

Correlation of Serum Total IgE, Eosinophil Granule Cationic Proteins, Sensitized Allergens and Family Aggregation in Atopic Dermatitis Patients with or without Rhinitis

Chih-Hung Lee¹, Hung-Yi Chuang², Chia-Chi Shih¹, Shiou-Hwa Jee³,
Li-Fang Wang³, Hsien-Ching Chiu³, Chung-Hsing Chang¹,
Chieh-Shan Wu¹ and Hsin-Su Yu^{1,3}

Abstract

Atopic dermatitis (AD) is a complex disease with both a genetic background and environmental interactions. Although multiple linkage-analyses about AD have been studied, there have been only a few family aggregation tests of AD or perennial allergic rhinitis (AR) to date. The association of allergen-specific IgE in AD and atopic dermatitis with allergic perennial rhinitis (ADR) have also been seldom discussed. The purpose of this study was to evaluate family aggregation and assess allergen-specific IgE in patients with AD and ADR. We also planned to investigate the effect of family history of AD on the prevalence of allergen-specific antibodies. The serum levels of IgE, eosinophil cationic protein (ECP) and major basic protein (MBP) were measured and compared in patients with AD and those with ADR. Proportional analysis compared allergen-specific IgE between AD and ADR. The family aggregation was conducted to estimate the odds ratio for various atopic diseases in different family members. Total IgE and allergen-specific antibodies in serum were compared between those patients who had AD with AR and those without. The result revealed that allergic rhinitis is the most common concomitant atopic disease associated with AD. The ADR group was more likely to have serum mite-, cockroach-, and feather-specific IgE. The positive rates for wheat, peanut and soybean were higher in those AD without rhinitis. In the family aggregation of AD, the odds ratio for siblings was higher than for parents, the ratios for brother and sister were 9.91 and 8.75, respectively. However, the odds ratio for parents of ADR was higher than siblings; the ratios for father and mother of ADR were 8.22 and 2.94, respectively. AD patients with family histories of AD were more likely to have mite-, soybean-, and peanut-specific antibodies in their serum. We concluded that aeroallergens are the most important allergens aggravating atopic diseases in Taiwan. Food plays an important role in the pathogenesis of AD. Measurement of serum total IgE combined with the MAST-CLA test could be helpful in the diagnosis of atopic diseases. The differential aggregation tendency for AD and ADR implicated the complexity of the gene-environment interaction in these atopic diseases.

Key words: atopic dermatitis; allergic rhinitis; family aggregation; allergen-specific IgE

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¹Department of Dermatology, Kaohsiung Medical University, Kaohsiung, Taiwan.

²Department of Occupational and Environmental Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

³Department of Dermatology, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan.

Reprint requests to: Dr. Hsin-Su Yu, No 7, Chung-Hsan South Road, Department of Dermatology, National Taiwan University Hospital, National Taiwan University College of Medicine, Taipei, Taiwan.

Introduction

Atopic dermatitis (AD) is a common inflammatory skin disease that belongs, along with allergic asthma and allergic rhinitis, to the group of atopic disease. The serum level of IgE has been reported to be closely related to the clinical severity of atopic disease (asthma, allergic rhinitis, and atopic dermatitis). However, allergen-specific IgE plays an even more crucial role in the patho-

genesis of atopic diseases (1). The level of allergen-specific IgE may reflect the disease activity of atopy (2). It is well established that the pathophysiology of atopic diseases is characterized by tissue inflammation because eosinophils are chemoattracted to the sites of inflammation (3). Previous studies have demonstrated that the number of eosinophils is increased in blood and tissue in patients with atopic diseases (4, 5). Major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil peroxidase (EPO) and eosinophil-derived neurotoxin (EDN) are four major cytoplasmic cationic proteins in eosinophils (6). MBP constitutes 50% of the total granule protein of the eosinophil (7). ECP and MBP are important eosinophil effective proteins in atopic diseases. The findings that MBP and ECP are increased in the serum of atopic patients implied they are involved in tissue damage in atopic diseases (8–10). Morita reported a significant correlation between serum MBP and clinical score in AD and suggested that MBP is a potential marker for disease activity (9). Compared to the research on bronchial asthma, that on perennial allergic rhinitis is relatively rare. Furthermore, the occurrences of allergen-specific antibodies in perennial allergic rhinitis (AR) combined with AD have seldom been investigated. This study was undertaken to further investigate the prevalence rates of these allergen-specific antibodies in each category of the disease.

