

Agreement between the Skin Prick Test and Specific Serum IgE for Egg White and Cow's Milk Allergens in Young Infant with Atopic Dermatitis

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ABSTRACT

Background: The skin prick test (SPT) for detecting atopic sensitization is not preferred in young infants with atopic dermatitis (AD) because of concerns about poor skin reactivity. This study aimed to evaluate whether the results of SPT agreed well with those of specific serum immunoglobulin E (sIgE) antibody test in young infants with AD.

Methods: This study included 2,077 eligible infants (age, <12 months) with AD who were tested by either SPT or sIgE between 2007 and 2011. Among them, 199 infants tested for egg white (EW) and 192 infants tested for cow's milk (CM), by both SPT and sIgE on the same day were identified and reviewed retrospectively. Kappa statistics and tests for equal kappa statistics were used to evaluate the agreement between the SPT and sIgE.

Results: The mean wheal diameter and the allergen-to-histamine ratio of SPT showed substantial agreement with those of sIgE for EW ($\kappa = 0.62, 0.69$) and CM ($\kappa = 0.34, 0.47$). The agreement for EW was significantly higher <6-month-old than in ≥ 6 -month-old infants ($\kappa = 0.79$ vs. $0.54, P = 0.02$), and that for CM was similar ($P = 0.60$). The mean wheal diameters for EW and CM were evenly distributed, and did not show increasing trends regardless of age in months ($P_{\text{trend}} = 0.13$ and 0.06 , respectively).

Conclusions: The results of SPT agreed well with those of sIgE. This finding provides a rationale for using SPT, and suggests that SPT can be used along with sIgE to detect food sensitization in young infants with AD.

KEY WORDS

atopic dermatitis, immunoglobulin E, infant, sensitization, skin tests

INTRODUCTION

Atopic dermatitis (AD) is one of the most common chronic, recurrent, allergic skin disease in childhood, with a prevalence of 10%-20% worldwide.¹ A previous study reported that 45% of children develop AD during the first 6 months of life and approximately 60% show symptoms within the first year of life.²

Recent evidence from longitudinal birth cohorts has consistently indicated that either AD or atopic sensitization during early life appears to be one of the

key predictors of later asthma or allergic rhinoconjunctivitis.^{3,4} Moreover, atopic eczema with sensitization (e.g., hen's egg allergy), rather than non-atopic eczema, during early life appears to have higher risk of progressing to later asthma.^{4,6} Therefore, detection of atopic sensitization is an important initial workup for infants with AD, in both clinical and research settings.

Allergen-specific serum immunoglobulin E (sIgE) and the skin prick test (SPT) were accepted as the first step for detecting the presence of IgE antibody

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in the diagnostic workup for AD or suspected food allergy.⁷ SPT has been widely used to confirm or exclude atopic sensitization and has many advantages in clinical practice: (1) it is easy to perform, (2) it provides fast results, and (3) it is inexpensive.⁷ Nevertheless, SPT does not seem to be preferred in infants because of concerns that their skin response to allergen might be poorer than that in older children, due to the immaturity of their skin mast cells.^{8,9} However, mast cells are not only potent effector cells in allergy but also important players in the process of sensitization to allergens.¹⁰ Moreover, skin exposure as well as oral intake of causative food could lead to considerable IgE-mediated reaction even in early infancy. It is therefore theoretically possible to perform skin tests to detect relevant food sensitization even in young infants.¹¹ Although, good agreement between SPT and sIgE for aeroallergens was consistently reported,^{12,13} that for food allergens is still under debate,^{14,15} and has not been fully evaluated, particular in young infants with AD.

We hypothesized that the skin of young infants with AD is sufficiently mature to react with allergens. Therefore, the skin response to SPT will be sufficient to detect atopic sensitization and will agree well with the results of sIgE. To test this hypothesis, we conducted a retrospective study on young infants with AD.

The aims of this study were to evaluate: (1) whether the results of SPT for food allergens agree well with those of sIgE, and (2) whether the wheal response of SPT is mature to detect atopic sensitization in young infants with AD.

METHODS

STUDY DESIGN AND SETTING

Subjects included in this study were young infants (age, <12 months) with AD who were referred to the Pediatric Allergy and Respiratory Center, Soonchunhyang University Hospital (a tertiary medical center in Seoul, Korea) from January 1, 2007 through December 31, 2011.

