

Total IgE at 6 months predicts remittance or persistence of atopic dermatitis at 14 months

Norio Kawamoto, M.D., Ph.D.,¹ Toshiyuki Fukao, M.D., Ph.D.,¹ Hideo Kaneko, M.D., Ph.D.,^{1,2} Kouichiro Hirayama, Ph.D.,¹ Satomi Sakurai, M.D., Ph.D.,¹ Takahiro Arai, M.D., Ph.D.,¹ Masashi Kondo, M.D., Ph.D.,¹ Minako Kawamoto, M.D., Ph.D.,¹ Eiko Matsui, M.D., Ph.D.,¹ Kenji Orii, M.D., Ph.D.,³ Kimiko Kasahara,¹ Masao Takemura, B.Sc., Ph.D.,⁴ Mitsuru Seishima, M.D., Ph.D.,⁴ Makoto Shiraki, M.D., Ph.D.,⁵ Shinichi Iwasa, M.D., Ph.D.,⁵ and Naomi Kondo, M.D., Ph.D.^{1,6}

ABSTRACT

Some patients with infantile atopic dermatitis (AD) achieve remission around 1 year old, but in others it persists. The difference between them is unclear. We performed a birth cohort study to find the markers predicting the outcome of infantile AD. We followed up a cohort ($n = 314$) from birth to 14 months of age, and cord blood was taken from the participants. Some of them ($n = 144$) had a physical examination and a blood test at 6 and 14 months of age. The subjects who had AD at 6 months ($n = 34$) were divided into two groups, named the transient group (those who had no AD at 14 months of age; $n = 16$) and the persistent group (those who still had AD at 14 months of age; $n = 18$). Then, laboratory data were compared between these two groups. Percentage of CD8 in cord blood lymphocytes and total IgE at 6 months of age in the persistent group was significantly higher than those of the transient group. The area under the curves of a receiver operating characteristic analysis were 0.792 ($p = 0.007$) and 0.722 ($p = 0.027$). In the persistent group, total IgE, percentages of T-helper (Th) 2 and phytohemagglutinin-induced IL-4 production from peripheral blood mononuclear cells at 14 months of age were also significantly higher than those of the transient group. Thus Th2 polarization in the persistent group was confirmed. In clinical use, total IgE at 6 months of age is the most useful predictive marker to know the outcome of infantile AD. The clinical trial registration ID is UMIN000002926.

(Allergy Asthma Proc 34:362–369, 2013; doi: 10.2500/aap.2013.34.3678)

Atopic dermatitis (AD) is a common chronic inflammatory skin disease in infants and children and is characterized by the itching of skin with exacerbations and remissions. Association between AD and cytokines was proposed. It seems that not only IgE-mediated type I hypersensitivity but also cell-mediated type IV hypersensitivity are involved in the pathogenesis of AD. Acute AD skin lesions are associated with the infiltration of T-helper (Th) 2 cells expressing increased levels of IL-4, IL-13, and IL-31. In contrast, chronic AD lesions deviate toward Th1 inflammation with predominant IL-12, IL-18, and interferon (IFN) γ .^{1–3}

The constant scratching associated with atopic eczema may result in skin damage, secondary infection, and sleep disturbance to both child and parents.⁴ AD has its onset during the first 6 months of life in 45% and the 1st year of life in 60% of affected individuals.⁵ Of 192 children in the German Multicenter Atopy Study, with early infantile AD, 43.2% were in complete remission by age 3 years.^{6,7} Previously, we reported that several cord blood factors are important as predictive indicators of pediatric allergy.^{8–10} Although several factors, including maternal history of AD,¹¹ cord blood IgE,^{10,12} reduced IFN- γ , and enhanced IL-4 producing CD4⁺ cord blood T cells¹³ and regulatory T cells,¹⁴ have been proposed as risks for infantile AD, there is no report predicting outcomes for infantile AD. In some patients, the symptoms of AD improve during or after the 1st year of life. However, there are some patients whose symptoms of AD persist beyond their first birthday. It is very useful for the patients and caregivers to know whether the patients will improve soon or not. In this article we evaluated the outcome of the subjects who were diagnosed by a pediatric allergist as having AD at 6 months and discovered some factors that predict the outcome of infantile AD.

