

Risk Factors for Wheezing, Eczema and Rhinoconjunctivitis in the Previous 12 Months among Six-Year-Old Children in Himeji City, Japan: Food Allergy, Older Siblings, Day-Care Attendance and Parental Allergy History

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ABSTRACT

Background: The aim of this study was to clarify whether some environmental and genetic factors (food allergy, older siblings, early day-care attendance and parents' allergy history) are related to the development of allergic symptoms (wheezing in the previous 12 months [WP], eczema symptoms in the previous 12 months [EP], and rhinoconjunctivitis symptoms in the previous 12 months [RP]) in Japanese children.

Methods: Using the modified version of the International Study on Asthma and Allergies in Childhood (ISSAC) questionnaire, we studied the prevalence of WP, EP and RP among six-year-old children attending 72 primary schools throughout Himeji City, Japan, during the two years from 2005 to 2006.

Results: Food allergy and parents' history of allergy showed a significant relationship with the prevalence of WP, EP and RP. Day-care attendance in the first two years of life and presence of older siblings showed a significant inverse relationship with the prevalence of RP. However, neither day-care attendance nor presence of older siblings was related to the development of W and ER.

Conclusions: Among Japanese children, food allergy and parents' history of allergy are risk factors for WP, ES or RS. However, early day-care attendance and presence of older siblings might be protective factors against RS. Infections in early life may affect the prevalence of rhinoconjunctivitis in six-year-old children.

KEY WORDS

day-care, food allergy, hygiene hypothesis, older siblings, rhinoconjunctivitis

INTRODUCTION

Environmental factors do not always pose a risk for

the development of allergic diseases. Some circumstantial conditions related to the environment of children, such as the presence of older siblings, early

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Table 1A The questionnaire for asthma, eczema and rhinoconjunctivitis[†]

- (1) For asthma, the relevant questions were as follows: Have you (has your child) had wheezing or whistling in the chest in the last 12 months? (yes /no).
- (2) For eczema, the relevant questions were as follows: Have you (has your child) ever had an itchy rash which was coming and going for at least 6 months? (yes/no); Has your child had this itchy rash at any time in the last 12 months? (yes/no). Has this itchy rash at any time affected any of the following places: the folds of the elbows, behind the knees, in front of the ankles, under the buttocks, or around the neck, ears, or eyes? (Yes/no).
- (3) For rhinoconjunctivitis, the relevant questions were as follows: In the last 12 months, have you (has your child) had a problem with sneezing or a running or blocked nose when you (he/she) did not have a cold or flu? (yes/no); In the past 12 months, has this nose problem been accompanied by itchy watery eyes? (yes/no).

[†]The actual questionnaire was asked in Japanese.

Table 1B The questionnaire for food allergy, animal allergy, siblings, attending the day-care and parental allergy[†]

- (1) Did the child experience allergy due to egg, cow's milk, wheat, buckwheat, crab and other foods that the parents reported?
- (2) Did the family keep animals with fur (dog, cat, hamster, rodent and bird) in the house? Since what age of the child did the family start to keep such animals?
- (3) Did the child have older siblings?
- (4) When did the child start to attend the day-care?
- (5) Did the parent(s) suffer from allergic diseases such as asthma, eczema, allergic rhinitis, allergic conjunctivitis, pollinosis and urticaria?

[†]The actual questionnaire was asked in Japanese.

day-care attendance, and lower than normal hygiene, may prevent the appearance of allergic diseases. In 1989, Strachan proposed a novel and speculative explanation for the increasing prevalence of hay fever in the United Kingdom.¹ He found that the increasing trend for smaller numbers of children in families was related to the prevalence of hay fever, and proposed that allergic diseases could be prevented by infection in early childhood (the "hygiene hypothesis").

Several epidemiological studies of the environmental factors related to allergic diseases have been published in Japan.²⁻⁷ We have reported an inverse relationship between current cat ownership and prevalence of allergic rhinitis among children in Himeji City.³ We have also shown that passive smoking is related to a significantly lower prevalence of allergic rhinitis.³ Recently, Ohfuji *et al.*⁷ reported an epidemiological study conducted among children aged 6-15 years in Okinawa. They demonstrated an inverse relationship between sibship size (especially the presence of older siblings) and the prevalence of allergic disorders.

With respect to the risk factors for allergic disorders among children, food sensitivity and/or genetic predisposition should also be considered, as well as environmental conditions. Some foods (e.g., egg, cow's milk, etc.) may cause allergic diseases, including not only food allergy but also eczema, asthma and rhinoconjunctivitis, in individuals who have sensitivity. Food sensitivity or food allergy may be closely associated with the development of different allergic diseases, and genetic factors also play a considerable role. Studies of family history also suggest that aller-

gic diseases (or allergic predispositions) in some patients are inherited from the parents.⁸

In this study, to clarify the relationship between environmental factors (parent-reported food allergy, older siblings, day-care attendance) and allergic symptoms (wheezing in the previous 12 months [WP], eczema symptoms in the previous 12 months [EP], and rhinoconjunctivitis symptoms in the previous 12 months [RP]), and the relationship between genetic factors (parents' allergy history) and allergic diseases (WP, EP and RP), we studied the prevalence of allergic symptoms (WP, EP and RP) among six-year-old children attending primary schools in Himeji City, Japan, during the two years from 2005 to 2006.

METHODS

Using the International Study on Asthma and Allergies in Childhood (ISSAC) questionnaire,⁹ we studied the epidemiology of allergic symptoms in six-year-old children attending primary schools throughout Himeji City, Japan, during a two-year period from 2005 to 2006. Himeji City, situated close to the Seto Inland Sea, has a population of about 530,000. The southern area of the city is industrial, with steel manufacture predominating, the central area is urban with a large population, and the northern area is rural with farmlands.

The questionnaires were distributed by teachers to 11,150 families, and received 11,116 responses, of which 11,116 (99.6%) were fully complete. The presence or absence of allergic symptoms in the children was determined from the answers to the disease-relevant questions.