The genetic predisposition to the development of AD has been confirmed by numerous epidemiological studies. The inheritance pattern of atopic disease is complex and does not follow simple Mendelian inheritance patterns (11). Multiple genes and environmental factors are implicated. The incidence of atopic disease is rising in both Western and Eastern countries. One current hypothesis proposes that changes in environmental factors have favored the expression of allergic disease in those who are genetically susceptible (12). Many genetic linkage studies had been performed and re-

viewed by Diepgen and Fartasch (13). However, there have been few family aggregation tests of AD to date, especially in Oriental countries. The aggregation tendencies between the family members, such as parents and siblings, may differ in each AD group with or without other concomitant perennial allergic rhinitis. These are reasons why we do family aggregation tests in these atopic diseases. When we combined the total serum IgE and allergen-specific antibody with family aggregation, we were interested in whether those AD patients with family histories of AD have higher serum IgE or allergen-specific antibodies than those without.

Materials and Methods

Patients

Patients who fitted Hanifin and Rajka's criteria for AD (14) were enrolled in this study. Diagnostic criteria for allergic perennial rhinitis included itching, sneezing, discharge and blockage of the nose (15) without vasomotor rhinitis (16) or any other known associated disease. The rhinitis symptoms were not seasonal. Seventy-two patients with AD (40 males and 32 females, mean age 17.2 years, range 1–68 years) and 152 patients with AD and contaminant perennial rhinitis (ADR) (75 males and 77 females, mean age 19.3 years, range 2–53 years) were collected from a outpatient clinic of dermatology (a total of 224 AD patients with or without perennial allergic rhinitis).

Personal and Family History of Atopic Disease

Among the 224 AD patients, 200 patients finished the complete interview with physicians that covered the personal and family histories of atopic disease. Individuals who had AD with or without concomitant bronchial asthma, perennial allergic rhinitis, or allergic conjunctivitis were selected by the physicians. The atopic diseases, including perennial allergic rhinitis, conjunctivitis, asthma and AD, among the family members were also obtained by physicians, based on a standard questionnaire in the outpatient department. The patients and their families were familiar with these atopic diseases be-

Table 1. The Levels of serological parameters in the AD and ADR groups

	Total IgE (IU/ml)	MBP (mg/ml)	ECP (μ g/L)	Age (years)
NC	<100	456.0 $\pm$ 123.1	<18	17.2 $\pm$ 24.3
AD	1,100.9 $\pm$ 1,264.9* (N=72)	1,117.1 $\pm$ 660* (N=10)	17.6 $\pm$ 16.8 (N=71)	17.2 $\pm$ 15.5 (N=72)
ADR	1,707.4 $\pm$ 4,246.4* (N=152)	1,077.0 $\pm$ 566.2* (N=17)	23.0 $\pm$ 24.1* (N=130)	19.3 $\pm$ 10.4 (N=152)

Values in parentheses represent the numbers of cases.

*: Compared to normal controls, $p < 0.05$, ANOVA with Scheffe's test

cause they had been in patient-family support groups and were well educated about the facts of these allergic diseases.

Serum Total IgE Measurement

Ten milliliters of venous blood sample were allowed to clot at room temperature. Serum was collected within two hours and was stored at -25°C until use. Serum concentration of total IgE was measured by IMMULITE[®] Total IgE kit (DPC, Los Angeles, CA) according to the manufacturer's instructions. IMMULITE[®] Total IgE kit is a solid-phase, two-site chemiluminescent enzyme immunometric assay. The intra- and inter-assay coefficients of variation were 5.3% and 5.9%, respectively. The cut-off value for positive result in this kit was set at 100 IU/ml.