From the ¹Department of Pediatrics, Graduate School of Medicine, Gifu University, Gifu, Japan, ²Department of Clinical Research, National Hospital Organization, Nagara Medical Center, Gifu, Japan, ³Neonatal Intensive Care Unit, Gifu University Hospital, Gifu, Japan, ⁴Department of Informative Clinical Medicine, Graduate School of Medicine, Gifu University, Gifu, Japan, and ⁵Iwasa Maternity, Gifu, Japan
Funded by Health and Labor Science Research Grants for Research on Allergic Disease and Immunology from the Ministry of Health, Labor and Welfare, Japan
The authors have no conflicts of interest to declare pertaining to this article
Address correspondence to Norio Kawamoto, M.D., Ph.D., Department of Pediatrics, Graduate School of Medicine, Gifu University, 1-1 Yanagido, Gifu 501-1194, Japan
E-mail address: norio-kawamoto@umin.ac.jp
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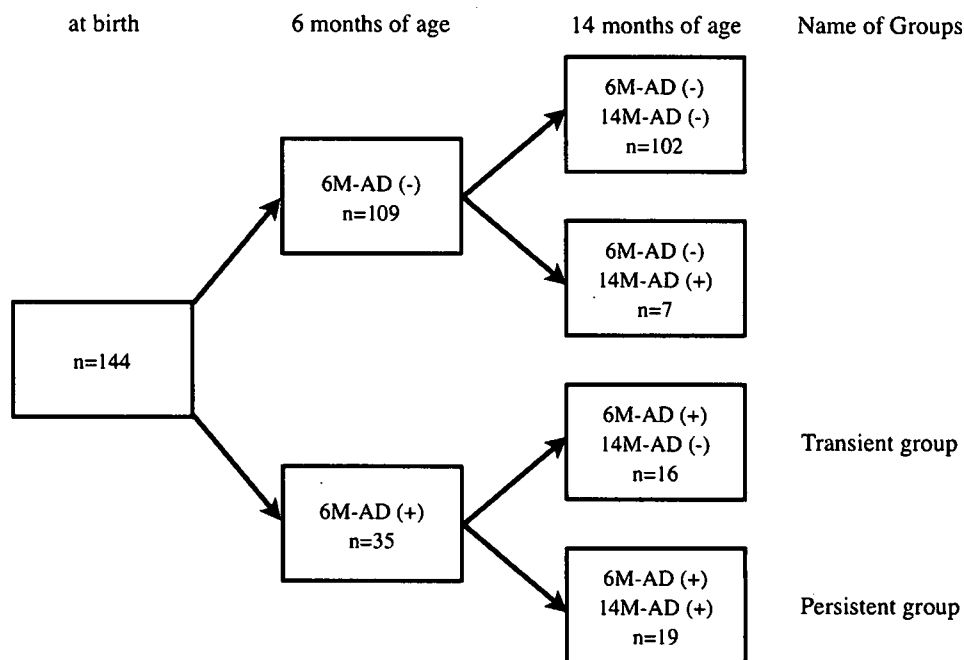


Figure 1. The groups according to the diagnosis at 6 and 14 months of age. Of the 314 subjects 144 (45.9%) had physical examinations at both 6 and 14 months.

METHODS

Study Subjects and Study Design

We performed this analysis as a part of the Gifu Allergy and Immunology Cohort Study (GAICS). The detail of this cohort study was written in our previous publication.¹² The outline was explained to the parent(s) before birth, and those who consented participated. Cord blood samples were obtained at the time of birth, and physical examination by a pediatric allergist and blood sampling at 6 and 14 months of age were performed with written agreements from their parents. To analyze the outcome of infantile AD, the participants of the GAICS who took the physical examination at both 6 and 14 month of age were enrolled in this study. The diagnosis of AD was made by pediatric allergists according to Hanifin's and Rajka's minor criteria.¹⁵ This cohort study was approved by the Ethical Committee of the Graduate School of Medicine, Gifu University.

Study Groups

As shown in Fig. 1, the subjects who had AD at 6 months of age were divided into two groups according to the diagnosis of AD at 14 months of age. Laboratory data were compared between the transient group (who had AD at 6 months and a remission at 14 months) and the persistent group (who had AD at 6 months, and which persisted to the age of 14 months).

Laboratory Determination

Total white blood cell (WBC) counts were performed by using an automated instrument. Blood smears from peripheral blood samples were stained (Wright-Gi-

emsa stain), and a 200-count WBC differential was performed. The percentages of eosinophil in WBC were named Eosinophil %.

