Environmental risk factors for early infantile atopic dermatitis

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Previous studies of predictors of atopic dermatitis (AD) in Asia have had limited sample size and small numbers of variables focused primarily on family history or dietary exposures. The purpose of this study was to evaluate the influence of various environmental risk factors for early infantile AD. We used multistage, stratified systematic sampling to recruit 2048 mother–child pairs from the Taiwan national birth registration in 2003. Information on environmental risk factors for infant AD gathered by questionnaire were available from 1760 infants at 6 months of age. Multiple logistic regression was used to estimate adjusted odds ratios (aORs) and their 95% confidence intervals (CIs) for risk factors for AD after adjusting for potential confounders. AD was noted in 118 of 1760 (6.7%) of the infants. After adjusting for maternal age and education, family history of atopy, infant gender, and gestational age, fungi on walls of the house [aOR 2.14 (95% CI 1.41–3.22)] and frequent use of microwave oven at home [aOR 1.71 (95% CI 1.13–2.58)] increased the risk of early infantile AD. This study suggests that environmental factors do play a role in early infantile AD. Fungi, a kind of aeroallergen, are especially important in humid climate as in Taiwan and their impacts might be felt at the early infant stage. The hazards of microwave use should be paid more attention.

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Atopic dermatitis (AD) is a common skin disease which affects 10–20% of the population, with onset usually during infancy. The frequency of AD appears to have increased over the past three decades, so it is not a purely hereditary disease (1, 2). The development and phenotypic expression of AD depend on a complex interaction among genetic factors, perinatal environmental exposure to allergens, and non-specific adjuvant factors, such as pollution, infections, and climates (3). Attempts to identify parameters predictive of the development of AD have been made by many investigators during the last decades. However, there are few large prospective studies on the various environmental factors

of the early-life presentation of AD, especially in Asian populations.

The purpose of this study was to investigate environmental factors for early infantile AD among infants enrolled in the Taiwan National Birth Cohort study. We assessed AD in the first 6 months of life, a period during which the condition causes considerable morbidity, in terms of sleep and feeding disruption, family stress, physician visits, health care expenditures, and later asthma, allergic rhinitis, and urticaria (4). These children with early AD may suffer severe or long-lasting symptoms and thus are very important for further studies. In addition, clarification of early environmental impacts for

prenatal allergy sensitization and postnatal development of AD will provide a better strategy to predict and prevent AD early.

Materials and methods

Study population and sampling strategy

In the pilot study of Taiwan National Birth Cohort Study, we used the multistage stratified systematic sampling design to obtain the representative samples from the national birth registration data between November and December 2003. We stratified a total of 369 towns in Taiwan into 12 strata according to the administrative division (four strata) and the total fertility rate (three strata). Using the principle of proportion probability to size, we randomly sampled 29 towns from the 12 strata (5, 6). All postpartum women and newborns, a total of 2048 pairs, from these 29 towns were recruited. Written consents were provided by the women. The study was approved by the Medical Ethics Committee and Data Protection Board in Taiwan.

Data collection and case definition

We conducted an interview with the 2048 postpartum women within 1 week after their delivery by means of a structured questionnaire. A total of 148 cases refused to participate. After 6 months of delivery, 140 cases were lost to follow-up because of moving home ($n = 50$), incorrect addresses ($n = 38$), going abroad ($n = 25$), infant deaths ($n = 14$), adopted infants ($n = 3$), and other miscellaneous reasons ($n = 10$). A total of 1760 women finished the home interview. The complete interview rate was 86%. Cases of AD were defined as children whose mothers reported that the child had AD diagnosed by a doctor (7). Exclusion criteria include multiple gestation (twins, triplets, etc.), inability to answer questions in Chinese, and plans to move out of the area before delivery.

Variables

Data were obtained from the home interview questionnaire. Questions about potential confounders and prenatal and postnatal risk factors were asked, including maternal age, maternal education, family income, family history of atopy, maternal smoking and drinking alcohol during pregnancy, maternal diet and supplements such as multivitamins or fish oils during pregnancy, duration of breast feeding and consumption of infant formula, age of introduction

of solid foods or highly allergenic foods, infant history of allergy, acute bronchiolitis, number of siblings, pet raising, cockroaches and carpets at home, environmental tobacco smoke, fungi on the walls of the house, frequent use of microwave oven or magnetic oven, moving into a new house, new paintings, etc.