Risk Factors for Allergic Diseases

Table 2 Risk factors for wheezing in the previous 12 months (WP) with unadjusted and adjusted odds ratios

	Total	WP	Prevalence(%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	10737	1061	9.9		1.00			1.00	
Yes	252	74	29.4	<i>p</i> < 0.001	3.79	2.87-5.01	<i>p</i> < 0.001	2.89	2.16-3.88
Cow's milk allergy									
No	10918	1113	10.2		1.00				
Yes	71	22	31.0	<i>p</i> < 0.001	3.96	2.38-6.57			
Buckwheat allergy									
No	10927	1118	10.2		1.00				
Yes	62	17	27.4	<i>p</i> < 0.001	3.32	1.89-5.81			
Crab allergy									
No	10912	1119	10.3		1.00				
Yes	77	16	20.8	0.003	2.30	1.32-4.00			
Wheat allergy									
No	10976	1131	10.3		1.00				
Yes	13	4	30.8	0.025	3.87	1.19-12.58			
Parental allergy									
No	3607	244	6.8		1.00			1.00	
Father or Mother	4529	504	11.1	<i>p</i> < 0.001	1.73	1.47-2.02	0.026	1.23	1.03-1.47
Parent	2875	392	13.6	<i>p</i> < 0.001	2.18	1.84-2.57	0.448	1.09	0.87-1.36
Parental asthma									
No	9538	827	8.7		1.00			1.00	
Father or Mother	1387	273	19.7	<i>p</i> < 0.001	2.58	2.22-3.00	<i>p</i> < 0.001	2.12	1.80-2.50
Parent	86	40	46.5	<i>p</i> < 0.001	9.16	5.96-14.08	<i>p</i> < 0.001	8.02	5.09-12.65
Parental eczema									
No	9525	908	9.5		1.00			1.00	
Father or Mother	1389	212	15.3	<i>p</i> < 0.001	1.71	1.46-2.01	0.018	1.24	1.04-1.47
Parent	97	20	20.6	<i>p</i> < 0.001	2.47	1.50-4.05	0.184	1.45	0.84-2.53
Parental rhinitis									
No	7993	709	8.9		1.00			1.00	
Father or Mother	2556	350	13.7	<i>p</i> < 0.001	1.63	1.42-1.87	0.003	1.27	1.08-1.48
Parent	462	81	17.5	<i>p</i> < 0.001	2.18	1.70-2.81	0.005	1.52	1.14-2.03
Parental urticaria									
No	9413	909	9.7		1.00			1.00	
Father or Mother	1436	201	14.0	<i>p</i> < 0.001	1.52	1.29-1.79	0.081	1.17	0.98-1.40
Parent	162	30	18.5	<i>p</i> < 0.001	2.13	1.42-3.18	0.087	1.47	0.95-2.28
Parental pollen allergy									
No	6052	580	9.6		1.00				
Father or Mother	3788	430	11.4	0.005	1.21	1.06-1.38			
Parent	1171	130	11.1	0.111	1.18	0.96-1.44			
Parental conjunctivitis									
No	9703	942	9.7		1.00				
Father or Mother	1179	177	15.0	<i>p</i> < 0.001	1.64	1.38-1.95			
Parent	129	21	16.3	0.014	1.81	1.13-2.90			
Gender									
F	5347	441	8.2		1.00			1.00	
M	5664	699	12.3	<i>p</i> < 0.001	1.57	1.38-1.78	<i>p</i> < 0.001	1.53	1.34-1.74
Cat in room at present									
No	10399	1064	10.2		1.00				
Yes	281	33	11.7	0.410	1.17	0.81-1.69			
Dog in room at present									
No	9889	1015	10.3		1.00				
Yes	791	82	10.4	0.927	1.01	0.80-1.28			
Cat in room before one year old									
No	10528	1083	10.3		1.00				
Yes	345	38	11.0	0.662	1.08	0.77-1.52			
Dog in room before one year old									
No	10345	1055	10.2		1.00				
Yes	529	66	12.5	0.093	1.26	0.96-1.64			
Bird in room before one year old									
No	10808	1113	10.3		1.00				
Yes	66	8	12.1	0.628	1.20	0.57-2.52			
Hamster in room before one year old									
No	10737	1098	10.2		1.00			1.00	
Yes	137	23	16.8	0.013	1.77	1.13-2.78	0.078	1.53	0.95-2.45

*Crude odds ratios of food and parental allergy showed the significant variables (*p* < 0.05) without duplicate information and the others showed variable with or without significance (*p* < 0.05) by using logistic regression.

‡The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + gender + hamster in room before one year old.

Hosmer Lemeshow test; the first step* *p* = 0.358, Step 7** *p* = 0.931.

Table 3 Risk factors for eczema in the previous 12 months (EP) with unadjusted and adjusted odds ratios

	Total	EP	Prevalence(%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	10737	1434	13.4		1.00				
Yes	252	139	55.2	$p < 0.001$	7.98	6.19-10.29	$p < 0.001$	4.71	3.52-6.29
Cow's milk allergy									
No	10918	1531	14.0		1.00				
Yes	71	42	59.2	$p < 0.001$	8.88	5.52-14.30	0.002	2.45	1.39-4.32
Buckwheat allergy									
No	10927	1544	14.1		1.00				
Yes	62	29	46.8	$p < 0.001$	5.34	3.23-8.82	0.031	1.94	1.06-3.55
Crab allergy									
No	10912	1541	14.1		1.00				
Yes	77	32	41.6	$p < 0.001$	4.32	2.74-6.83	0.006	2.07	1.24-3.47
Wheat allergy									
No	10976	1563	14.2		1.00				
Yes	13	10	76.9	$p < 0.001$	20.08	5.52-73.02	0.073	3.68	0.89-15.29
Parental allergy									
No	3607	321	8.9		1.00				
Father or Mother	4529	651	14.4	$p < 0.001$	1.72	1.49-1.98	0.016	1.22	1.04-1.43
Parent	2875	606	21.1	$p < 0.001$	2.73	2.36-3.16	0.002	1.35	1.11-1.63
Parental asthma									
No	9538	1258	13.2		1.00				
Father or Mother	1387	287	20.7	$p < 0.001$	1.72	1.49-1.98	0.321	1.08	0.92-1.27
Parent	86	33	38.4	$p < 0.001$	4.10	2.64-6.36	0.001	2.26	1.39-3.68
Parental eczema									
No	9525	1121	11.8		1.00				
Father or Mother	1389	405	29.2	$p < 0.001$	3.09	2.71-3.52	$p < 0.001$	2.38	2.06-2.75
Parent	97	52	53.6	$p < 0.001$	8.66	5.78-12.97	$p < 0.001$	5.68	3.66-8.83
Parental rhinitis									
No	7993	991	12.4		1.00				
Father or Mother	2556	468	18.3	$p < 0.001$	1.58	1.40-1.79	0.049	1.15	1.01-1.32
Parent	462	119	25.8	$p < 0.001$	2.45	1.97-3.05	0.091	1.26	0.96-1.65
Parental urticaria									
No	9413	1212	12.9		1.00				
Father or Mother	1436	312	21.7	$p < 0.001$	1.88	1.63-2.16	$p < 0.001$	1.36	1.17-1.59
Parent	162	54	33.3	$p < 0.001$	3.38	2.43-4.72	$p < 0.001$	1.99	1.37-2.89
Parental pollen allergy									
No	6052	791	13.1		1.00				
Father or Mother	3788	575	15.2	0.003	1.19	1.06-1.34			
Parent	1171	212	18.1	$p < 0.001$	1.47	1.25-1.74			
Parental conjunctivitis									
No	9703	1284	13.2		1.00				
Father or Mother	1179	251	21.3	$p < 0.001$	1.77	1.52-2.06	0.039	1.20	1.01-1.42
Parent	129	43	33.3	$p < 0.001$	3.28	2.26-4.75	0.020	1.66	1.08-2.54
Cat in room at present									
No	10399	1508	14.5						
Yes	281	34	12.1	0.259	0.81	0.57-1.17			
Dog in room at present									
No	9889	1429	14.5						
Yes	791	113	14.3	0.899	0.99	0.80-1.21			
Cat in room before one year old									
No	10528	1521	14.4						
Yes	345	41	11.9	0.183	0.80	0.57-1.11			
Dog in room before one year old									
No	10345	1479	14.3						
Yes	529	83	15.7	0.373	1.12	0.88-1.42			
Bird in room before one year old									
No	10808	1546	14.3		1.00				
Yes	66	16	24.2	0.024	1.92	1.09-3.38	0.024	1.99	1.10-3.61
Older siblings									
<2	4748	718	15.1		1.00				
≥2	6035	833	13.8	0.053	0.90	0.81-1.00			

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + bird in room before one year old.