Total IgE was measured in serum obtained from the blood samples with LUMIPULSE IgE (Fujirebio, Inc., Tokyo, Japan). Although the practical detection range of this product was originally defined from 1 to 1500 IU/mL, technical information from the company showed the detection limit of this product was 0.02 IU/mL. Because we also confirmed the linearity with sequential dilution until 0.07 IU/mL, we defined 0.1 IU/mL as the detection limit of total IgE in this study. Specific IgE was measured with the radioallergosorbent test and sensitization was defined as a specific IgE concentration higher than 0.34 UA/mL for certain allergens (egg white, cow's milk, wheat, soybean, house-dust 1, *Dermatophagoides pteronyssinus*, dog dander, and cat dander). Cord blood serum IgA was examined to evaluate the contamination of maternal blood, and samples of IgA ≥ 1 mg/dL were excluded.¹⁶

Flow Cytometric Analysis of Lymphocyte Subpopulations

Whole blood samples were stained with CD3, CD19, CD4, CD8, CD56/CD16, and CD4/CD25 antibodies and treated with ammonium chloride to lyse the erythrocytes. The tubes were washed twice with phosphate-buffered saline and analyzed immediately by Cytomics FC500 (Beckman Coulter, Brea, CA). The percentages of CD3⁺, CD19⁺, and CD4⁺ cells in the lymphocytes were respectively named CD3% (T cell), CD19% (B cell), and CD4% (Th cell). The CD8⁺ cells were divided into CD8^{bright} and CD8^{dull}. Most of the CD8^{dull} cells

Table 1 Immunological factors of transient and persistent group at birth

		Transient			Persistent			p Value#
		Mean	SD	n	Mean	SD	n	
Cord blood								
WBC	×10 ³ /μL	10.41	3.28	12	12.84	4.28	16	0.150
Eosinophil%	%	2.78	1.05	12	2.96	0.84	16	0.762
IgE	IU/mL	0.80	1.23	14	0.52	0.56	19	0.623
Th1%	%	0.24	0.17	13	0.28	0.24	18	0.857
Th2%	%	0.23	0.28	13	0.14	0.15	18	0.559
Tc1%	%	0.58	0.67	13	0.61	0.66	18	0.920
Tc2%	%	0.02	0.02	13	0.01	0.02	18	0.056
CD3%	%	53.86	19.90	13	55.95	13.63	18	0.936
CD19%	%	6.95	4.53	13	9.55	4.83	18	0.150
CD4%	%	42.80	16.45	13	42.51	10.15	17	0.722
CD8%	%	17.81	6.17	13	23.28	4.46	17	0.007*
CD8 ^{Bright} %	%	11.42	4.67	12	13.58	5.22	16	0.286
CD56/CD16%	%	7.83	4.39	13	12.13	6.68	18	0.072
CD4/CD25%	%	12.23	2.97	13	12.50	3.30	18	0.904
IFN-γ (PHA)	pg/mL	426.70	328.86	11	1218.51	1888.77	16	0.921
IL-4 (PHA)	pg/mL	6.10	5.21	12	5.56	4.41	19	0.776

* $p < 0.05$.

#Statistical significance determined by Mann-Whitney U test.

WBC = white blood cell; Th = T helper; Tc = cytotoxic T cell; IFN = interferon; PHA = phytohemagglutinin; SD = standard deviation.

expressed CD56 and CD16 (data not shown) and were considered to be natural killer (NK) cells. On the other hand, most of the CD8^{Bright} cells expressed CD3, but not CD16 or CD56 (data not shown). Hence, the percentages of CD8⁺ cells, CD8^{Bright}, and CD8^{dull} in the lymphocytes were named CD8%, CD8^{Bright}% (cytotoxic T [Tc] cell), and CD8^{dull}% (some parts of the NK cells). The percentages of CD56⁺ and CD16⁺ cells in the lymphocytes were named CD56/CD16%. The CD25⁺ cells in CD4⁺ lymphocytes were named CD25/CD4%.

Intracellular Cytokine Analysis

A total of 0.5 mL of heparinized whole blood was added to 0.5 mL of RPMI-1640 medium and incubated with a combination of 25 ng/mL of phorbol myristate acetate and 1 $\mu\text{g/mL}$ of ionomycin in the presence of 10 $\mu\text{g/mL}$ of breferrdin A (Sigma, St. Louis, MO) and cultured for 4 hours at 37°C, in a humidified atmosphere containing 5% CO₂. Surface staining (CD4 and CD8) was then performed and the samples were then fixed and permeabilized with an IntraPrep Permeabilization Reagent (Beckman Coulter). Finally, the cells were incubated with monoclonal antibodies of anti-IFN- γ -fluorescein isothiocyanate (Beckton Dickinson, Franklin Lakes, NJ) or anti-IL-4-phycoerythrin (Beckton Dickinson), and analyzed using Cytomics FC500. The percentage of IFN- γ -producing cells in a CD4⁺ or CD8^{Bright} cell was considered as Th-1% or Tc1%, re-

spectively. The percentage of IL-4-producing cells in a CD4⁺ or CD8^{Bright} cell was considered as Th2% or Tc2%, respectively.