This study was designed to evaluate the agreement between SPT and sIgE in detecting food sensitization, and the distribution of wheal responses according to age in months in young infants with AD, retrospectively. We comprehensively reviewed medical records, demographic data, and results of SPT and sIgE of all subjects by using electronic and paper charts. This study protocol was approved by the Soonchunhyang University Hospital Research Ethics Committee (J2012-145). The written consent requirement was waived.

STUDY SUBJECTS

All subjects with AD were identified from electronic medical records of our institute, using the International Classification of Diseases 9 code. A total of

2,878 infants (age, <12 months) with mild-to-moderate AD graded by the SCORAD index¹⁶ were identified. The medical records of 2,077 infants with AD who underwent either SPT or sIgE for egg white (EW) and cow's milk (CM) were reviewed by the primary investigator. Among these 2,077 eligible infants, we identified 233 infants tested for EW and 225 infants tested for CM, who were evaluated by both SPT and sIgE at the same date. The detailed subject inclusion process is summarized in Figure 1. The exclusion criteria were as follows: wheal diameter for histamine <1 mm or saline $\geq$ 1 mm. Subjects who exhibited dermographism ($n = 1$) and histamine reactivity <1 mm ($n = 33$) to EW, and dermographism ($n = 1$) and histamine reactivity <1 mm ($n = 32$) to CM were excluded.

DATA COLLECTION

The results of SPT and sIgE, which were performed at the same date, were collected from the database and reviewed by the primary investigator. In this study, sIgE was measured using Pharmacia CAP System FEIA (Pharmacia & Upjohn Diagnostics, Uppsala, Sweden). SPT was performed by a trained and experienced nurse by using commercial allergen extracts (Allergopharma, Reinbek, Germany) according to the standard technique.¹⁷ Briefly, a single drop of allergen extracts was applied to the pricked (using a standardized lancet) normal skin on the dorsal surface of the upper back. Saline was used as a negative control, and histamine (1 mg/mL) was used as a positive control. Wheal and flare reactions were read at 15 min after the test. SPT was not performed on patients with history of systemic reactions or those who anti-histamines were administered within the last 4 weeks. We collected data on reported systemic adverse reactions, such as angioedema or anaphylaxis.

DIAGNOSTIC DECISION POINT

In the SPT, food sensitization was defined when the mean wheal diameter was ≥ 3 mm larger than that of the negative control. Besides the mean wheal diameter, we also calculated the allergen-to-histamine ratio (A/H). An A/H ratio of ≥ 1 was defined as positive.

Food sensitization was defined as sIgE level ≥ 0.35 kU/L which is a positive cutoff value recommended by the manufacturer.

STATISTICAL ANALYSIS

The distributions of demographic characteristics, laboratory results, and mean wheal diameter in SPT and sIgE according to age groups (ages, <6 and ≥ 6 months) were analyzed using the χ^2 -test or Fisher's exact test for categorical variables and by the Mann Whitney *U* test for continuous variables, as appropriate. As a measure of agreement between SPT and sIgE, kappa statistics were calculated. Tests for equal kappa statistics were used to compare kappa statistics