Hosmer Lemeshow test; the first step* $p = 0.372$, Step 2** $p = 0.077$.

Risk Factors for Allergic Diseases

Table 4 Risk factors for rhinoconjunctivitis in the previous 12 months (RP) with unadjusted and adjusted odds ratios

	Total	RP	Prevalence (%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	10737	1100	10.2		1.00			1.00	
Yes	252	74	29.4	$p < 0.001$	3.64	2.76-4.81	$p < 0.001$	2.68	1.96-3.67
Cow's milk allergy									
No	10918	1152	10.6		1.00			1.00	
Yes	71	22	31.0	$p < 0.001$	3.81	2.29-6.32			
Buckwheat allergy									
No	10927	1155	10.6		1.00			1.00	
Yes	62	19	30.6	$p < 0.001$	3.74	2.17-6.44	0.039	1.92	1.03-3.57
Crab allergy									
No	10912	1156	10.6		1.00			1.00	
Yes	77	18	23.4	$p < 0.001$	2.58	1.51-4.38			
Wheat allergy									
No	10976	1170	10.7		1.00			1.00	
Yes	13	4	30.8	0.029	3.73	1.15-12.12			
Parental allergy									
No	3608	140	3.9		1.00			1.00	
Father or Mother	4530	499	11.0	$p < 0.001$	3.07	2.53-3.72	$p < 0.001$	1.64	1.29b-2.09
Parent	2875	538	18.7	$p < 0.001$	5.70	4.70-6.92	0.001	1.64	1.23-2.20
Parental asthma									
No	9540	941	9.9		1.00			1.00	
Father or Mother	1387	218	15.7	$p < 0.001$	1.70	1.45-2.00			
Parent	86	18	20.9	0.001	2.42	1.43-4.08			
Parental eczema									
No	9526	929	9.8		1.00			1.00	
Father or Mother	1390	227	16.3	$p < 0.001$	1.81	1.54-2.11	0.024	1.22	1.03-1.46
Parent	97	21	21.6	$p < 0.001$	2.56	1.57-4.17	0.221	1.44	0.81-2.56
Parental rhinitis									
No	7995	580	7.3		1.00			1.00	
Father or Mother	2556	471	18.4	$p < 0.001$	2.89	2.53-3.29	$p < 0.001$	1.97	1.69-2.29
Parent	462	126	27.3	$p < 0.001$	4.79	3.84-5.98	$p < 0.001$	1.97	1.50-2.59
Parental urticaria									
No	9414	904	9.6		1.00			1.00	
Father or Mother	1437	231	16.1	$p < 0.001$	1.80	1.54-2.11	0.073	1.17	0.99-1.39
Parent	162	42	25.9	$p < 0.001$	3.30	2.30-4.71	0.008	1.73	1.15-2.59
Parental pollen allergy									
No	6054	400	6.6		1.00			1.00	
Father or Mother	3788	516	13.6	$p < 0.001$	2.23	1.94-2.56	$p < 0.001$	1.43	1.21-1.69
Parent	1171	261	22.3	$p < 0.001$	4.05	3.42-4.81	$p < 0.001$	2.29	1.780-2.92
Parental conjunctivitis									
No	9705	873	9.0		1.00			1.00	
Father or Mother	1179	249	21.1	$p < 0.001$	2.71	2.32-3.17	$p < 0.001$	1.56	1.31-1.85
Parent	129	55	42.6	$p < 0.001$	7.52	5.27-10.73	$p < 0.001$	2.78	1.87-4.14
Gender									
F	5347	532	9.9		1.00			1.00	
M	5666	645	11.4	0.015	1.16	1.03-1.31	0.064	1.13	0.99-1.29
Cat in room at present									
No	10399	1117	10.74						
Yes	281	20	7.12	0.054	0.64	0.40-1.01			
Dog in room at present									
No	9889	1062	10.74						
Yes	791	75	9.48	0.270	0.87	0.68-1.11			
Cat in room before one year old									
No	10528	1133	10.76						
Yes	345	27	7.83	0.084	0.70	0.47-1.05			
Dog in room before one year old									
No	10345	1097	10.60						
Yes	529	63	11.91	0.343	1.14	0.87-1.49			
Bird in room before one year old									
No	10808	1146	10.6		1.00			1.00	
Yes	66	14	21.2	0.007	2.27	1.25-4.11	0.027	2.06	1.09-3.92
Day-care attendance more than two years old									
No	9215	1027	11.1		1.00			1.00	
Yes	1737	143	8.2	$p < 0.001$	0.72	0.60-0.86	0.003	0.74	0.61-0.90
Older siblings more than two years old									
<2	4748	585	12.3		1.00			1.00	
≥2	6036	567	9.4	$p < 0.001$	0.74	0.65-0.83	$p < 0.001$	0.73	0.64-0.83

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + gender + bird in room before one year old + day-care attendance less than two years old + older siblings more than two years old.

Hosmer Lemeshow test; the first step* $p = 0.273$, Step 7** $p = 0.559$.

Table 5 Risk factors for complications of wheezing and eczema in the previous 12 months (WP_EP) with unadjusted and adjusted odds ratios