Cell Preparation and Cell Culture

Cord blood mononuclear cells or peripheral blood mononuclear cells (PBMCs) were isolated by centrifugation on Ficoll/Paque (Pharmacia AB, Uppsala, Sweden) and washed three times. The isolated cord blood mononuclear cells/PBMCs were suspended at a final concentration of 1×10^6 cells/mL in an RPMI-1640 medium supplemented with 10% heat-inactivated fetal calf serum, 2 mM of L-glutamine, 100 IU/mL of penicillin, and 100 $\mu\text{g/mL}$ of streptomycin. The cell suspensions were cultured in the presence or absence of 10 $\mu\text{g/mL}$ of phytohemagglutinin (PHA; Gibco BRL, Grand Island, NY) for 24 hours at 37°C in a humidified atmosphere containing 5% CO₂. The culture supernatants were measured through use of a human IFN- γ ELISA kit (Ohtsuka, Tokyo, Japan) and an IL-4 U.S. ELISA kit (Invitrogen Corporation, Camarillo, CA). The detection limits of the ELISAs are as follows: IFN- γ , 15.6–1000 pg/mL; IL-4, 0.39–25.0 pg/mL.

Statistics

Statistical evaluations were performed using the Mann-Whitney U test and univariate logistic regres-

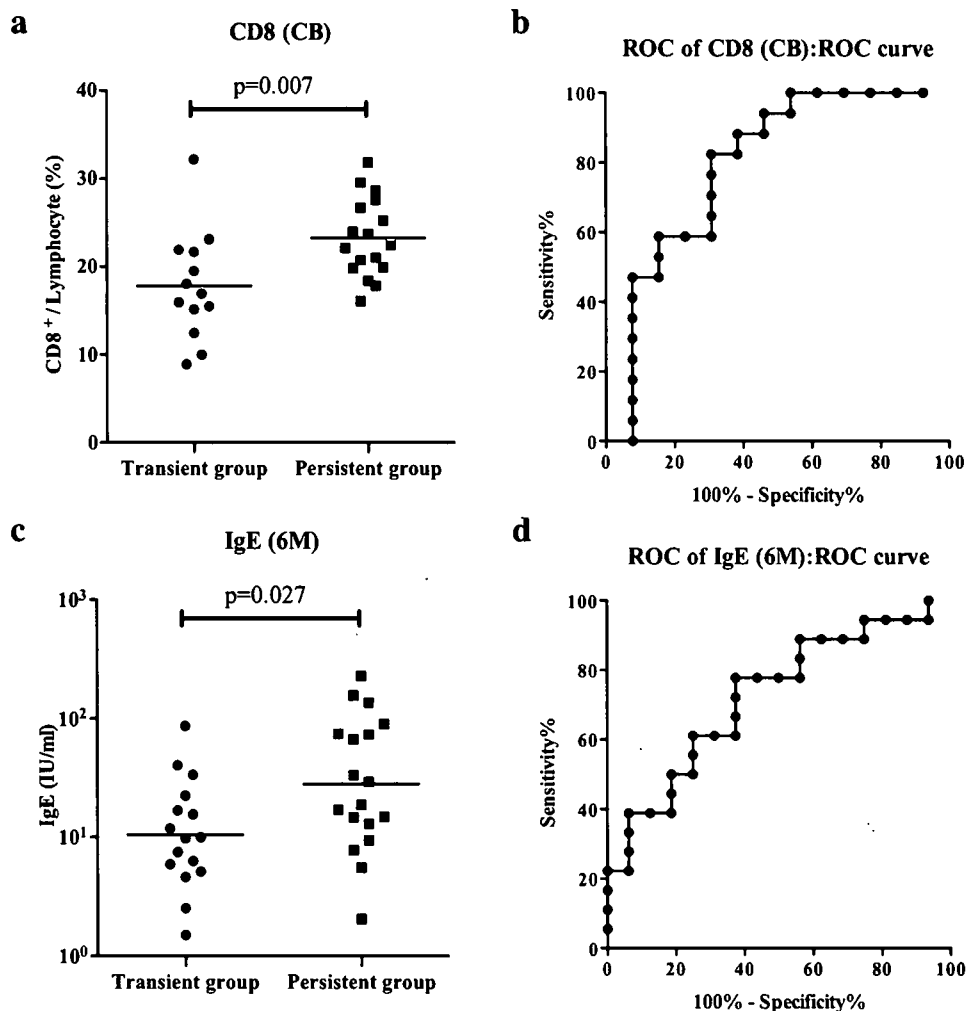


Figure 2. (a and c) Representative scatter plot and its (b and d) receiver operating characteristic (ROC) curve analysis of the laboratory data at birth and 6 months of age. Horizontal lines represent (a) mean or (c) geometric mean). (a and c) CD8% of cord blood and total IgE at 6 months of age were compared between transient and persistent groups.

sion analysis. The ability of measured parameters to discriminate between the persistent group and the transient group was evaluated using receiver operating characteristic (ROC) curves. The Mann-Whitney *U* test and ROC curve analysis were performed using JMP (SAS Institute, Inc., Cary, NC) and GraphPad Prism (GraphPad Software, Inc., La Jolla, CA) to analyze some of the laboratory data. Univariate logistic regression analysis was performed using SPSS (SPSS, Inc., Chicago, IL) to analyze specific IgE. Two-tailed values of $p < 0.05$ were considered statistically significant.

RESULTS

Study Participants and Baseline Characteristics