From the records of the hospitals included in the study, we collected neonate health data at birth, such as gender, head circumference, birth body weight, height, weeks of gestation, parity, type of delivery, and vaccination history.

Statistical analysis

The odds ratios (ORs) with 95% confidence intervals (95% CIs) for prenatal and postnatal predictors were calculated by means of logistic regression. Analyses were performed in both univariate and multivariate models. Significant variables from univariate analysis and other potential confounders from literature were selected by stepwise multivariate logistic regression. Potential confounders including maternal age and education, family history of atopy, infant gender, and gestational age were adjusted. All hypothesis testing was two-sided at the significance level of 0.05 and performed with the SAS software version 8.2.

Results

First, we compared the information between 1760 responders and 288 non-responders. The mean of maternal age was 28.4 years in the non-responder group which was similar to that of the responder group. The mean of infant birth weight and gestational age were 3046.8 g and 38.0 weeks in the non-responder group, and 3096.9 g and 38.4 weeks in the responder group, respectively. There were no significant difference in the characteristics between the non-responders and the responders, including maternal age, family history of atopy, birth weight, gestational age, gender, parity, and preterm delivery. About 970 of 1760 (55.1%) infants were male and 125 of 1760 (25.7%) were premature infants. Table 1 displays the demographic characteristics of infants and mothers.

During the study period, a diagnosis of a maternal report of provider-diagnosed AD was made in 118 of 1760 (6.7%) of children by the age of 6 months. The results of prenatal exposure influence on AD are shown in Table 2. Maternal smoking, maternal supplements, and use of Chinese herbal medicine during pregnancy were not significantly associated with AD. As to

Table 1. Demographic characteristics

Variable	No. of subject (%)
Maternal age (years)	
≤19	58 (3.30)
20–34	1541 (87.56)
≥35	161 (9.04)
Maternal education	
≤Junior high school	293 (16.65)
Senior high school	747 (42.44)
≤University	720 (40.91)
Maternal nationality	
Taiwan	1527 (86.76)
Foreign countries	233 (13.24)
Place of residence	
Urban area	883 (50.17)
Suburban area	360 (20.45)
Rural area	517 (29.38)
Family Income	
<400,000 NTS	366 (20.80)
400,000–1,000,000 NTS	975 (55.40)
>1,000,000 NTS	415 (23.58)
Family history of atopy	
Yes	21 (1.19)
No	1745 (98.03)
Infant gender	
Male	970 (55.11)
Female	790 (44.89)
Gestational age	
<36 weeks	453 (25.74)
≥36 weeks	1307 (74.26)
Birth body weight	
<2500	125 (7.10)
≥2500	1635 (92.90)
Delivery method	
Normal spontaneous delivery	1161 (66.72)
Cesarean section	599 (34.03)

postnatal exposures, duration of breast feeding and consumption of infant formula, frequent respiratory tract infections, older siblings, furry pets, carpets, and cockroaches at home were not associated with AD (Table 3). *Haemophilus influenza* vaccine had the potential to increase the risk of AD [OR 1.69 (95% CI 1.07–2.44)] (Table 3); however, it turned out to be not significant after adjusting for potential confounders. The presence of fungi in the walls of houses enhanced the risk of AD in the first 6 months of life and it seemed that increment of one wall increased the risk of AD – a dose–response relationship. Moving into a new house, frequent use of microwave oven, and electric magnetic oven (more than five times per week) increased the risk of AD. The ORs and their 95% CIs were 2.18 (1.01–4.70), 1.89 (1.28–2.72), and 1.56 (1.03–2.33), respectively (Table 3). Newly painted dwellings also enhanced the risk of AD, though not statistically significantly. After stepwise multivariate logistic regression, only significant variables, fungi in walls of houses [aOR 2.14 (95%