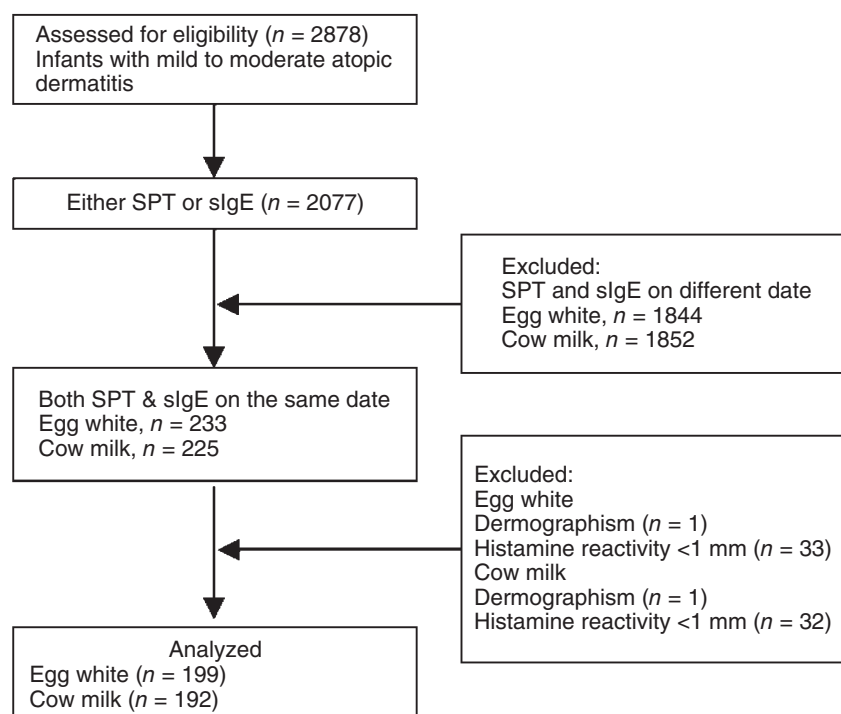


Fig. 1 Flow chart depicting the selection of study subjects.

between the 2 age groups (ages, <6 and ≥6 months). A restricted cubic spline graph was used to estimate the increasing trends of the mean wheal diameter for EW and CM according to age in months. We also estimated the correlation between the mean wheal size for food allergens and age in months. If data were normally distributed, we calculated Pearson correlation statistics for continuous variables. Otherwise, Spearman correlation statistics were calculated. All statistical analyses were performed with SAS software version 9.3 (SAS Institute Inc., Cary, NC, USA). A *P* value of <0.05 was considered the minimum level of statistical significance. All hypothesis tests were 2-sided.

RESULTS

STUDY POPULATION

Complete test results of SPT and sIgE were available for EW in 199 infants and for CM in 199 infants. No systemic adverse reactions were observed in only subjects tested for EW or CM.

EGG WHITE

Of the 199 infants, 60 (30.2%) were aged <6 months. The sensitization rates were 40.2% (80 of 199) in SPT, 54.8% (109 of 199) in sIgE, and 57.3% (114 of 199) in either SPT or sIgE. The median wheal diameters for histamine were not different significantly between the 2 age groups (*P* = 0.46), whereas those for EW were greater in infants aged ≥6 months (*P* < 0.05).

COW MILK

Of the 192 infants, 61 (31.8%) were aged <6 months. The sensitization rates were 17.7% (34 of 192) in SPT, 38.5% (74 of 192) in sIgE, and 42.2% (81 of 192) in either SPT or sIgE. The median wheal diameters for histamine were not significantly different between the 2 age groups (*P* = 0.19), whereas those for CM were greater in infants aged ≥6 months (*P* = 0.02) (Table 1).

AGREEMENT BETWEEN MEAN WHEAL DIAMETER OF SPT AND sIgE

As to EW, 68.8% for sensitivity, 94.4% for specificity, 93.8% for positive predictive value, and 71.4% for negative predictive value were observed between SPT and sIgE. As to CW, 36.5% for sensitivity, 94.1% for specificity, 79.4% for positive predictive value, and 70.3% for negative predictive value were observed. Substantial agreement was observed as to EW (κ = 0.62), whereas fair agreement was observed as to CM (κ = 0.34).

As to EW, the kappa value was significantly higher in the age group of <6 months than in the age group of ≥6 months (κ = 0.79 vs. 0.54, *P* = 0.02), while that for CM was not different (κ = 0.26 versus 0.35, *P* = 0.60) (Table 2).

AGREEMENT BETWEEN THE A/H RATIO AND sIgE

As to EW, 77.1% for sensitivity, 93.3% for specificity, 93.3% for positive predictive value, and 77.1% for negative predictive value were observed between SPT and sIgE.

Table 1 Characteristics of the study subjects tested by both SPT and sIgE for egg white ($n = 199$) and cow's milk ($n = 192$)