MAST-CLA Assay

The MAST[®]-CLA[®] allergen-specific IgE Assay (MAST Immunosystem, Inc, Mountain View, CA) is an *in vitro* test for the semiquantitative determination of circulating allergen-specific IgE concentrations in human serum. The sensitized allergens were determined according to the manufacturer's specification. The intensity of the result was determined by a densitometer scored semiquantitative from 0–4 plus. The result was assumed to be positive when the score was ≥ 2 .

Major Basic Protein Assessment

Our serum samples were entrusted to Dr. Gleich (Allergic Diseases Research Laboratory, Mayo Clinic, Rochester, MN) for measurement of MBP by radioimmunoassay using two different monoclonal antibodies against MBP.

Eosinophil Cationic Protein Measurement

ECP was measured in serum samples by a solid-phase, two-site chemiluminescent enzyme immunometric assay (DPC, Los Angeles, CA) according to the manufacturer's instructions. The intra- and inter assay coefficients of variation were 4.2% and 8.1%, respectively. The normal range of serum ECP is less than 18 ng/L.

Statistical Analysis

Results were expressed as mean $\pm$ SD, unless otherwise indicated. The Student t test was used to analyze differences of IgE, MBP, and ECP among groups. Atopy family aggregation was estimated by the generalized estimation equation (GEE) with adjustment of gender and age in different atopic diseases (17, 18). The two sample test of proportion analysis was applied to the allergen-specific IgE by various atopic diseases in these AD patients. (SAS 6.12, PROC GENMOD) Mann-Whitney test was utilized to compare the differences of the MAST values between the AD and ADR groups. Logistic regression analysis was performed to estimate the influence of some allergen-specific IgEs, including mites, soybeans, and peanuts, on the family history of AD. A p-value of less than 0.05 was considered statistically significant.

Results

Comparison of total serum IgE, MBP and ECP among control, AD and ADR groups

These values are listed in Table 1. The IgE levels in serum were 1100.9 ± 1264.9 IU/ml and 1707.4 ± 4246.4 IU/ml in the AD (range 13–15,800 IU/ml) and ADR groups (range 15–33,875 IU/ml), respectively. IgE

Table 2.

(a) Positive rates (%) of allergen-specific IgE and proportional analysis between AD and ADR groups

Allergen/Group	AD (N=57) (%)	Mean MAST score	ADR (N=141) (%)	Mean MAST score
Housedust**	33 (19/57)	1.15	59 (83/141)	2.13
Mite (D.F.)***	54 (31/57)	1.94	83 (117/141)	3.30
Mite (D.P.)***	56 (32/57)	2.00	83 (117/141)	3.32
Cockroach mix***	32 (18/57)	0.79	69 (97/141)	1.49
Feather mix*	19 (10/57)	0.47	36 (51/141)	0.87
Dog dander*	2 (1/57)	0.16	11 (16/141)	0.75
Cat dander	2 (1/57)	0.13	6 (9/141)	0.15
Candida	6 (3/57)	0.33	6 (8/141)	0.16
Aspergillus	4 (2/57)	0.12	6 (9/141)	0.15
Cladosporum	6 (3/57)	0.33	1 (1/141)	0.31
Penicillium	11 (6/57)	0.51	4 (5/141)	0.37
Alterana	4 (2/57)	0.06	4 (5/141)	0.10
Ragweed mix	9 (5/57)	0.45	3 (4/141)	0.27
Grass	11 (6/57)	0.57	4 (5/141)	0.29
Pine	0 (0/57)	0.00	0 (0/141)	0.00
Cotton	0 (0/57)	0.00	2 (3/141)	0.05
Eucalyptus	0 (0/57)	0.00	0 (0/141)	0.00
Mulberry	0 (0/57)	0.00	2 (3/141)	0.04
Bermuda grass	6 (3/57)	0.45	2 (3/141)	0.29
Pigweed mix	9 (5/57)	0.36	3 (4/141)	0.16
Corn	7 (4/57)	0.24	1 (2/141)	0.13
Wheat***	19 (10/57)	0.77	4 (5/141)	0.39
Vegetable mix	13 (7/57)	0.24	4 (6/141)	0.35
Crab	13 (7/57)	0.66	22 (31/141)	0.66
Clam	11 (6/57)	0.36	19 (27/141)	0.40
Shellfish mix	2 (1/57)	0.12	4 (6/141)	0.33
Pork	2 (1/57)	0.12	6 (8/141)	0.16
Beef	2 (1/57)	0.05	5 (7/141)	0.22
Egg white	9 (5/57)	0.26	4 (6/141)	0.15
Egg yolk	2 (1/57)	0.13	4 (5/141)	0.14
Milk	11 (6/57)	0.36	22 (31/141)	0.66
Shrimp	20 (11/57)	0.42	29 (41/141)	0.64
Yeast	4 (2/57)	0.18	4 (6/141)	0.18
Soybean**	19 (10/57)	0.89	5 (7/141)	0.51
Peanut***	15 (8/57)	0.91	2 (3/141)	0.47