Table 2. Univariate analysis of prenatal factors for infant atopic dermatitis

Variable	No. of subject	No. of AD	AD rate (%)	OR	95% CI
Maternal smoking during pregnancy					
Yes	37	4	10.81	1.71	0.60–4.91
No	1723	114	6.62	1.00	(referent)
Consumption of shrimps or crabs during pregnancy					
≤3 times per week	903	68	7.53	1.00	(referent)
>3 times per week	557	50	8.98	1.21	0.78–1.59
Deep sea fish oil supplements during pregnancy					
Yes	152	9	5.92	1.00	(referent)
No	1608	109	6.78	1.15	0.91–2.83
Calcium supplements during pregnancy					
Yes	611	46	7.53	1.22	0.83–1.79
No	1149	72	6.27	1.00	(referent)
Chinese herbal medicine during pregnancy					
Yes	351	25	7.12	1.07	0.67–1.72
No	1109	74	6.67	1.00	(referent)
Pearl powder during pregnancy					
Yes	65	5	7.69	1.15	0.45–2.94
No	1395	94	6.74	1.00	(referent)
Huang-Liang during pregnancy					
Yes	65	6	9.23	1.42	0.56–3.38
No	1395	93	6.67	1.00	(referent)
Szu-Wu-Tang during pregnancy					
Yes	49	3	6.12	1.00	(referent)
No	1411	96	6.80	1.12	0.34–3.67
Ginseng during pregnancy					
Yes	24	1	4.17	1.00	(referent)
No	1436	98	6.82	1.69	0.23–12.61

*p < 0.05.

OR, odd ratio; CI, confidence interval.

The major category of Chinese herbal medicines: 1 – Pearl powder (a single product; ground into powder); Margarita. 2 – Huanglian (a single product; ground and put into capsules); Coptidis Rhizoma. 3 – Szu-Wu-Tang (a compound product; boiled/cooked in water); Rehmanniae Radix, Paeoniae Radix, Angelicae Sinensis Radix, and Chuanxiong Rhizoma. 4 – Ginseng (a single product): Ginseng Radix.

CI: 1.41–3.22)] and frequent use of microwave oven at home [aOR 1.71 (95% CI: 1.13–2.58)] were left in the model (Table 4).

Discussion

The observed prevalence of 6.7% was lower than that reported in other cohort studies of children of similar ages (7). However, many cohorts tend to include more children with risk factors for AD defined by the mother, the diagnosis of whom is non-specific (8). Among various prenatal and postnatal environmental factors, we did find that fungi in the walls of houses and a frequent use of microwave oven at home increased the risk of early infantile AD, after adjusting for potential confounders. Season of birth has been reported to be associated with risk of AD (9). However, we did not include birth season as a factor in this analysis, because we chose samples within two continuous months and assessed the outcome at

Table 3. Univariate analysis of postnatal factors and indoor environmental factors for infant atopic dermatitis

Variable	No. of subject	No. of AD	AD rate (%)	OR	95% CI
Duration of breast feeding					
No breast feeding (consumption only infant formula)	286	17	5.94	1.07	0.49–2.35
<3 months breast feeding (exclusive breast feeding in first 3 months of life)	976	71	7.27	1.33	0.69–2.57
≥3 months breast feeding	198	11	5.56	1.00	(referent)
Acute bronchiolitis					
Yes	111	11	9.91	1.52	0.58–2.45
No	1349	88	6.52	1.00	(referent)
Older siblings					
0	661	47	7.11	1.00	(referent)
1	171	12	7.02	0.94	0.82–1.08
≥2	928	59	6.36	1.03	0.95–1.12
BCG vaccine					
Yes	1451	99	6.82	-	-
No	7	0	0	-	-
HBV vaccine					
Yes	1420	96	6.76	1.00	(referent)
No	38	3	7.89	1.18	0.36–3.91
Polio vaccine					
Yes	1439	98	6.81	1.32	0.17–9.95
No	19	1	5.26	1.00	(referent)
DTP vaccine					
Yes	1441	97	6.73	1.00	(referent)
No	17	2	11.76	1.76	0.23–6.51
<i>Haemophilus influenza</i> type b vaccine					
Yes	663	56	8.45	1.69	1.07–2.44*
No	795	43	5.41	1.00	(referent)
Furry pets at home					
Yes	500	30	6.00	1.00	(referent)
No	1260	88	6.98	1.19	0.58–1.36
Carpets at home					
Yes	115	9	7.83	1.20	0.59–2.43
No	1645	109	6.63	1.00	(referent)
Cockroaches at home					
Yes	1366	86	6.30	1.00	(referent)
No	394	32	8.12	1.32	0.86–2.01
Fungus at house wall (per increment of one wall)					
No	1189	58	4.88	1.00	(referent)
1	338	36	10.65	2.33	1.51–3.59*
2	131	14	10.69	2.33	1.26–4.31*
3	46	3	6.52	1.36	0.41–4.52
≥4	56	7	12.50	2.79	1.21–6.42*
Moving into a new house					
Yes	61	8	13.11	2.18	1.01–4.70*
No	1699	110	6.47	1.00	(referent)
House with newly brushed paints					
Yes	102	11	10.78	1.75	0.91–3.38
No	1658	107	6.45	1.00	(referent)
Environmental exposure to tobacco smoke					
>1 time per week	1003	64	6.38	1.00	(referent)
No	756	54	7.14	1.14	0.61–1.29
Pesticides					
>1 time per week	761	46	6.04	1.00	(referent)
No	999	72	7.21	1.20	0.82–1.77
Frequent use of natural gas heater					
>5 times per week	1296	90	6.94	1.16	0.75–1.80
No	464	28	6.03	1.00	(referent)