The characteristics of the 314 study subjects in our cohort study named GAICS have been described in detail previously.¹² Of the 314 subjects 171 (54.5%) were girls, the mean gestational age of the 314 subjects was 278.0 days (equal to 39 weeks and 5.0 days) and the standard deviation (SD) was 7.5. The mean birth weight was 3120.5 g (SD, 388.2). One hundred forty-four of the 314 subjects (45.9%) had physical examina-

tions at both 6 and 14 months (Fig. 1). Also, 140 of the 314 subjects (44.6%) had a blood test at both 6 and 14 months with informed consent.

Eighty of the 144 subjects (55.6%) were girls, the mean of gestational age of 144 subjects was 278.2 days (equal to 39 weeks and 5.2 days), and the SD was 7.0. The mean birth weight was 3098.9 g (SD 384.3). Of the 144 subjects who had a physical examination at 6 and 14 months, 35 (24.3%) and 26 (18.1%) suffered from AD at the time of diagnosis. The number of subjects in the transient and persistent group was 16 and 19, the number of girls was 5 (31.3%) and 11 (57.9%), the mean gestational age was 278.9 (SD, 7.0) days and 279.2 (SD, 8.0) days, the mean birth weight was 3280.9 g (SD, 443.0) and 3102.4 g (SD, 359.4), respectively.

Laboratory Data of Cord Blood

We compared the laboratory data of cord blood (Table 1 and Fig. 2 a). The percentage of CD8⁺ cells in cord blood of the persistent group was higher than that of the transient group. There was no significant difference in other laboratory data of cord blood between them.

Table 2 Immunological factors of transient and persistent group at 6 mo of age

		Transient			Persistent			<i>p</i> Value#
		Mean	SD	<i>n</i>	Mean	SD	<i>n</i>	
6 mo of age								
WBC	×10 ³ /μL	9.91	2.96	16	10.54	2.82	18	0.398
Eosinophil%	%	3.87	1.84	16	5.94	4.31	18	0.240
IgE	IU/mL	17.51	21.40	16	55.02	62.96	18	0.027*
Th1%	%	2.08	0.78	15	2.09	0.99	17	0.836
Th2%	%	0.34	0.23	15	0.42	0.29	17	0.385
Tc1%	%	7.26	6.75	14	5.22	4.51	17	0.302
Tc2%	%	0.04	0.07	14	0.05	0.08	17	0.563
CD3%	%	64.25	12.14	16	56.34	14.77	18	0.105
CD19%	%	14.20	12.23	16	16.31	10.06	18	0.417
CD4%	%	46.03	14.31	16	39.84	11.14	18	0.317
CD8%	%	16.37	5.10	16	17.54	5.94	18	0.334
CD8 ^{Brighto} %	%	12.62	4.11	16	12.39	3.94	18	0.730
CD56/CD16%	%	4.45	1.49	16	5.84	4.44	18	0.629
CD4/CD25%	%	11.21	2.13	16	11.15	2.37	18	0.890
IFN-γ (PHA)	pg/mL	2591.20	2397.61	15	1931.08	2952.05	16	0.058
IL-4 (PHA)	pg/mL	12.36	6.99	16	12.03	7.40	17	0.746

* $p < 0.05$.