**p<0.01, *p<0.05 using proportional analysis of MAST test by the AD and ADR groups.

***p<0.01, #p<0.05 using Mann-Whitney test to compare the MAST values between the AD and ADR groups.

(b) Numbers of patients with different MAST scores of wheat, soybean, and peanut in the AD and ADR groups.

MAST score	Wheat		Soybean		Peanut	
	AD	ADR	AD	ADR	AD	ADR
0	30	95	26	88	24	79
1	17	41	21	44	25	59
2	5	2	3	2	1	2
3	3	2	4	3	3	1
4	2	1	3	4	4	0
Mean MAST score	0.77	0.39	0.89	0.51	0.91	0.47
P (Chi-square test for trend)	<0.01		0.01		<0.01	

There are statistical differences of wheat-, soybean-, and peanut-specific IgE between the AD and ADR groups (Chi-square test for trends).

Table 3. Numbers and percentages of coexistent allergic rhinitis in AD patients, parents, and siblings

	AD patients	Father	Mother	Elder brother	Younger brother	Elder sister	Younger sister
Total AD (AD+ADR)	200 (100%)	25 (12.5%)	13 (6.5%)	7 (13%)	14 (21%)	9 (10%)	14 (19%)
ADR	112 (56%)	51 (25.5%)	41 (20.5%)	16 (27.6%)	17 (25%)	19 (21%)	13 (17%)
N*	200	200	200	54	67	90	75

*N indicates the total number of patients, parents, or siblings that have atopic dermatitis (AD), including atopic dermatitis with allergic rhinitis (ADR).

Table 4. Family aggergation (196 family numbers) estimated by the generalized estimation equation (GEE) with adjustment of gender and age by AD and ADR

		Odds ratio (95% CI)	P value
AD	Father	1.22 (0.33– 4.48)	0.760
	Mother	4.39 (1.37–14.02)	0.013
	Brother	9.91 (3.68–26.71)	<0.001
	Sister	8.75 (3.33–23.02)	<0.001
ADR	Father	8.22 (5.10–13.26)	<0.001
	Mother	2.94 (1.36– 6.34)	0.006
	Brother	2.41 (1.36– 4.26)	0.003
	Sister	6.33 (3.90–10.27)	<0.001

level in both groups was elevated significantly as compared to that in normal controls ($P < 0.05$). The serum MBP levels were $1,117.1 \pm 660.0$ mg/ml and $1,077.0 \pm 566.2$ mg/ml in the AD (range 523–2,642 mg/ml) and ADR groups (range 498–2,341 mg/ml), respectively. The MBP levels in both groups were also elevated significantly as compared to that in normal controls ($p < 0.05$). The serum ECP levels was significantly elevated ($p < 0.05$) in the ADR (23.0 ± 24.1 μ g/L, range 1–198 μ g/L) group over that in the control group (< 18 μ g/L). No significant age differences were noticed between the AD (17.2 ± 15.5 y/o) and the ADR groups (19.3 ± 10.4 y/o).