	Egg white				Cow milk			
	Total $n = 199$	<6 mo $n = 60$	≥6 mo $n = 139$	P	Total $n = 192$	<6 mo $n = 61$	≥6 mo $n = 131$	P
Age, mo	7.0 (5.0-9.0)	4.0 (3.25-5.0)	8.0 (7.0-10.0)		7.0 (5.0-9.0)	4.0 (3.5-5.0)	8.0 (7.0-9.0)	
Sex (M), n (%)	119 (59.8)	41 (68.3)	78 (56.1)		115 (59.9)	42 (68.9)	73 (55.7)	
Wheal size (mm) ^{†, ‡}	2.0 (2.0-3.0)	2.0 (2.0-3.0)	2.0 (2.0-3.0)	0.46	2.0 (2.0-3.0)	2.0 (2.0-3.0)	2.0 (2.0-3.0)	0.19
Distribution of wheal size, n (%) [‡]				0.35				0.09
1 ≤ <1.5	14 (7.0)	1 (1.7)	13 (9.4)		15 (7.8)	1 (1.6)	14 (10.7)	
1.5 ≤ <2	19 (9.5)	6 (10.0)	13 (9.4)		18 (9.4)	6 (9.8)	12 (9.2)	
≥2	166 (83.4)	53 (88.3)	113 (81.3)		159 (82.8)	54 (88.5)	105 (80.2)	
Wheal size (mm) ^{†, §}	2.0 (0.0-4.0)	0.0 (0.0-3.4)	2.0 (0.0-4.0)	<0.05	0.0 (0.0-2.0)	0.0 (0.0-0.0)	0.0 (0.0-2.0)	0.02
Distribution of wheal size, n (%) [§]				0.22				0.00 [#]
<2 mm	98 (49.2)	36 (60.0)	62 (44.6)		141 (73.4)	51 (83.6)	90 (68.7)	
2 mm ≤ <3 mm	21 (10.6)	4 (6.7)	17 (12.2)		17 (8.9)	2 (3.3)	15 (11.5)	
3 mm ≤ <4 mm	27 (13.6)	8 (13.3)	19 (13.7)		9 (4.7)	6 (9.8)	3 (2.3)	
≥4 mm	53 (26.6)	12 (20.0)	41 (29.5)		25 (13.0)	2 (3.3)	23 (17.6)	
sIgE (kU/L), n (%)				0.02 [#]				<0.01 [#]
<0.35	90 (45.2)	36 (60.0)	54 (38.8)		118 (61.5)	48 (78.7)	70 (53.4)	
0.35-95% PPV	18 (9.0)	4 (6.7)	14 (10.1)		51 (26.6)	9 (14.8)	42 (32.1)	
≥95% PPV [¶]	91 (45.7)	20 (33.3)	71 (51.1)		23 (12.0)	4 (6.6)	19 (14.5)	

[†] Median (interquartile range).

[‡] Mean wheal diameter for histamine.

[§] Mean wheal diameter for allergen.

[¶] The 95% positive predictive value for positive oral challenge test ≤2 years was defined as egg white ≥2 kU/L, and cow's milk ≥5 kU/L.

^{||} Mann Whitney U test, $P < 0.05$.

[#] Chi-square test, $P < 0.05$.

tive predictive value were observed between SPT and sIgE. As to CW, 51.4% for sensitivity, 92.4% for specificity, 80.9% for positive predictive value, and 75.2% for negative predictive value were observed. Substantial agreement was observed as to EW ($\kappa = 0.69$), whereas moderate agreement was observed in CM ($\kappa = 0.47$).

Differences in kappa values between the 2 age groups were not significant as to EW and CM (EW, $\kappa = 0.75$ vs. 0.66, $P = 0.37$; CM, $\kappa = 0.26$ vs. 0.47, $P = 0.58$) (Table 3).

DISTRIBUTION OF MEAN WHEAL DIAMETERS IN EW AND CM ACCORDING TO AGE IN MONTHS

The mean wheal diameter in EW was not positively correlated with age ($\gamma = 0.134$, $P = 0.06$); however, after adjustment for sIgE, it was weakly positively correlated with age ($\gamma = 0.139$, $P = 0.04$). On the contrary, the mean wheal diameter in CM was weakly positively correlated with age ($\gamma = 0.147$, $P = 0.04$), but was not significant after adjustment for sIgE ($\gamma = 0.126$, $P = 0.08$). The mean wheal diameters in EW and CM were evenly distributed, and did not show increasing trends regardless of age in months ($P_{\text{trend}} = 0.13$ and $P_{\text{trend}} = 0.06$, respectively) (Fig. 2).