Table 3. (Continued)

Variable	No. of subject	No. of AD	AD rate (%)	OR	95% CI
Frequent use of electric magnetic oven					
>5 times per week	399	36	9.02	1.56	1.03–2.33*
No	1361	82	6.02	1.00	(referent)
Frequent use of microwave oven					
>5 times per week	730	66	9.04	1.89	1.28–2.72*
No	1030	52	5.05	1.00	(referent)
Frequent use of baking oven					
>5 times per week	616	43	6.98	1.07	0.73–1.58
No	1144	75	6.56	1.00	(referent)

*p < 0.05.

Table 4. Multivariate analysis of risk factors for infant atopic dermatitis

Variable	No. of Subject	No. of AD	AD rate (%)	aOR	95% CI
Fungi at house wall					
Yes	1139	81	7.11	2.14	1.41–3.22*
No	321	18	5.61	1.00	(referent)
Frequent use of microwave oven					
>5 times per week	38	3	7.89	1.71	1.13–2.58*
No	1420	96	6.76	1.00	(referent)

*p < 0.05.

aOR, adjusted odds ratio; CI, confidence interval.

The following potential confounders were included in the multivariate models: maternal age and education, family history of atopy, infant gender, and gestational age. After stepwise multivariate logistic regression, only fungi at house wall and frequent use of microwave oven were left in the model.

only 6 months of age before every infant had experienced each season. Available evidence from the literature suggested that early solid feeding may increase the risk of infant AD; however, we did not include age of introduction to solid foods and consumption of highly allergenic foods in the analysis because the age of introduction of non-staple foods was usually after 6 months in Taiwan and in this study infants were all <6 months of age.

Prenatal predictors

Little is known about the effects of maternal diet, supplementation, and Chinese herbal mixture use during pregnancy on the risk of AD in the offspring. Some studies proved that deep fish oil could modify immune responses in infants after maternal dietary supplementation during pregnancy because of potential role of anti-inflammatory n-3 polyunsaturated fatty acids (10). Although no significant difference in the frequency of AD was identified in our study, fish oil suggests a potential protection.

Chinese traditionally consider that supplementation of herbal medicine during pregnancy may strengthen the body of the mother and can make the skin of the infant beautiful. It is believed that pearl powder contains various kinds of amino acids, trace elements, and calcium which have anti-aging effect and can refresh the skin in humans (11). However, we did not find a significant relationship between pearl powder and early infantile AD. Some studies actually demonstrated that Chinese herbal mixtures were useful as an alternative therapy for atopic eczema. However, the results were heterogeneous (12). Further well-designed and larger randomized controlled trials are required to determine whether prenatal supplementation or Chinese herbal medicine can reduce the risk of atopic diseases.