	Total	WP_EP	Prevalence(%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	8768	263	3.0		1.00			1.00	
Yes	137	49	35.8	$p < 0.001$	18.01	12.43-26.08	$p < 0.001$	7.91	5.03-12.43
Cow's milk allergy									
No	8858	292	3.3		1.00			1.00	
Yes	47	20	42.6	$p < 0.001$	21.73	12.05-39.20	$p < 0.001$	4.45	2.03-9.74
Buckwheat allergy									
No	8861	298	3.4		1.00			1.00	
Yes	44	14	31.8	$p < 0.001$	13.41	7.04-25.55	0.001	4.41	1.89-10.29
Crab allergy									
No	8856	302	3.4		1.00			1.00	
Yes	49	10	20.4	$p < 0.001$	7.26	3.59-14.69	0.077	2.10	0.92-4.80
Wheat allergy									
No	8898	308	3.5		1.00				
Yes	7	4	57.1	$p < 0.001$	37.19	8.29-166.87			
Parental allergy									
No	3138	48	1.5		1.00				
Father or Mother	3630	128	3.5	$p < 0.001$	2.35	1.68-3.29			
Parent	2153	138	6.4	$p < 0.001$	4.41	3.16-6.15			
Parental asthma									
No	7865	206	2.6		1.00			1.00	
Father or Mother	1003	88	8.8	$p < 0.001$	3.58	2.76-4.63	$p < 0.001$	1.95	1.45-2.63
Parent	53	20	37.7	$p < 0.001$	22.53	12.71-39.94	$p < 0.001$	13.71	6.99-26.92
Parental eczema									
No	7906	205	2.6		1.00			1.00	
Father or Mother	964	96	10.0	$p < 0.001$	4.16	3.23-5.35	$p < 0.001$	2.84	2.13-3.78
Parent	51	13	25.5	$p < 0.001$	12.85	6.74-24.49	$p < 0.001$	6.25	2.82-13.84
Parental rhinitis									
No	6627	167	2.5		1.00			1.00	
Father or Mother	1956	109	5.6	$p < 0.001$	2.28	1.78-2.92	0.023	1.39	1.05-1.83
Parent	338	38	11.2	$p < 0.001$	4.90	3.38-7.10	$p < 0.001$	2.29	1.46-3.58
Parental urticaria									
No	7752	230	3.0		1.00			1.00	
Father or Mother	1063	70	6.6	$p < 0.001$	2.31	1.75-3.04	0.015	1.48	1.08-2.03
Parent	106	14	13.2	$p < 0.001$	4.98	2.79-8.87	0.003	2.64	1.38-5.08
Parental pollen allergy									
No	4985	152	3.0		1.00				
Father or Mother	3031	124	4.1	0.013	1.36	1.07-1.73			
Parent	905	38	4.2	0.073	1.39	0.97-2.00			
Parental conjunctivitis									
No	7959	241	3.0		1.00				
Father or Mother	875	62	7.1	$p < 0.001$	2.44	1.83-3.26			
Parent	87	11	12.6	$p < 0.001$	4.64	2.43-8.84			
Gender									
F	4369	117	2.7		1.00			1.00	
M	4552	197	4.3	$p < 0.001$	1.64	1.30-2.08	0.002	1.48	1.15-1.91
Cat in room at present									
No	8415	294	3.5		1.00				
Yes	236	11	4.7	0.339	1.35	0.73-2.50			
Dog in room at present									
No	7999	277	3.5		1.00				
Yes	652	28	4.3	0.269	1.25	0.84-1.86			
Cat in room before one year old									
No	8532	304	3.6		1.00				
Yes	284	9	3.2	0.724	0.89	0.45-1.74			
Dog in room before one year old									
No	8393	291	3.5		1.00				
Yes	424	22	5.2	0.063	1.52	0.98-2.38			
Piliferous animals in room before one year old									
No	7987	269	3.4		1.00				
Yes	827	44	5.3	0.004	1.61	1.16-2.24			
Day-care attendance more than two years old									
No	1419	52	3.7		1.00				
Yes	7447	259	3.5	0.726	0.95	0.70-1.28			
Older siblings more than two years old									
<2	3818	141	3.7		1.00				
≥2	4909	168	3.4	0.497	0.92	0.74-1.16			

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + gender + piliferous animals in room before one year old.

Hosmer Lemeshow test: the first step* $p = 0.488$. Step 9** $p = 0.251$.

Risk Factors for Allergic Diseases

Table 6 Risk factors for complications of wheezing and rhinoconjunctivitis in the previous 12 months (WP_RP) with unadjusted and adjusted odds ratios

	Total	WP_RP	Prevalence(%)	p value	Unadjusted ^{†*}		p value	Adjusted ^{‡**}	
					exp ^β	95% CI		exp ^β	95% CI
Egg allergy									
No	8946	185	2.1		1.00			1.00	
Yes	164	30	18.3	$p < 0.001$	10.60	6.95-16.17	$p < 0.001$	5.57	3.34-9.31
Cow's milk allergy									
No	9061	204	2.3		1.00			1.00	
Yes	49	11	22.4	$p < 0.001$	12.57	6.33-24.94	0.011	3.06	1.30-7.25
Buckwheat allergy									
No	9072	209	2.3		1.00				
Yes	38	6	15.8	$p < 0.001$	7.95	3.29-19.22			
Crab allergy									
No	9055	209	2.3		1.00				
Yes	55	6	10.9	$p < 0.001$	5.18	2.20-12.23			
Wheat allergy									
No	9101	213	2.3		1.00				
Yes	9	2	22.2	0.002	11.92	2.46-57.73			
Parental allergy									
No	3259	18	0.6		1.00				
Father or Mother	3698	86	2.3	$p < 0.001$	4.29	2.57- 7.14			
Parent	2173	114	5.2	$p < 0.001$	9.97	6.05-16.44			
Parental asthma									
No	8066	148	1.8		1.00			1.00	
Father or Mother	1012	58	5.7	$p < 0.001$	3.25	2.38-4.44	0.001	1.85	1.30-2.62
Parent	52	12	23.1	$p < 0.001$	16.05	8.25-31.22	$p < 0.001$	9.48	4.29-20.94
Parental eczema									
No	8012	162	2.0		1.00				
Father or Mother	1050	50	4.8	$p < 0.001$	2.42	1.75-3.35			
Parent	68	6	8.8	$p < 0.001$	4.69	2.00-11.00			
Parental rhinitis									
No	6880	88	1.3		1.00			1.00	
Father or Mother	1929	97	5.0	$p < 0.001$	4.09	3.05-5.48	$p < 0.001$	2.64	1.90-3.66
Parent	321	33	10.3	$p < 0.001$	8.84	5.83-13.42	$p < 0.001$	2.75	1.60-4.74
Parental urticaria									
No	7900	150	1.9		1.00			1.00	
Father or Mother	1114	55	4.9	$p < 0.001$	2.68	1.96-3.68	0.012	1.56	1.10-2.22
Parent	116	13	11.2	$p < 0.001$	6.52	3.58-11.87	0.014	2.43	1.20-4.94
Parental pollen allergy									
No	5216	72	1.4		1.00			1.00	
Father or Mother	3036	97	3.2	$p < 0.001$	2.36	1.73-3.21	0.013	1.53	1.10-2.14
Parent	878	49	5.6	$p < 0.001$	4.22	2.92-6.12	$p < 0.001$	2.38	1.55-3.66
Parental conjunctivitis									
No	8186	149	1.8		1.00			1.00	
Father or Mother	867	57	6.6	$p < 0.001$	3.80	2.77-5.19	0.002	1.78	1.24-2.56
Parent	77	12	15.6	$p < 0.001$	9.96	5.27-18.82	0.013	2.69	1.24-5.86
Gender									
F	4540	83	1.8		1.00			1.00	
M	4590	135	2.9	0.001	1.63	1.23-2.15	0.001	1.65	1.23-2.22
Cat in room at present									
No	8626	204	2.4		1.00				
Yes	238	5	2.1	0.791	0.89	0.36-2.17			
Dog in room at present									
No	8192	190	2.3		1.00				
Yes	672	19	2.8	0.405	1.23	0.76-1.98			
Cat in room before one year old									
No	8728	208	2.4		1.00				
Yes	288	4	1.4	0.279	0.58	0.21-1.56			
Dog in room before one year old									
No	8593	200	2.3		1.00				
Yes	424	12	2.8	0.506	1.22	0.68-2.21			
Bird in room before one year old									
No	8965	208	2.3		1.00				
Yes	52	4	7.7	0.017	3.51	1.25-9.82			
Day-care attendance more than two years old									
No	1486	27	1.8		1.00				
Yes	7593	189	2.5	0.122	1.38	0.92-2.07			
Older siblings more than two years old									
<2	3893	112	2.9		1.00				
≥2	5043	102	2.0	0.009	0.70	0.53-0.91			

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + gender + bird before one year old + older siblings.