#Statistical significance determined by Mann-Whitney U test.

WBC = white blood cell; Th = T helper; Tc = cytotoxic T cell; IFN = interferon; PHA = phytohemagglutinin; SD = standard deviation.

To evaluate the predictability of the CD8% of cord blood for distinguishing the persistent group from the transient group, an ROC curve analysis was performed (Fig. 2 b). The area under the curve of the CD8 of cord blood was 0.792 (95% confidence interval [CI], 0.615–0.969; $p = 0.007$); the optimal cutoff point was 19.84%. This cutoff point produced the following values: sensitivity of 82.4% and specificity of 69.2%. Hence, the CD8% of cord blood is a predictive factor in regard to whether a patient of AD at 6 months of age will improve by 14 months of age.

Laboratory Data at 6 Months of Age

We compared the laboratory data at 6 months of age between the two groups (Table 2 and Fig. 2 c). In the persistent group, total IgE at 6 months of age was significantly higher than that of the transient group. There was no significant difference in other laboratory data at 6 months of age between them. To evaluate the predictability of total IgE at 6 months of age for distinguishing the persistent group from the transient group, an ROC curve analysis was performed (Fig. 2 d). The area under the curve of total IgE at 6 months was 0.722 (95% CI, 0.550–0.894; $p = 0.027$); the optimal cutoff point was 12.99 IU/mL. This cutoff point produced the following values indicating diagnostic utility: sensitivity of 77.78% and specificity of 62.50%. Hence, total IgE at 6 months of age is also a predictive factor as to

whether a patient of AD at 6 months of age will improve by 14 months of age.

The risk of sensitization at 6 months of age was analyzed (Table 3). The risk of persistence increased significantly among the egg white-sensitized group (odds ratio [OR], 8.00; 95% CI, 1.37–46.81; $p = 0.021$).

Laboratory Data at 14 Months of Age

We compared the laboratory data at 14 months of age between the transient and persistent groups (Table 4 and Fig. 3, a–c). Total IgE, Th2% and IL-4 production by PHA-stimulated PBMCs in the persistent group were higher than those of the transient group ($p = 0.013$, $p = 0.047$, and $p = 0.006$, respectively). These data indicate that Th2 polarization was confirmed in the persistent group.

The risk of sensitization at 14 months of age was analyzed (Table 5). The risk of persistence increased significantly among the egg white-sensitized group (OR, 7.50; 95% CI, 1.28–44.08; $p = 0.026$) or cow's milk-specific (OR, 5.50; 95% CI, 1.22–24.81; $p = 0.027$) IgE.

DISCUSSION

Many cases of infantile AD occur during the first 6 months of life.⁵ After then, some achieve remission at ~1 year old, but with others it persists. It is very im-

Table 3 Univariate risk for persistence of infantile AD

		Persistent (n/total)	Transient (n/total)	p Value	OR	95% CI for OR	
						Lower	Upper
6 mo of age							
Egg white	class 1≤	88.89% (16/18)	50.00% (8/16)	0.021*	8.00	1.37	46.81
Cow's milk	class 1≤	44.44% (8/18)	18.75% (3/16)	0.119	3.47	0.73	16.53
Wheat	class 1≤	36.36% (4/11)	37.50% (3/8)	0.960	0.95	0.14	6.28
Soy	class 1≤	5.56% (1/18)	0.00% (0/16)	1	NC		—
Dog dander	class 1≤	33.33% (6/18)	25.00% (4/16)	0.596	1.50	0.34	6.7
Cat dander	class 1≤	5.56% (1/18)	6.25% (1/16)	0.932	0.88	0.05	15.37
<i>Dermatophagoides farinae</i>	class 1≤	5.56% (1/18)	6.25% (1/16)	0.932	0.88	0.05	15.37

*Significant in univariate logistic regression analysis.

AD = atopic dermatitis; CI = confidence interval; OR = odds ratio.