Postnatal environmental factors

The correlation and mechanism of fungus and AD have not been well understood. AD may be associated with chronic dermatophytic infections. In contrast, dermatophytes in the skin may cause allergic reaction leading to dermatitis (13). Preliminary data from a Danish-Swedish investigation had shown that AD patients with head-neck-shoulder dermatitis demonstrated positive prick test and specific IgE to *Pityrosporum ovale* more often than normal individuals. These findings indicated that the presence of *P. ovale* on the skin might cause an allergic reaction leading to AD (14). Some studies found that sensitization to fungi is prevalent in childhood with an age-dependent distribution reaching maximum values at 7 years (15, 16). Other previous studies reported that fungal colonization might be detected as early as 2 months (14, 17). However, the exact onset of the fungi influence and sensitization had not been established. We found that fungi may play a role in the development of AD in the first 6 months of age. Even after adjusting for potential confounders, fungi remained the important risk factor for early infantile AD and had dose and response relationship.

If fungi were a significant risk factor for AD in infants as early as 6 months old, an interesting question arises. How can fungi enter the bodies of such young infants? Do they enter by inhalation as an aeroallergen or by direct invasion via skin? Routes of allergen entry are important for the outcome of the resultant allergic reactions. Terui et al. (18) found that levels of immunoglobulin E (IgE) against airborne allergens, which enter the body mainly through the respira-

tory tract, were higher in AD with asthma and allergic rhinitis. On the contrast, levels of IgE against allergens such as *Candida albicans* and *Malassezia furfur*, which can colonize the skin, were higher in pure AD. Some AD show immediate reactions while others show delayed-type hypersensitivity responses to fungal allergens (18). Further research on the mechanism of fungi impacts on AD in the early life seems warranted.

It is very fascinating that we found microwave oven enhanced the risk of AD. The possible mechanisms are that exposure to microwave radiation might have thermal effects and enhance allergic responses with a concomitant increased release of substance P, vasoactive intestinal peptide and nerve growth factor, and skewing of the cytokine pattern toward Th2 type (19–21). Adjustment for several potential confounders did not change the estimates for the effect of microwave on AD substantially. Therefore, the health risk of microwave should be paid more attention. More detailed follow-up studies are required in larger cohorts to establish the robustness of these findings and to ascertain their significance in relation to longer-term modification of AD in children.

Another interesting finding is that moving into a new house potentially increased the risk of AD. Moving into a new dwelling might increase the chemical indoor exposure of formaldehyde and volatile organic compounds (VOCs) to infants either through inhalation or contact. The major source of formaldehyde in the home is the building materials. It can cause burning sensations in throat, nausea, asthma attack, contact dermatitis, and severe allergic reactions (22). VOCs can be found in newly painted dwellings (23). They are widely used as ingredients in household products, including paints, wax, building materials, furnishings, and pesticides. Throat irritation, fatigue, allergic skin reaction, and damage to liver and kidney are found to be associated with inadequate exposures. The reported association between cord blood IgE levels and placental persistent organic pollutant levels has raised concerns about potential immunological effects early in life (24). Therefore, our finding indicated that exposure to indoor chemicals should be minimized from birth on to prevent allergies. As to the sources of combustion products in homes, environmental tobacco smoke, natural gas heaters, and baking oven are common. The major pollutants are carbon monoxide, nitrogen dioxide, and particles, which are released when fuels are incompletely burned. We did not find significant associations between indoor combustion products and AD in our

study. This might be explained by the fact that the indoor air pollutants might irritate lung tissue and mainly cause respiratory symptoms and asthma instead of skin disease (25).

In our study, we found that *H. influenza* vaccination had potential effects in the promotion of AD. This was consistent with the 'hygiene hypothesis', which demonstrated that increased immunization in modern society had led to decreased Th1-type responses and the development of atopic diseases (26, 27). Some studies found little evidence for an association between this vaccination and some atopic outcomes (28, 29). The reasons for this controversy included different age of study population, ethnicity and, possibly, different adjusting potential confounders. Further follow up of this cohort might give us an answer.