Hosmer Lemeshow test; the first step* $p = 0.317$, Step 6** $p = 0.411$.

Table 7 Risk factors for complications of eczema and rhinoconjunctivitis in the previous 12 months (EP_RP) with unadjusted and adjusted odds ratios

	Total	EP_RP	Prevalence(%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	8771	284	3.2		1.00			1.00	
Yes	133	47	35.3	$p < 0.001$	16.33	11.23-23.76	$p < 0.001$	9.12	5.73-14.53
Cow's milk allergy									
No	8863	314	3.5		1.00			1.00	
Yes	41	17	41.5	$p < 0.001$	19.29	10.26-36.26	0.001	4.46	1.90-10.46
Buckwheat allergy									
No	8870	321	3.6		1.00			1.00	
Yes	34	10	29.4	$p < 0.001$	11.10	5.26-23.40	0.077	2.53	0.91-7.06
Crab allergy									
No	8857	321	3.6		1.00			1.00	
Yes	47	10	21.3	$p < 0.001$	7.19	3.54-14.58	0.075	2.35	0.92-6.00
Wheat allergy									
No	8899	328	3.7		1.00				
Yes	5	3	60.0	$p < 0.001$	39.20	6.53-235.38			
Parental allergy									
No	3208	31	1.0		1.00				
Father or Mother	3623	122	3.4	$p < 0.001$	3.57	2.40-5.31			
Parent	2089	179	8.6	$p < 0.001$	9.61	6.53-14.12			
Parental asthma									
No	7841	251	3.2		1.00			1.00	
Father or Mother	1020	69	6.8	$p < 0.001$	2.19	1.67-2.89	0.755	1.05	0.76-1.46
Parent	59	12	20.3	$p < 0.001$	7.72	4.05-14.73	0.003	3.30	1.50-7.27
Parental eczema									
No	7935	230	2.9		1.00			1.00	
Father or Mother	941	92	9.8	$p < 0.001$	3.63	2.82-4.67	$p < 0.001$	2.30	1.72-3.08
Parent	44	10	22.7	$p < 0.001$	9.85	4.81-20.19	0.004	3.81	1.54-9.40
Parental rhinitis									
No	6714	146	2.2		1.00			1.00	
Father or Mother	1889	136	7.2	$p < 0.001$	3.49	2.75-4.43	$p < 0.001$	2.30	1.75-3.02
Parent	317	50	15.8	$p < 0.001$	8.42	5.97-11.88	$p < 0.001$	2.65	1.68-4.20
Parental urticaria									
No	7767	235	3.0		1.00			1.00	
Father or Mother	1047	77	7.4	$p < 0.001$	2.54	1.95-3.32	0.068	1.33	0.98-1.81
Parent	106	20	18.9	$p < 0.001$	7.45	4.51-12.33	$p < 0.001$	3.68	2.04-6.64
Parental pollen allergy									
No	5073	106	2.1		1.00			1.00	
Father or Mother	2991	147	4.9	$p < 0.001$	2.42	1.88-3.12	$p < 0.001$	1.66	1.26-2.20
Parent	856	79	9.2	$p < 0.001$	4.76	3.53-6.44	$p < 0.001$	2.76	1.93-3.94
Parental conjunctivitis									
No	8006	230	2.9		1.00			1.00	
Father or Mother	835	78	9.3	$p < 0.001$	3.48	2.67-4.55	0.003	1.60	1.17-2.20
Parent	79	24	30.4	$p < 0.001$	14.75	8.97-24.25	$p < 0.001$	4.04	2.19-7.46
Cat in room at present									
No	8396	311	3.7		1.00				
Yes	245	9	3.7	0.980	0.99	0.51-1.95			
Dog in room at present									
No	7990	296	3.7		1.00				
Yes	651	24	3.7	0.981	1.00	0.65-1.52			
Cat in room before one year old									
No	8516	321	3.8		1.00				
Yes	291	7	2.4	0.231	0.63	0.30-1.34			
Dog in room before one year old									
No	8389	310	3.7		1.00				
Yes	419	18	4.3	0.527	1.17	0.72-1.90			
Bird in room before one year old									
No	8758	321	3.7		1.00			1.00	
Yes	50	7	14.0	$p < 0.001$	4.28	1.91-9.59	0.008	3.70	1.42-9.67
Day-care attendance more than two years old									
No	1416	42	3.0		1.00				
Yes	7451	288	3.9	0.102	1.32	0.95-1.83			
Older siblings more than two years old									
<2	3763	159	4.2		1.00			1.00	
≥2	4965	165	3.3	0.028	0.78	0.62-0.97	0.062	0.80	0.63-1.01

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + bird in room before one year old + day-care attendance more than two years old + older siblings more than two years old.

Hosmer Lemeshow test; the first step* $p = 0.271$, Step 3** $p = 0.343$.

Risk Factors for Allergic Diseases

Table 8 Risk factors for complications of wheezing, eczema and rhinoconjunctivitis in the previous 12 months (WP_EP_RP) with unadjusted and adjusted odds ratios

