solely on the basis of a history of a suspected allergic reaction to peanut. Sixteen of 34 children with a history of an anaphylactic reaction had a negative food challenge result. Eight of these children were able to eat peanuts without an allergic

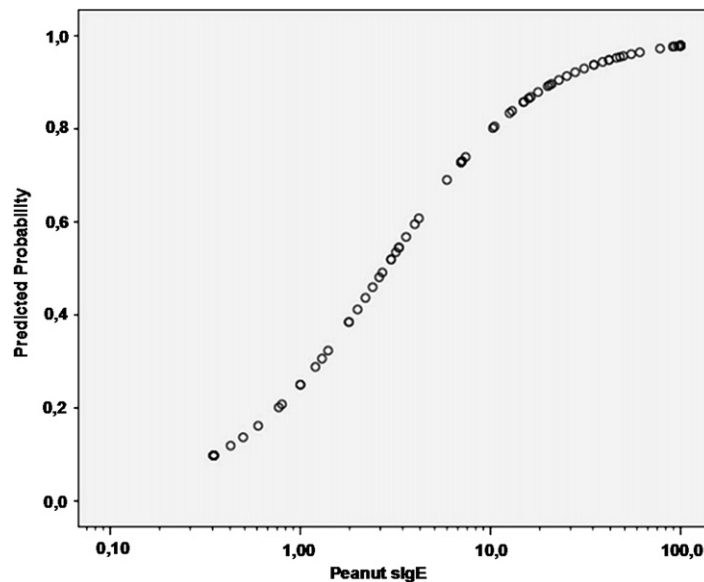


FIG 1. Probability curve of a positive DBPCFC for peanut at a given peanut-specific IgE (*sIgE*) level using logistic regression analysis with $\ln$ *sIgE*.

reaction: 1 child only eats traces of peanut, 2 children still have allergic reactions, and data on the remaining 5 children could not be discovered. We emphasize that a history of an anaphylactic reaction does not automatically indicate a diagnosis of peanut allergy. Bock and Atkins⁹ previously concluded that a history of anaphylaxis was validated by a DBPCFC in less than 50% of the subjects.

Another factor that usually draws little attention is the influence of the statistical method used. We used 2×2 tables to describe our data and logistic regression analysis to generate probability curves that predict the likelihood of patients with a particular peanut-specific IgE level reacting during a food challenge.

In conclusion, our study has several strengths compared with the studies previously mentioned. We performed DBPCFCs in all children suspected of peanut allergy independent of a history of anaphylaxis to peanut. Another strength of our study was the relatively large group of children analyzed and that the analysis was performed with specific IgE levels determined within 6 months before the challenge. A weakness of our study is the fact that the clinician supervising the DBPCFCs was not blind to the peanut-specific IgE level and the retrospective nature of this study. However, all children underwent a standardized DBPCFC. We do not expect that blinding of the clinician or a prospective study would lead to a different outcome.

The clinical relevance of the present study is the ability to predict the outcome of a DBPCFC at every specific IgE level. As many as 54% of DBPCFC results were positive. By using the logistic regression curve, a physician will be able to estimate the probability of a certain patient reacting to peanut during the DBPCFC. The previously formulated cutoff levels can be used by physicians in case of a similarity in patient characteristics to decide whether a DBPCFC is indicated. By using the (90%, 95%, and 100% positive predictive value) specific IgE cutoff levels, DBPCFCs would be superfluous in at least some of the children who were planning to undergo a DBPCFC. However, DBPCFCs still remain important to determine the severity of the allergic

reaction and the amount of peanut that will lead to an allergic reaction.

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Disclosure of potential conflict of interest: The authors have declared that they have no conflict of interest.

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