The strengths of our study include the large sample size and the population-based cohort design and because of the large sample size we were able to control for numerous potential confounders. The multistage, stratified systematic sampling including both urban, suburban, and rural population has enhanced generality. Our study is limited by the use of maternal report of doctor-diagnosed AD as the outcome variable, which might not be so specific as the standard diagnostic criteria of AD. However, maternal report of doctor-diagnosed AD has been previously validated versus clinical examination in a study performed in the United States (30). Another limitation is the measurements of dose-response relationships in maternal supplementation during pregnancy and exposure levels of environmental smoking, chemicals, microwave, and electric magnetic wave. Quantification of the maternal supplementation and Chinese herbal medicine use during pregnancy is very difficult because of its variability and recall bias. Pregnant women might purchase Chinese herbal medicine and supplementation without doctors' prescription at any time. Although we assessed visible molds during the home interview, environmental tobacco smoke exposures were collected by parental report of any smoking in the home by a resident. Further measurements in the infant's bedrooms using passive sampling systems will be tried to identify the true causal relationship.

In conclusion, we observed an increased risk of early infantile AD with fungi in walls of houses and frequent use of microwave oven at home. Environmental factors do play a influential role in infant AD as early as 6 months of age. Fungi are especially important in humid climates prevalent in Taiwan. An enhanced understanding of

the environmental causes of infant atopic diseases will allow for early prevention of these increasingly frequent diseases.

Acknowledgments

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References

1. DIEPGEN TL. Is the prevalence of atopic dermatitis increasing? In: WILLIAMS HC, ed. *Epidemiology of Atopic Eczema*. Cambridge: Cambridge University.
2. YAN DC, OU LS, TSAI TL, WU WF, HUANG JL. Prevalence and severity of symptoms of asthma, rhinitis, and eczema in 13- to 14-year-old children in Taipei, Taiwan. *Ann Allergy Asthma Immunol* 2005; 95: 579–85.
3. ARRUDA LK, SOLE D, BAENA-CAGNANI CE, NASPITZ CK. Risk factors for asthma and atopy. *Curr Opin Allergy Clin Immunol* 2005; 5: 153–9.
4. GUSTAFSSON D, SJOBERG O, FOUCARD T. Development of allergies and asthma in infants and young children with atopic dermatitis—a prospective follow-up to 7 years of age. *Allergy* 2000; 55: 240–45.
5. CHUANG CH, CHANG PJ, HSIEH WS, et al. A combined effect of employment status and trans-cultural marriage on breast feeding: a population-based survey in Taiwan. *Paediatr Perinat Epidemiol* in press.
6. CHUANG CH, HSIEH WS, GUO YL, et al. Chinese herbal medicines used in pregnancy: a population-based survey in Taiwan. *Pharmacoepidemiol Drug Saf* in press.
7. MOORE MM, RIFAS-SHIMAN SL, RICH-EDWARDS JW, et al. Perinatal predictors of atopic dermatitis occurring in the first six months of life. *Pediatrics* 2004; 113: 468–74.
8. BENN CS, BENFELDT E, ANDERSEN PK, OLESEN AB, MELBYE M, BJORKSTEN B. Atopic dermatitis in young children: diagnostic criteria for use in epidemiological studies based on telephone interviews. *Acta Derm Venereol* 2003; 83: 347–50.
9. KUSUNOKI T, ASAI K, HARAZAKI M, KOREMATSU S, HOSOI S. Month of birth and prevalence of atopic dermatitis in schoolchildren: dry skin in early infancy as a possible etiologic factor. *J Allergy Clin Immunol* 1996; 103: 1148–52.
10. DUNSTAN JA, MORI TA, BARDEN A, et al. Fish oil supplementation in pregnancy modifies neonatal allergen-specific immune responses and clinical outcomes in infants at high risk of atopy: a randomized, controlled trial. *J Allergy Clin Immunol* 2003; 112: 1178–84.
11. CAO G, XU Z, WEI H, YAO S, LIU Y. Pearl and mother-of-pearl powder in health-care. *Zhongguo Zhong Yao Za Zhi* 1996; 21: 635–8.