Table 2 Kappa statistics between mean wheal diameter of SPTs and those of sIgE for egg white and cow milk, and comparison of Kappa statistics between the age groups of <6 months and ≥6 months with mild-to-moderate atopic dermatitis

		SPT †	sIgE ‡		Observed agreement	Kappa (95% CI)	P §
			Positive (%)	Negative (%)			
Egg white	Total, <i>n</i> = 199	Positive	75 (37.7)	5 (2.5)	0.80	0.62 (0.51-0.72)	0.02
		Negative	34 (17.1)	85 (42.7)			
	≥6 mo, <i>n</i> = 139	Positive	56 (40.3)	4 (2.9)	0.76	0.54 (0.41-0.67)	
		Negative	29 (20.9)	50 (36.0)			
	<6 mo, <i>n</i> = 60	Positive	19 (31.7)	1 (1.7)	0.90	0.79 (0.62-0.95)	
		Negative	5 (8.3)	35 (58.3)			
Cow milk	Total, <i>n</i> = 192	Positive	27 (14.1)	7 (3.7)	0.72	0.34 (0.21-0.47)	0.60
		Negative	47 (24.5)	111 (57.8)			
	≥6 mo, <i>n</i> = 131	Positive	23 (17.6)	3 (2.3)	0.69	0.35 (0.21-0.48)	
		Negative	38 (29.0)	67 (51.1)			
	<6 mo, <i>n</i> = 61	Positive	4 (6.6)	4 (6.6)	0.79	0.26 (-0.03-0.55)	
		Negative	9 (14.8)	44 (72.1)			

[†] Positivity defined as 3 mm ≥ negative control.

[‡] Positivity defined as ≥0.35 kU/L.

[§] Test for equal kappa statistics between the age groups of <6 and ≥6 months.

Table 3 Kappa statistics between the allergen to histamine ratio of SPT and sIgE for egg white and cow's milk, and comparison of the Kappa statistics between the age groups of <6 months and ≥6 months with mild-to-moderate atopic dermatitis

		SPT †	sIgE ‡		Observed agreement	Kappa (95% CI)	P §
			Positive (%)	Negative (%)			
Egg white	Total, <i>n</i> = 199	Positive	84 (42.2)	6 (3.0)	0.84	0.69 (0.59-0.79)	0.37
		Negative	25 (12.6)	84 (42.2)			
	≥6 mo, <i>n</i> = 139	Positive	65 (46.8)	4 (2.9)	0.83	0.66 (0.53-0.78)	
		Negative	20 (14.4)	50 (36.0)			
	<6 mo, <i>n</i> = 60	Positive	19 (31.7)	2 (3.3)	0.88	0.75 (0.58-0.92)	
		Negative	5 (8.3)	34 (56.7)			
Cow milk	Total, <i>n</i> = 192	Positive	38 (19.8)	9 (4.7)	0.77	0.47 (0.34-0.60)	0.58
		Negative	36 (18.8)	109 (56.8)			
	≥6 mo, <i>n</i> = 131	Positive	33 (25.2)	6 (4.6)	0.74	0.47 (0.32-0.61)	
		Negative	28 (21.4)	64 (48.9)			
	<6 mo, <i>n</i> = 61	Positive	5 (8.2)	3 (4.9)	0.82	0.26 (0.08-0.67)	
		Negative	8 (13.1)	45 (73.8)			

[†] Positivity defined as an A/H ratio of ≥1.

[‡] Positivity defined as ≥0.35 kU/L.

[§] Test for equal kappa statistics between the age groups of <6 and ≥6 months.

DISCUSSION

In this study, we evaluated agreements between SPT and sIgE for EW and CM allergens in young infants with mild-to-moderate AD. A previous study reported that results of SPT do not agree well with those of sIgE in young infants.^{14,15} However, our results showed that 1) the results of SPTs for food allergens agreed well with those of sIgE in young infants with AD, and 2) the mean wheal diameters for EW and CM were evenly distributed, and did not show increasing trends regardless of age in months. To the

best of our knowledge, this is the first study to investigate the distribution of wheal response to food allergens according to age in months in young infants with mild-to-moderate AD.