	Total	WP_EP_RP	Prevalence(%)	Unadjusted ^{†*}			Adjusted ^{‡**}		
				p value	exp ^β	95% CI	p value	exp ^β	95% CI
Egg allergy									
No	7874	78	1.0		1.00			1.00	
Yes	91	23	25.3	$p < 0.001$	33.81	20.04-57.02	$p < 0.001$	14.45	7.44-28.07
Cow's milk allergy									
No	7932	90	1.1		1.00			1.00	
Yes	33	11	33.3	$p < 0.001$	43.57	20.52-92.51	$p < 0.001$	7.54	2.72-20.87
Crab allergy									
No	7928	96	1.2		1.00			1.00	
Yes	37	5	13.5	$p < 0.001$	12.75	4.86-33.42	0.002	6.02	1.91-19.04
Buckwheat allergy									
No	7938	97	1.2		1.00				
Yes	27	4	14.8	$p < 0.001$	14.06	4.77-41.4			
Wheat allergy									
No	7961	99	1.2		1.00				
Yes	4	2	50.0	$p < 0.001$	79.41	11.08-569.43			
Parental allergy									
No	2999	9	0.3		1.00				
Father or Mother	3211	34	1.1	0.001	3.56	1.70-7.43			
Parent	1770	59	3.3	$p < 0.001$	11.46	5.67-23.16			
Parental asthma									
No	7117	69	1.0		1.00			1.00	
Father or Mother	824	24	2.9	$p < 0.001$	3.06	1.92-4.90	0.580	1.17	0.67-2.04
Parent	39	9	23.1	$p < 0.001$	30.64	14.02-66.96	0.000	11.51	4.29-30.93
Parental eczema									
No	7164	68	0.9		1.00			1.00	
Father or Mother	783	30	3.8	$p < 0.001$	4.16	2.69-6.43	0.015	1.91	1.14-3.22
Parent	33	4	12.1	$p < 0.001$	14.39	4.93-42.06	0.329	2.10	0.47-9.31
Parental rhinitis									
No	6114	36	0.6		1.00			1.00	
Father or Mother	1609	45	2.8	$p < 0.001$	4.86	3.12-7.56	$p < 0.001$	3.04	1.83-5.04
Parent	257	21	8.2	$p < 0.001$	15.02	8.64-26.14	$p < 0.001$	6.08	2.96-12.47
Parental urticaria									
No	7003	67	1.0		1.00			1.00	
Father or Mother	894	25	2.8	$p < 0.001$	2.98	1.87-4.74	0.414	1.25	0.73-2.16
Parent	83	10	12.0	$p < 0.001$	14.18	7.02-28.65	$p < 0.001$	4.94	2.03-12.04
Parental pollen allergy									
No	4611	33	0.7		1.00				
Father or Mother	2635	48	1.8	$p < 0.001$	2.57	1.65-4.02			
Parent	734	21	2.9	$p < 0.001$	4.09	2.35-7.10			
Parental conjunctivitis									
No	7224	66	0.9		1.00			1.00	
Father or Mother	699	28	4.0	$p < 0.001$	4.53	2.89-7.09	0.008	2.07	1.21-3.55
Parent	57	8	14.0	$p < 0.001$	17.71	8.07-38.85	0.014	3.79	1.31-10.97
Cat in room at present									
No	7519	94	1.3		1.00				
Yes	219	3	1.4	0.875	1.10	0.35-3.49			
Dog in room at present									
No	7146	85	1.2		1.00				
Yes	592	12	2.0	0.082	1.72	0.93-3.16			
Cat in room before one year old									
No	7624	100	1.3		1.00				
Yes	259	2	0.8	0.455	0.59	0.14-2.39			
Dog in room before one year old									
No	7515	94	1.3		1.00				
Yes	369	8	2.2	0.133	1.75	0.84-3.63			
Bird in room before one year old									
No	7841	99	1.3		1.00			1.00	
Yes	43	3	7.0	0.004	5.87	1.79-19.28	0.008	6.67	1.66-26.84
Day-care attendance more than two years old									
No	1293	11	0.9		1.00				
Yes	6638	89	1.3	0.152	1.58	0.84-2.97			
Older siblings more than two years old									
<2	3363	50	1.5		1.00				
≥2	4441	49	1.1	0.135	0.74	0.50-1.10			

[†] Crude odds ratios of food and parental allergy showed the significant variables ($p < 0.05$) without duplicate information and the others showed variables with or without significance ($p < 0.05$) by using logistic regression.

[‡] The significant unadjusted variables were adjusted by using backwards elimination (likelihood) method. Design; egg + cow's milk + buckwheat + crab + wheat + parental allergy + parental asthma + parental eczema + parental rhinitis + parental urticaria + parental pollen allergy + parental conjunctivitis + bird in room before one year old + day-care attendance more than two years old + older siblings more than two years old.

Hosmer Lemeshow test; the first step* $p = 0.197$, Step 8** $p = 0.507$.

Our questionnaire included our own items regarding the household, as well as the original questions in the ISSAC questionnaire (Table 1A, Table 1B).

STATISTICAL ANALYSIS

Relationships between allergies such as WP, EP, and RP and food allergy, parental allergy, keeping animals, presence of older siblings, and early day-care attendance were estimated using logistic regression analysis. Significant variables that excluded duplicate information were chosen as candidates for multivariate analysis and adjusted by using the backward elimination (likelihood) method. The results of analyses were expressed in terms of odds ratio with 95% confidence interval and *p* value. All analyses were two-tailed, and a *p* value of <0.05 was considered to indicate statistical significance. Statistical analyses were performed on a personal computer with the SPSS statistical software package (ver. 17.02 SPSS, Chicago, USA).

RESULTS

WHEEZING IN THE PREVIOUS 12 MONTHS (Table 2)

Gender: The overall prevalence of WP was 10.4% among the children enrolled in this study (boys 12.3%; girls 8.2%). The prevalence of WP was significantly higher in boys than in girls (adjusted odds ratio [aOR] 1.53, 95% confidence interval [95% CI] 1.35-1.74).

Food allergy: According to our data, 29.4% of the children with egg allergy suffered from WP. Having egg allergy had a significant positive relationship with the prevalence of WP (aOR 2.89, 95% CI 2.16-3.88).

Family history: The occurrence of WP was higher in children whose parents had a history of allergy than in children whose parents did not. History of asthma in one parent (aOR 2.12, 95% CI 1.80-2.50) or both (aOR 8.02, 95% CI 5.09-12.65), and history of rhinitis in one parent (aOR 1.27, 95% CI 1.08-1.48) or both (aOR 1.52, 95% CI 1.14-2.03) showed a significant positive relationship with the prevalence of WP in the children.

ECZEMA IN THE PREVIOUS 12 MONTHS (Table 3)

Gender: The overall prevalence of EP was 14.3% among the children enrolled in this study, and there was no significant difference between the genders (boys 14.2%; girls 14.4%).

Food allergy: According to our data, 55.2% of the children with egg allergy, 59.2% of the children with cow's milk allergy, 46.8% of the children with buckwheat allergy, 41.6% of the children with crab allergy, and 76.9% of the children with wheat allergy suffered from EP. Allergy to egg (aOR 4.71, 95% CI 3.52-6.29), cow's milk (aOR 2.45, 95% CI 1.39-4.32), buckwheat (aOR 1.94, 95% CI 1.06-3.55) and crab (aOR 2.03, 95%

CI 1.24-3.47) was significantly related to the prevalence of EP in the children.

Family history: The occurrence of EP was higher in children whose parents had a history of allergy than in children whose parents did not. History of asthma in both parents (aOR 2.26, 95% CI 1.39-3.68), history of eczema in one parent (aOR 2.38, 95% CI 2.06-2.75) or both (aOR 5.63, 95% CI 3.66-8.83), history of rhinitis in one parent (aOR 1.15, 95% CI 1.01-1.32), history of urticaria in one parent (aOR 1.36, 95% CI 1.17-1.59) or both (aOR 1.88, 95% CI 1.37-2.89), and history of conjunctivitis in one parent (aOR 1.20, 95% CI 1.01-1.42) or both (aOR 1.66, 95% CI 1.08-2.54) were significantly related to the prevalence of EP in the children.