Positive rate of different allergens in AD and ADR by MAST-CLA test

The specific allergens in AD and ADR groups measured by MAST-CLA allergen test system are listed in Table 2. Patients with ADR had higher positive rates of aeroallergen-specific IgEs to housedust (59% vs 33%), mite (D.F.) (83% vs 54%), mite (D.P.) (83% vs 56%), cockroach (69% vs 32%), and feather (36% vs 19%) than patients with AD ($p < 0.01$). In addition, the MAST score was statistically higher in the ADR group than in the AD group, including housedust-, mite (D.F.)-, mite (D.P.)-, and cockroach-specific IgE ($p < 0.05$). However, patients with AD had higher positive rates to food allergens than those with ADR, especially for wheat (19% vs 4%), peanut (15% vs 2%), and soybean (19% vs 5%) ($p < 0.05$). The mean MAST score of wheat-specific IgE was statistically increased in the AD group

Table 5. Total serum IgE level and prevalence rate of specific-IgE grouped by AD/ADR and positive/negative family history

	AD		ADR	
Family history (AD)	Yes	No	Yes	No
No	20	37	102	39
IgE (IU/ml)	1,143±1,356	1,086±1,723	1,689±4,239	1,826±5,343
Housedust (No/%)	8 (40%)	11 (31%)	73 (72%)	29 (77%)
Mite (D.F.)	15 (75%)*	16 (43%)	82 (80%)	35 (89%)
Mite (D.P.)	16 (80%)*	16 (43%)	82 (80%)	34 (89%)
Cockroach	7 (35%)	11 (29%)	59 (68%)	38 (72%)
Wheat	6 (30%)	4 (11%)	2 (2%)	3 (8%)
Soybean	7 (35%)*	3 (8%)	3 (3%)	4 (10%)
Peanut	6 (30%)*	2 (5%)	2 (2%)	1 (3%)

*denotes $p < 0.05$ between the groups with or without family history

Table 6. Logistic regression of AD patients with or without family history by the presence of mite (D.F.)-, mite (D.P.)-, soybean-, and peanut-specific IgE in their sera

Factors	Estimated β	S.E.	Odds Ratio	95% Confidence level	
Mite (D.F.)	0.106	1.556	1.112	0.053	23.459
Mite (D.P.)	0.311	1.468	1.365	0.077	24.252
Soybean	1.355	0.640	3.878*	1.105	13.607
Peanut	1.43	0.826	4.174	0.827	21.074
Intercept	0.026	0.565	1.026		

*denotes $p < 0.05$ between the groups with or without family history. The AD patients with the presence of soybean-specific antibody in their sera were 3.878-fold more likely than those without to have a family history of A.D.

(0.77) over that in the ADR group (0.39) ($p < 0.01$). The mean MAST score of soybean-specific IgE was statistically increased in the AD group (0.89) over that in the ADR group (0.51) ($p < 0.01$). The mean MAST score of peanut-specific IgE was statistically increased in the AD group (0.91) over that in the ADR group (0.47) ($p < 0.01$). Chi-square test for trends also revealed the statistical differences of Mast score of wheat ($p < 0.01$), soybean- ($p = 0.01$), and peanut-specific IgE ($p < 0.01$) between the AD and ADR groups (Table 2b). Finally, the prevalence of specific IgE towards seafood, including crab, clam, shrimp and shellfish did not show significant differences between AD and ADR groups.

Family aggregation estimation

There were 196 families and 200 AD patients enrolled in the family aggregation test. The age distribution was 12.2 ± 7.4 years (mean $\pm$ S.D.). The AD patients tended to have concomitant allergic rhinitis (56%), asthma (27.5%), or conjunctivitis (24.5%). Allergic rhinitis was the most common concomitant allergic disorder among these AD patients (Table 3). Among these 200 AD patients, 25 of their fathers (12.5%) had AD; 13 (6.5%) mothers had AD; 7 elder brothers (13% in 54) had AD; 14 younger brothers (21% in 67) had AD; 9 elder sisters (10% in 90) had AD; and 14 younger sisters (19% in 75) had AD. Among the 112 patients with ADR, 51 of their fathers (25.5%)

had AD; 41 (20.5%) mothers had AD; 16 elder brothers (27.6% in 54) had AD; 17 younger brothers (25% in 67) had AD; 19 elder sisters (21% in 90) had AD; and 14 younger sisters (19% in 75) had AD (Table 3).