12. KOBAYASHI H, MIZUNO N, TERAMAE H, et al. Diet and Japanese herbal medicine for recalcitrant atopic dermatitis: efficacy and safety. *Drugs Exp Clin Res* 2004; 30: 197–202.
13. SVEJGAARD E, FAERGEMAN J, JEMEC G, KIEER M, OTTEVANGER V. Recent investigations on the relationship between fungal skin diseases and atopic dermatitis. *Acta Derm Venereol Suppl* 1989; 144: 140–2.
14. BROBERG A. *Pityrosporum ovale* in healthy children, infantile seborrhoeic dermatitis and atopic dermatitis. *Acta Derm Venereol Suppl* 1995; 191: 1–47.
15. NOLLES G, HOEKSTRA MO, SCHOUTEN JP, GERRITSEN J, KAUMAN HF. Prevalence of immunoglobulin E for fungi in atopic children. *Clin Exp Allergy* 2001; 31: 1564–70.
16. WANG IJ, LIN YT, YANG YH, et al. Correlation between age and allergens in pediatric atopic dermatitis. *Ann Allergy Asthma Immunol* 2004; 93: 334–8.
17. BROBERG A, FAERGEMANN J, JOHANSSON S, JOHANSSON SG, STRANNEGARD IL, SVEJGAARD E. *Pityrosporum ovale* and atopic dermatitis in children and young adults. *Acta Derm Venereol* 1992; 72: 187–92.
18. TERUI T, MAKINO Y, HASHIMOTO A, TAGAMI H. Learning from fungus allergy in atopic dermatitis patients. *Nippon Ishinkin Gakkai Zasshi* 2000; 41: 157–60.
19. KIMATA H. Microwave radiation from cellular phones increases allergen-specific IgE production. *Allergy* 2005; 60: 838–9.
20. KIMATA H. Enhancement of allergic skin wheal responses in patients with atopic eczema/dermatitis syndrome by playing video games or by a frequently ringing mobile phone. *Eur J Clin Invest* 2003; 33: 513–7.
21. KIMATA H. Enhancement of allergic skin wheal responses by microwave radiation from mobile phones in patients with atopic eczema/dermatitis syndrome. *Int Arch Allergy Immunol* 2002; 129: 348–50.
22. KASHANI MN, GOROUHI F, BEHNIA F, NAZEMI MJ, DOWLATI Y, FIROOZ A. Allergic contact dermatitis in Iran. *Contact Dermatitis* 2005; 52: 154–8.
23. DIEZ U, KROESSNER T, REHWAGEN M, et al. Effects of indoor painting and smoking on airway symptoms in atopy risk children in the first year of life results of the LARS-study. *Leipzig Allergy High-Risk Children Study. Int J Hyg Environ Health* 2000; 203: 23–8.
24. NOAKES PS, TAYLOR P, WILKINSON S, PRESCOTT SL. The relationship between persistent organic pollutants in maternal and neonatal tissues and immune responses to allergens: A novel exploratory study. *Chemosphere* 2006; 63: 1304–11.
25. COELHO C, STEERS M, LUTZLER P, SCHRIVER-MAZZUOLI L. Indoor air pollution in old people's homes related to some health problems: a survey study. *Indoor Air* 2005; 15: 267–74.
26. BENN CS, MELBYE M, WOHLFAHRT J, BJORKSTEN B, AABY P. Cohort study of sibling effect, infectious diseases, and risk of atopic dermatitis during first 18 months of life. *BMJ* 2004; 328: 1223.
27. ADLER UC. The influence of childhood infections and vaccination on the development of atopy: a systematic review of the direct epidemiological evidence. *Homeopathy* 2005; 94: 182–95.
28. BERNSEN RM, KOES BW, DE JONGSTE JC, VAN DER WOUDE JC. Haemophilus influenzae type b vaccination and reported atopic disorders in 8–12-year-old children. *Pediatr Pulmonol* 2006; 41: 463–9.
29. LAUBEREAU B, GROTE V, HOLSCHER G, et al. Vaccination against Haemophilus influenzae type b and atopy in east German schoolchildren. *Eur J Med Res* 2002; 7: 387–92.
30. LAUGHTER D, ISTVAN JA, TOFTE SJ, HANIFIN JM. The prevalence of atopic dermatitis in Oregon schoolchildren. *J Am Acad Dermatol* 2000; 43: 649–55.

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