AD AND EARLY SENSITIZATION AS PREDICTORS OF LATER ASTHMA

The etiologies of allergic diseases, including asthma, have been considered multifactorial. Numerous factors have been investigated as potential predictors for the development and severity of asthma.^{4-6,18} Nevertheless there is no biomarker to clearly predict subse-

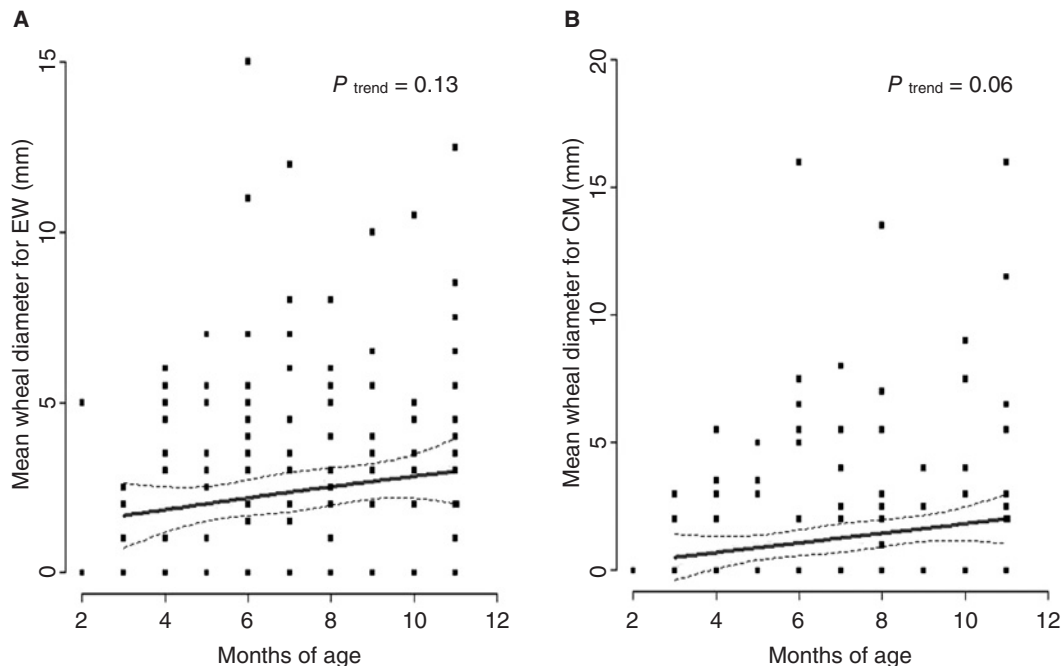


Fig. 2 Restricted cubic spline graph showing no trend ($P = 0.13$ and $P = 0.06$, respectively) in the distribution of skin reactivity to EW and CM according to age in months. **(A)** Mean wheal diameters for EW were evenly distributed regardless of age ($\gamma = 0.134$, $P = 0.06$); however, after adjustment for sIgE, they were weakly positively correlated with age ($\gamma = 0.139$, $P = 0.04$). On the contrary, **(B)** Mean wheal diameters for CM were weakly positively correlated with age ($\gamma = 0.147$, $P = 0.04$), but were not statistically significant after adjustment for sIgE ($\gamma = 0.126$, $P = 0.08$).

quent development of allergic disease.

Numerous longitudinal observational studies have proved the natural course of allergic disease from early sensitization and eczema in infancy to later childhood (*i.e.*, allergic march). Early sensitization to foods^{4,19} or inhalant allergens,²⁰ and AD have been emphasized as a strong predictors of later allergic diseases. In particular, atopic eczema with food sensitization in early life, rather than non-atopic eczema, was strongly associated with increased risk of later asthma.^{4,18}

Although there is the possibility that early food sensitization is confounded by early eczema, early food sensitization appears to be an independent risk factor for later development of asthma and allergic rhinitis regardless of AD.^{4,5} Moreover, early atopic sensitization in young infants with AD appears to be associated with the risk of severe exacerbations of early asthma.³ To date, there have been few effective preventive strategies for the development of asthma, and it has been emphasized that early identification and intervention are the best ways to reduce associated morbidities and socioeconomic burden.²¹ Therefore, early identification of children at high risk of later asthma has numerous clinical implications. However, atopic eczema and non-atopic eczema could not be differentiated by physical examination alone.

Thus, detection of atopic sensitization in young infants with AD is essential in clinical practice. For these reasons, early food sensitization and/or AD would be a target for further interventional studies, and therefore atopic sensitization should be identified in young infants with AD.