We found (Table 4) nine times the family aggregation among siblings of atopic dermatitis as compared to normal controls (OR 9.91 and 8.75 for brothers and sisters, respectively). Among the ADR group, apparent aggregations were shown in all family members ($p < 0.01$), including father (OR 8.22), mother (OR 2.94), brother (OR 2.41) and sister (OR 6.33). Paternal preponderance was most evident in the ADR group (OR 8.22, 95% CI=5.10–13.26) while maternal preponderance was most prominent in the AD group (OR 8.22, 95% CI=5.10–13.26) as compared to that in other groups.

Effect of AD family history on IgE and allergen-specific IgE in AD (Table 5, 6)

As in Table 2, we found that housedust-, mite-, and cockroach-specific IgE was more prevalent in the ADR than in the AD group, but that wheat-, soybean-, and peanut-specific IgE was less frequent in ADR than in AD. Thus we became interested in whether the family history of AD would influence the distribution of allergen-specific IgE. Therefore, 198 patients were stratified into AD (N=57) and ADR (N=141) groups. These patients were further divided by the factor of a family history of AD. The numbers of AD with family history, AD without family history, ADR with family history, and ADR without family history were 20, 37, 102, and 39, respectively. Family history of AD made a greater impact in allergen-specific IgE in AD than in ADR. In the ADR group, there were no statistical differences in any allergen-specific IgE between those with or without family histories of AD. However, in the AD group, mite-, soybean-, and peanut-specific IgE was more prevalent in AD with family history than in those without. Total IgE, as might be expected, was not affected by family history of atopy (Table 5). For multi-

ple factors analysis rather than single factor analysis, we performed a logistic regression to estimate the contributions of mite-, soybean-, and peanut-specific IgE to the family history of AD in AD patients. The only significant factor was soybean-specific IgE, that had an odds ratio equal to 3.878. The odds ratios for mite (D.F.), mite (D.P.), and peanut were 1.112, 1.365, and 4.174, which did not reach statistical significance (Table 6).

Discussion

Serum IgE, eosinophil, and allergen-specific IgE are believed to play critical roles in the pathogenesis of atopic disease. Several research papers have reported that higher serum levels of total IgE, MBP, ECP and eosinophilia were present in patients with AD (7, 19, 20). In this study, more than half of the AD patients had concomitant allergic rhinitis (Table 3). AD with or without allergic rhinitis may present as separate entities. Our result, demonstrated that there were no significant differences between patients with AD and patients with ADR with regard to the serum IgE levels or age distribution (Table 1). This result suggested that the total serum IgE level was not merely influenced by single or overlapping atopic diseases.

Allergen-specific IgE undoubtedly plays a specific role in the pathogenesis of atopic disease (1). Total serum IgE is the summation of different sorts of allergen-specific IgE and is not thought to linearly correlate with the severity of atopic diseases (1). Furthermore, allergen-specific IgE is thought to be closely related to recent disease activity in atopic diseases (2). A significant association between the severity score of AD and the concentration of allergen-specific IgE to dust mites and cats was demonstrated by Schafer and colleagues (21). Many studies have demonstrated that the MAST-CLA® allergen test system provides an equal efficiency compared with skin test and radioallergen sorbent test (RAST) in the evaluation of sensitized allergens in atopic patients

(22–24). AD patients with concomitant perennial allergic rhinitis are more likely to have specific antibodies to mites, housedust, cockroaches, and feathers (Table 2). This reflects the fact that AD patients with concomitant perennial allergic rhinitis are more likely to have higher serum IgE levels, as in our study (Table 1), because the level of allergen-specific IgE is in proportion to total serum IgE levels (25). These aeroallergens become the most important indoor allergens in causing or aggravating the combined form of atopic disease (ADR) in Taiwan. Another important finding from our study was higher positive rates of wheat-, peanut-, and soybean-specific IgEs among the patients with AD than those with ADR. These allergens may be closely related to hypersensitivity in AD in Taiwan. These data suggest that the combination of serum total IgE level and MAST-CLA tests are useful in the diagnosis of atopic diseases.