Table 4 Immunological factors of transient and persistent groups at 14 mo of age

		Transient			Persistent			p Value#
		Mean	SD	n	Mean	SD	n	
14 mo of age								
WBC	×10 ³ /μL	10.59	2.70	14	9.20	2.38	17	0.159
Eosinophil%	%	2.43	1.22	14	2.73	1.94	16	0.677
IgE	IU/mL	26.84	24.74	14	102.38	128.63	16	0.013*
Th1%	%	3.44	1.35	14	4.09	1.41	17	0.132
Th2%	%	0.53	0.18	14	0.76	0.38	17	0.047*
Tc1%	%	14.69	8.77	14	16.37	9.33	17	0.552
Tc2%	%	0.22	0.38	14	0.13	0.11	17	0.766
CD3%	%	65.68	7.63	14	63.91	6.76	17	0.525
CD19%	%	12.93	6.49	14	14.89	5.61	17	0.383
CD4%	%	44.75	8.71	14	43.97	6.30	17	0.578
CD8%	%	21.54	6.97	14	22.28	5.47	17	0.578
CD8 ^{Bright} %	%	16.10	6.92	14	15.77	5.07	17	0.812
CD56/CD16%	%	5.82	2.52	14	7.46	4.25	17	0.383
CD4/CD25%	%	11.79	1.40	14	11.91	2.34	17	0.500
IFN-γ (PHA)	pg/mL	1383.76	1665.92	14	1520.55	1462.60	17	0.451
IL-4 (PHA)	pg/mL	8.65	5.19	14	14.73	7.02	17	0.006*

*p < 0.05.

#Statistical significance determined by Mann-Whitney U test.

WBC = white blood cell; Th = T helper; Tc = cytotoxic T cell; IFN = interferon; PHA = phytohemagglutinin; SD = standard deviation.

portant to find the predictive markers to know whether the subjects who had AD at 6 months of age will continue to have it or not. Here, we showed a cohort study, named GAICS, in which the CD8% of cord blood and total IgE at 6 months of age were positive predictive markers for the outcome of infantile AD.

The meaning of elevated CD8% at birth is unclear. Although Leonardi *et al.* reported that CD8 was significantly lower in the patient with AD aged 2–13 years,¹⁷ there was no report concerning CD8 in cord blood. There was no significant difference in the CD8^{Bright}% of

cord blood between the persistent and transient groups. CD8⁺ cells were divided into two subpopulations, named CD8^{Bright} and CD8^{dull}. CD8^{dull} cells were considered to be NK cells.^{18,19} The majority of peripheral blood NK cells exhibit the phenotypic characterization CD56⁺ and CD16⁺.²⁰ NK cells are classically considered as large granular lymphocytes of the innate immune system. They are involved in direct innate immune reactions against viruses, bacteria, parasites, and tumors.²¹ Recently, it was revealed that NK cells link not only innate immune response but also adap-

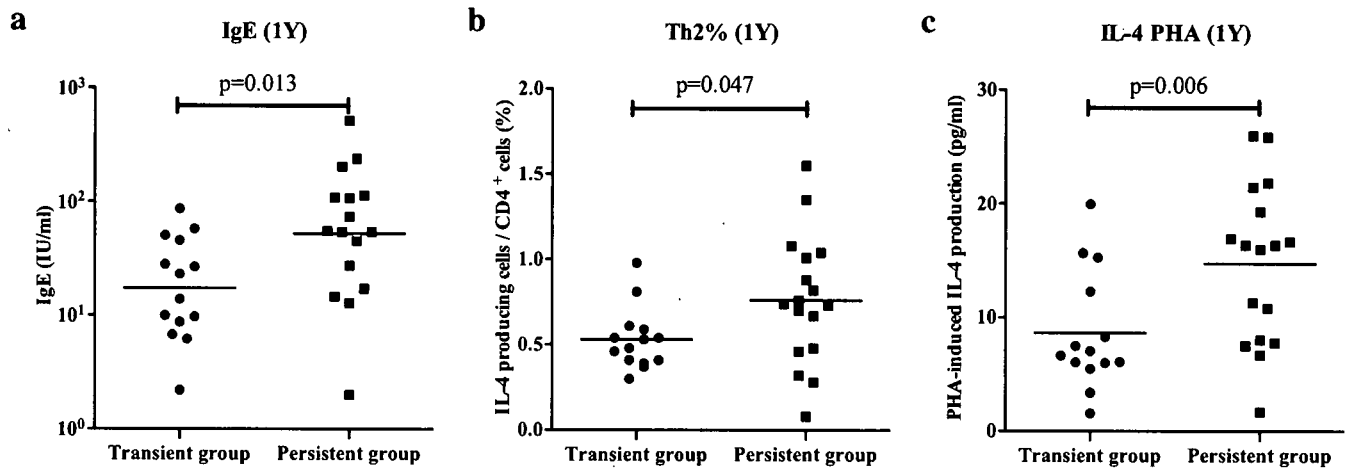


Figure 3. (a–c) Representative scatterplot of the laboratory data at 14 months of age. Horizontal lines represent geometric (a) mean or (b and c) means. (a–c) Total IgE, T-helper (Th) 2%, phytohemagglutinin (PHA)-induced IL-4 production from peripheral blood mononuclear cells (PBMCs) at 14 months of age were compared between transient and persistent groups.