Keeping pets: Keeping a bird before the child was one year old (aOR 1.99, 95% CI 1.10-3.61) was significantly related to the prevalence of EP in the children.

RHINOCONJUNCTIVITIS IN THE PREVIOUS 12 MONTHS (Table 4)

Gender: The overall prevalence of RP was 10.7% among the children enrolled in this study, and there was no significant difference between the genders (boys 11.4%; girls 9.9%).

Food allergy: According to our data, 29.4% of the children with egg allergy and 30.6% of the children with buckwheat allergy suffered from RP. Allergy to egg (aOR 2.68, 95% CI 1.96-3.67) and buckwheat (aOR 1.92, 95% CI 1.03-3.57) was significantly related to the prevalence of RP in the children.

Older siblings: The occurrence of RP in children who had one or more older siblings was lower than that in the children who had no older siblings. Having older siblings showed a significant inverse relationship with the prevalence of RP (aOR 0.73, 95% CI 0.64-0.83). Thus the presence of older siblings appeared to be a protective factor against RP.

Early day-care attendance: The occurrence of RP in the children who had attended a day-care center in the first two years of life was lower than that in the children who had not. Day-care attendance in the first two years of life showed a significant inverse relationship with the prevalence of RP (aOR 0.74, 95% CI 0.61-0.90). Early day-care attendance may thus be a protective factor against RS.

Family history: The occurrence of RP was higher in children whose parents had a history of allergy than in children whose parents did not. History of eczema in one parent (aOR 1.22, 95% CI 1.03-1.46), history of rhinitis in one parent (aOR 1.97, 95% CI 1.69-2.29) or both (aOR 1.97, 95% CI 1.50-2.59), history of urticaria in both parents (aOR 1.73, 95% CI 1.15-2.59), history of pollen allergy in one parent (aOR 1.43, 95% CI 1.21-1.69) or both (aOR 2.29, 95% CI 1.78-2.92) and history of conjunctivitis in one parent (aOR 1.56, 95% CI 1.31-1.85) or both (aOR 2.78, 95% CI 1.87-4.14) were significantly related to the prevalence RP in the children.

Keeping pets: The occurrence of RP was higher in children whose families had kept a bird before the child was one year old (aOR 2.06, 95% CI 1.09-3.92).

The results for complications of WP and EP, complications of WP and RP, complications of EP and RP, and complications of WP, EP and RP are shown in Table 5-8.

DISCUSSION

RATE OF RESPONSE TO THE QUESTIONNAIRE

The extremely high response rate was obtained through close cooperation between the parents (or caregivers) and primary school teachers in Himeji City. This study was performed as soon as the children entered elementary school, and thus their parents (or caregivers) were highly motivated regarding health aspects of their children in school. The teachers, for their part, were asked to ensure that questionnaires were returned by all of their pupils. This survey was part of an investigation of the effects of air pollution on health in Himeji City. We have continued this survey every year since 1995, and have already reported an increase in the prevalence of allergic rhinitis and pollinosis due to Japanese cedar, and a decrease of eczema (atopic dermatitis).³ This survey is still ongoing.

GENDER

In this study, the prevalence of WP was significantly higher in boys than in girls. This finding was compatible with the results of Arshad *et al.*¹⁰ Being male may be a risk factor for the development of asthma. However, there were no significant relationships between gender and WP, or between gender and RP.

FOOD ALLERGY

Parent-reported food allergy in the children was significantly associated with the prevalence of WP, EP and RP. Egg allergy in particular was associated with all allergic diseases in this study, including WP, EP and RP.

With regard to the relationship between food allergy and asthma, it should be noted that asthma is an important factor of food-associated death.¹¹ Novembre *et al.*¹² reported that respiratory symptoms induced by food allergy are almost always associated with other clinical manifestations in the skin and/or gastrointestinal organs. Ito and Morishita¹³ reported that respiratory symptoms were seen in 50 out of 154 children who showed some symptoms in food challenge tests (32.5%). Ahshad *et al.*¹⁰ reported that among the early life factors associated with asthma at the age of 10 years, the presence of food allergy at 1 year and 4 years of age was statistically significant. Schroeder *et al.*¹⁴ reported an association and a temporal relationship between food allergy and asthma in children aged six years and older in Chicago, USA;

there were significant associations between symptomatic food allergy (OR 5.1, 95% CI 3.1-8.4) and asthma, and between asymptomatic food sensitization (OR 1.9, 95% CI 1.0-3.6) and asthma.¹⁴ Schroeder *et al.*¹⁴ also reported that asthma had a temporal relationship with food allergy, preceding the development of asthma by approximately 1.25 years in their selected cohort.

There is a strong relationship between food allergy and EP. In our study, allergy towards egg, cow's milk, buckwheat and crab was associated with eczema: more than 50% of the children with egg and cow's milk allergy had eczema (Table 3). Eigenmann *et al.*¹⁵ reported that approximately one third of children with refractory, moderate to severe eczema had IgE mediated clinical reactivity to food proteins. Ito *et al.*¹⁶ reported that the prevalence of food allergy in patients with eczema was 86% at the age of 0 years. Talbot¹⁷ reported a pathogenic role of food allergy in the development of eczema in 1918, and indicated that elimination of the offending food improved eczema.

Our results and other reports have suggested that food allergy is also associated with the development of RS. In a report from Denmark by Kjaer *et al.*,¹⁸ 9 out of 55 children with rhinoconjunctivitis were sensitized by egg (16.4%), and the occurrence of rhinoconjunctivitis in the children with egg sensitization was 9 among 18 children (50.0%). However, in a report from the UK by Marinho *et al.*,¹⁹ egg sensitization had no significant association with rhinoconjunctivitis.

ALLERGY HISTORY IN THE PARENTS

A family history of allergic diseases may indicate the presence of genetic risk factors for the development of allergic diseases. Our study also showed that the presence of allergic diseases in the parents was significantly related to the presence of allergic diseases in their 6-year-old children. This finding was in accordance with many studies reported previously. Arshad²⁰ reported that a positive family history of allergy was a significant risk factor for any allergic condition, including asthma, eczema and rhinitis, in 2-year-old children on the Isle of Wight, UK. Tanaka *et al.*⁸ reported that the risk for allergic diseases may be increased in children, irrespective of the type of allergic disease in the family members. Nishima *et al.*²¹ also reported that bronchial asthma was more prevalent among Japanese primary school students with a family history of allergic disease. Kjellman²² reported that the incidence of atopic disease was 24.8% in 7-year-old Swedish children with a family history of atopic disease, and 10.4% in those without atopic disease, and that the incidence of a positive family history of atopic disease was 73.5% in children with two or more different types of atopic disease, in contrast to 44.6% in children who had only one manifestation of atopic disease.