AGREEMENT BETWEEN SPT AND sIgE FOR FOOD ALLERGEN

Of an unselected cohort of 353 infants (age 2 years) from The Prevention of Allergy among Children in Trondheim (PACT) study, 15.6% were sensitized to food allergens and 34.3% had AD. That study reported weak agreement between SPT and sIgE for both EW ($\kappa = 0.37$) and CM ($\kappa = 0.19$); therefore, these 2 tests should not be used interchangeably, but complementarily, for the detection of atopic sensitization.¹⁴ However, our results did not support the results of The PACT study but rather showed that STP and sIgE agreed well with each other. This discordance might be due to the different study populations and low sensitization rates in The PACT study (*e.g.*, EW, 11.4%; CM, 5.1%) compared to our higher sensitization rates for both EW (57.3%) and CM (42.2%).

SKIN REACTIVITY IN YOUNG INFANTS

Contrary to sIgE levels, which represent the pres-

ence of circulating allergen-specific IgE antibody, SPT represents the overall response according to the levels of histamine and other mediators (*e.g.*, prostaglandin, leukotrienes, and platelet-activating factor) released from mast cells activated by the interaction between allergen and sIgE antibodies on the cell surface. Therefore, it has been suggested that SPT should not be interchangeably used with sIgE because circulating IgE is not equivalent to cell-bound histamine-releasing active mediators.²² However Hill *et al.*²³ have reported that although the responses of mast cells in the skin to allergens are lower in younger infants, the diagnostic accuracy of SPT is either similar or more sensitive than sIgE measurement, and SPT for food allergens is more clinically relevant. Skin reactions vary with age, and infants may react predominantly with large erythematous flares and small wheals. However, since large wheals are observed even in young infants, skin tests are useful for the diagnosis of allergic diseases in this population.

SAFETY CONCERNS ABOUT THE USE OF SPT IN YOUNG INFANTS

Despite the usefulness and safety of SPT, concerns about severe systemic reactions such as anaphylaxis seem to be a reason for avoiding SPT in young infants. Although we did not find systemic reactions in the subjects included in the current study, the overall incidence of adverse reactions is approximately 0.04% in children,²⁴ and deaths (<0.02%) by SPT with fresh foods have been reported.²⁵ Because infants cannot effectively complain of the early symptoms of a systemic reaction,²⁶ physicians should be aware of the possibility of fatal systemic reactions, particularly in infants who have had severe reactions, and should carefully perform the test and observe the results in an office fully equipped with emergency kits.

STRENGTHS AND LIMITATIONS

The major strengths of this study are as follows: 1) Since SPT and sIgE measurement were performed at the same date, and SPT was performed by the same trained technician and interpreted by the same physician, our study provided more consistent results than multicenter studies. 2) The sample size was large to analyze the agreement due to the high sensitization rate. 3) Infants with severe AD were excluded to avoid any misinterpretation that could originate from poor or severe response of inflamed skin, even looking clear.

However, this study also has inherent limitations due to its retrospective design. The interferences of drugs, such as antihistamines or local corticosteroids, as well as systemic illness before SPT, may not be completely excluded. For example, 33 of the 233 subjects (14.2%) tested for EW were excluded because of poor skin responses to histamine. However, we did

our best to reduce the interference by excluding subjects with poor skin responses to histamine. Repeated comparison between SPT and sIgE are necessary to evaluate the maturity of skin response by age. However, even in a prospective study, monthly measurements in young infants may be impossible because of ethical issues.

Food allergens have been reported to be an important risk factor for the development and exacerbation of AD. The prevalence of food allergy (FA) is known to be up to 5%-6% in infancy,^{7,27} and about 35% of children with moderate-to-severe atopic dermatitis (AD) have FA as a trigger.²⁸ Therefore, detection of causative food allergens in AD coincident with FA would be important in clinical practice. In our study, 26.6% (52/192) of the patients were clinically diagnosed with milk allergy, and 31.2% (62/199) with egg allergy. This low prevalence of FA may be due to the retrospective design and younger subjects.

Taken together, although the detection rate of food sensitization is lower in SPT, the results of SPT for food allergens agreed well with those of sIgE in young infants with AD. Moreover, skin responses to food allergens were evenly distributed regardless of age. These findings suggest that SPT can be used along with sIgE to detect food sensitization in young infant with AD and may predict the risk of later asthma in order to prevent disease progression.

In conclusion, our findings may provide the rationale for the use of SPT in young infants with AD in both clinical and research settings, and may deserve future research into better prediction methods for allergic diseases.

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