MBP and ECP are major cytotoxic proteins released from activated eosinophils in inflammation (20–26). Both of them may reflect the disease activity of atopic diseases through damage to cells. For example, MBP can induce hyperactivity of bronchial smooth muscles and provoke cutaneous inflammatory reactions in human skin (27). The serum ECP level is useful as an inflammatory marker in asthma (10, 28). In our study, the serum levels of MBP and ECP were not significantly different between patients with AD and patients with ADR (Table 1). Nevertheless, the serum MBP, but not the ECP level in both groups, was obviously higher than that in normal controls. These results indicated that serum MBP may be more relevant to atopic disease than serum ECP and suggested the possibility of an active participation of eosinophils in the pathogenesis of AD and ADR (29). They also implied that the release of eosinophil proteins in patients with AD and patients with ADR may be through identical pathways.

A family or personal history of atopic diseases is an important feature in atopic der-

matitis, allergic conjunctivitis, asthma, and perennial allergic rhinitis. The study of complex genetic illness demands accurate definitions of the phenotypes being investigated. The clinical definitions of atopic disease need to encompass the wide variation of disease expression that exists among individuals. Furthermore, the heterogeneity of these subsets of atopic diseases can complicate the genetic epidemiology of individual atopic diseases. Different approaches including population studies, family aggregation and twin studies have been done to study the roles of genetic factors in the development of allergic disease (13). In a molecular base, both genome-wide scans and candidate region approaches were studied extensively. Linkage analysis has discovered several loci that contribute to the expression of AD (3q21, 5q31–33, 11q13, 13q12–14, 14q11.2, etc.) (13).

The use of estimation equation, an alternative to traditional maximum likelihood analysis, had been advocated for analyzing correlated data, such as family data (30). In the study of family aggregation of AD estimated by Diepgen and Blettner (11), analyses within the members of the family showed a high OR among siblings (OR=3.86; 95%-CI 2.10–7.09), while the OR between parents and siblings was only 1.90 (95%-CI 1.31–2.97). Our results were consistent with this study with OR 9.91 and 8.75 in brothers and sisters, respectively. The maternal preponderance of AD, present in our study (Table 6), was also demonstrated in Bradley's study (12). Among patients with one parent with AD, 37% had a father with AD and 63% had a mother with AD (12). This can be explained by stronger maternal heritability, shared physical environment of mother and child, or environmental events that affect the fetus in utero. In our study, the family aggregation was evident in all fathers, mothers, and siblings in the ADR group as compared to the group of AD with or without other concomitant allergic diseases.

The influence of family history of AD on

distribution of allergen-specific IgE in AD has seldom been discussed previously. The fact we did find that mite-, peanut-, and soybean-specific IgE is more likely to appear in AD patients with family histories of AD than those without (Table 5) is far more interesting. These allergens, apart from the likelihood of enhanced production of specific IgE, may also be related to family aggregation. These data further demonstrated the complexity of AD and atopic diseases in family aggregation, genetic background, and environmental effects. The differential pattern of family aggregation among the AD and ADR groups reveals the complexity of the gene-environment interactions involved. Furthermore, the incidence of atopic disease is increasing in both Western and Eastern countries. Environmental factors, including differential serum allergen-specific IgE in the AD and ADR groups, seem to be related to the differential pattern of family aggregation in the AD and ADR groups and the recently increasing prevalence of atopic diseases in Taiwan.

In conclusion, four original observations are made in the present study. First, the aeroallergens are most important allergens causing and aggravating atopic disease, although food allergens may play a relevant role in the pathogenesis of AD in Taiwan. Second, the measurement of serum total IgE combined with MAST-CLA test is helpful in the diagnosis of atopic diseases. Third, although the tendency of aggregation in atopic dermatitis is higher among siblings than parents, that in atopic dermatitis with concomitant allergic rhinitis (ADR) is similarly high among parents and siblings. Fourth, the family history of AD affected the distribution of some allergen specific IgEs in the serum of AD patients. The differential pattern of family aggregation tests and allergen-specific IgEs in AD and ADR patients suggests that environmental factors are only one of the components in the complexity of atopic diseases.

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