Safafino²³ suggested that maternal atopy was more strongly related to asthma and hay fever in children than parental atopy, and that the severity of specific atopic illness in children was not affected by the number of their parents who had the same condition, nor was it strongly related to the severity of the condition in the parents. However, our present study showed that parents had significantly the same kind of allergic disease as the child. When a child had asthma, the parents also showed a significant tendency to have asthma, and the same phenomenon was observed for eczema. Furthermore, when a child had rhinoconjunctivitis, the parents also had a significant tendency to have rhinitis, pollinosis and conjunctivitis. A positive family history of some allergic disease appeared to be the main risk factor for the prevalence of allergy in the children.

OLDER SIBLINGS

In our study, the presence of older siblings showed a significant inverse relationship with the prevalence of RP. This may be explained by Strachan's hygiene hypothesis that allergic diseases can be prevented by infection in early childhood, transmitted by unhygienic contact with older siblings, or acquired prenatally from a mother infected by contact with her older children.¹ Many reports have addressed the relationship between family size and allergic diseases, or the relationship between the presence of older siblings and allergic diseases. Jarvis *et al.*²⁴ also reported an inverse relationship between family size and hay fever. Bråbäck *et al.*,²⁵ Räsänen *et al.*²⁶ and Bodner *et al.*²⁷ reported an inverse relationship between the number of older siblings and prevalence of hay fever. Bodner *et al.*²⁷ and Strachan *et al.*²⁸ reported that the number of older siblings exerted a stronger effect than the number of younger siblings. Strachan *et al.*²⁹ reported that the presence of brothers was more protective against the development of inhalant allergy than the presence of sisters. Westergaard *et al.*³⁰ also reported that the presence of brothers was more protective against the development of allergic rhinitis than the presence of sisters.

However, in our study, no relationship was found between the presence of older siblings and WP, or between the presence of older siblings and EP. Although some reports have indicated protective effects of family size (or the presence of older siblings) against the development of asthma,^{24,31} many others have shown that the effects of older siblings are insignificant.²⁵⁻²⁷ There is also considerable controversy regarding the relationship between family size (or the presence of older siblings) and eczema. Some studies have found an inverse relationship between family size or day-care attendance and eczema,²⁷ whereas others have not.²⁴ Zutavern *et al.*³² concluded that there was no evidence to support the hygiene hypothesis with regard to eczema.

EARLY DAY-CARE ATTENDANCE

Attendance at a day care center in the first two years of life showed a significant inverse relationship with the prevalence of RP in our study. This result was in accord with the report by Svane *et al.*³³ on the relationship between early day care attendance and hay fever. However, other studies have found no protective effects of early day care attendance against the development of hay fever.^{34,35}

In our study, we were unable to find any significant relationship between early day-care attendance and the occurrence of WP or EP. There have been some conflicting reports regarding the relationship between early day-care attendance and the occurrence of allergic disease, some indicating protective effects against asthma,^{36,37} whereas others have reported no protective effects against the development of wheezing or asthma.³³⁻³⁵ According to Svanes *et al.*,³³ the environment in early life may well influence the development of the immune system and the lung airways in different ways, thus creating complex patterns. Asthma is a disease not only of the immune system but also of the respiratory system.

The debate regarding the relationship between early attendance at a day care center and eczema is still ongoing. Some studies have found an inverse relationship with eczema,³⁷ whereas others have demonstrated no protective effects against eczema.³³

KEEPING PETS

The evidence regarding the relationship between exposure to animals and risk allergy/atopy is conflicting.³⁸ Our results showed that current ownership of a cat or dog or having kept one before a child was one year old was not significantly related to allergy. These findings were different from our previous study indicating that current cat ownership appeared to be associated with a lower prevalence of atopic dermatitis, allergic rhinitis, and Japanese cedar pollinosis.³ After that previous finding, we informed pediatricians, teachers and citizens in Himeji that keeping pets might protect allergic diseases. However, the timing of exposure may have been important; we showed that the occurrence of ES and RS in children of families who had kept birds before the child was one year old was higher than that in children of families who had not kept birds. Svanes *et al.* reported that respiratory symptoms were more common in adults who had owned birds during childhood.³⁹ However, the number of children of families who kept birds was small in the present study, and further investigation of this issue will be necessary.

RHINOCONJUNCTIVITIS, POLLINOSIS AND NON-SEASONAL RHINITIS

Our questionnaire was conducted according the ISAAC.⁴⁰ There is a possibility that rhinoconjuncti-

tis could have included pollinosis, non-seasonal rhinitis and non-seasonal conjunctivitis. However, Nishima mentioned that the seasonal pattern of prevalence of rhinoconjunctivitis using the ISAAC in Japan differed from the pattern of pollinosis due to Japanese cedar.⁴¹ Therefore, an ISSAC modified Japanese edition may be necessary.

COMPLICATIONS OF ALLERGIC DISEASES (WP and EP, WP and RP, EP and RP, and WP, EP and RP)

Complications of each allergic disease showed the characteristic features of the various allergic symptoms in our study. The odds ratios of the parental same allergic histories as the children's complications were higher than the odds ratios of the parental different allergic histories from the children's complications.

RHINOCONJUNCTIVITIS AND HYGIENE HYPOTHESIS

Our study demonstrated that the prevalence of RP in 6-year-old children was inversely related to the presence of older siblings and early day-care attendance. This might only partially support hygiene hypothesis as we did not show microbial infections among our investigated children. Romagnani *et al.* reported that 'Natural immunity' to bacterial and viral infections induces a Th1 pattern of cytokine release, potentially suppressing the Th2 immune response involved in IgE-mediated allergy.⁴² Although the Th1/Th2 paradigm may not be as clear in humans as it first appeared in rodents,⁴³ it has been thought that microbial pathogens may have similar Th1-stimulatory effects in humans.⁴⁴ If microbial stimulation is enough during infancy, Th1 function may be enough to suppress Th2 responses. According to Prescott *et al.*,⁴⁵ there is rapid suppression of Th2 responses during the first year of life in non-atopic children, but there is consolidation of such responses in atopic children. The development of allergic rhinitis cannot be simply explained by the hygiene hypothesis. Matheson *et al.*⁴⁶ reported that greater cumulative exposure to siblings before the age of 2 years showed a strong inverse association with early-onset (before 7 years of age) allergic rhinitis, but less so with later-onset allergic rhinitis. Although we focused on six-year-old children in this study, and observed an inverse relationship between RP and the presence of older siblings or early day-care attendance, different results might have been obtained if we had examined children in another age group.

CONCLUSION

Among Japanese children, food allergy and a history of parental allergy appear to be risk factors for WP, EP or RP. However, early day-care attendance and the presence of older siblings might be protective

against RP. Infections in early life may affect the prevalence of rhinoconjunctivitis in children by the time they have become six years old.

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