Table 5 Univariate risk for persistence of infantile AD

		Persistent (n/total)	Transient (n/total)	p Value	OR	95% CI for OR	
						Lower	Upper
14 mo of age							
Egg white	class 1≤	88.24% (15/17)	50.00% (8/16)	0.026*	7.50	1.28	44.08
Cow's milk	class 1≤	64.71% (11/17)	25.00% (4/16)	0.027*	5.50	1.22	24.81
Wheat	class 1≤	35.29% (6/17)	18.75% (3/16)	0.293	2.36	0.48	11.73
Soy	class 1≤	29.41% (5/17)	6.25% (1/16)	0.115	6.25	0.64	60.94
Dog dander	class 1≤	29.41% (5/17)	20.00% (3/15)	0.541	1.67	0.32	8.59
Cat dander	class 1≤	11.76% (2/17)	13.33% (2/15)	0.894	0.87	0.11	7.05
<i>Dermatophagoides farinae</i>	class 1≤	23.53% (4/17)	18.75% (3/16)	0.738	1.33	0.25	7.17
House-dust 1	class 1≤	35.29% (6/17)	18.75% (3/16)	0.293	2.36	0.48	11.73

*Significant in univariate logistic regression analysis.

AD = atopic dermatitis; CI = confidence interval; OR = odds ratio.

tive immune responses.²² Although there was no significant difference in the CD56/CD16% of cord blood between the persistent and transient groups, the mean value of the persistent group is 1.5 times higher than that of the transient group. Hence, NK cells of cord blood may play some important role, but the role of NK cells of cord blood remains to be elucidated.

Elevated serum IgE levels were considered to be associated with AD. However, the predictability of future allergic disease by serum total IgE or specific IgE is still unclear. Our results showed that total IgE at 6 months of age was elevated in the persistent group and positive for egg white-specific IgE at 6 months was the risk for the persistent group.

We compared the usefulness of the CD8% of cord blood and total IgE at 6 months of age. The ROC analysis showed that the CD8% of cord blood is better for predicting the outcome of infantile AD. Because many cases of infantile AD occur during the first 6

months of life, it is difficult to take cord blood when the patient is diagnosed as having AD. In contrast, total IgE is an important factor for diagnosing AD^{23,24} and is ordinarily used to diagnose the disease at ~6 months of age. Thus, we concluded that total IgE at 6 months of age is the most useful factor for predicting the outcome of infantile AD.

IgE food sensitization is also closely associated with atopic eczema in infancy.^{25,26} Our results showed that total IgE, percentages of Th2 cells, and PHA-induced IL-4 production from PBMCs at 14 months of age were elevated in the persistent group, and positive for egg white-specific and cow's milk-specific IgE were the risks for the persistent group. IL-4 induces polarization to the Th2 phenotype as well as the isotype switch from IgM to IgE synthesis by B lymphocytes.^{27,28} Therefore, this result showed that patients of the persistent group were polarized to Th2 and their production of IgE increased.

Th2 cells or PHA-induced IL-4 production from PB-MCs at 14 months of age were elevated in the persistent group. Several studies have reported that naïve T cells, which make up most of the cord blood, develop into memory T cells with increasing age.^{29,30} We previously reported that the Th1, Th2, Tc1, and Tc2 of cord blood are very low and that Th2 polarization in allergic subjects becomes obvious with increasing age.¹⁸ Our present study showed a similar tendency.

In conclusion, total IgE at 6 months is the most useful laboratory data for predicting the outcome of infantile AD. The CD8⁺ cells of cord blood are also important laboratory data for predicting the outcome of infantile AD. According to our results, there were two risk factors for the persistence of AD to 14 months of age: (1) >13 IU/mL of total IgE and (2) being positive for egg white-specific IgE at 6 months of age and it was confirmed that these subjects were polarized to Th2.

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