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Dissociation between the Prevalence of Atopy and Allergic Disease in Rural China among Children and Adults

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Abstract

Background—The prevalence of allergic diseases is increasing worldwide, but the reasons are not well understood. Previous studies suggest that this trend may be associated with lifestyle and urbanization.

Objective—To describe patterns of sensitization and allergic disease in an unselected agricultural Chinese population.

Methods—The data was derived from a community-based twin study in Anqing, China. Skin prick testing was performed to foods and aeroallergens. Atopy was defined as sensitization to ≥1 allergen. Allergic disease was ascertained by self-report. The analysis was stratified by sex and age (children [11-17 years] and adults [≥18 years]) and included 1059 same-sex twin pairs.

Results—Of 2118 subjects, 57.6% were male (n=1220). Ages ranged from 11-71 years; 43.3% were children (n=918). Atopy was observed in 47.2% (n=999) of participants. The most common sensitizing foods were shellfish (16.7%) and peanut (12.3%). The most common sensitizing aeroallergens were dust mite (30.6%) and cockroach (25.2%). Birth order and zygosity had no effect on sensitization rates. Multivariate logistic regression models revealed risk factors for sensitization include age for foods and sex for aeroallergens. The rates of food allergy and asthma were estimated to be <1%.

Conclusions—Atopic sensitization was common in this rural farming Chinese population, particularly to shellfish, peanut, dust mite, and cockroach. The prevalence of allergic disease, in contrast, was quite low.

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Clinical Implications—Allergen sensitization was far more common than the rate of self-reported allergic disease in this community. Evidence of sensitization is an inadequate marker of allergic disease and better correlates with clinical disease are needed.

Capsule summary—Among this large unselected Chinese rural farming community, atopy was observed in nearly half of the study subjects, but the rate of allergic disease was comparatively very low.

Keywords

aeroallergens; rural; farming community; Chinese; food allergens; prevalence; sensitization; skin prick tests

Introduction

The prevalence of allergic diseases such as asthma and allergic rhinitis (AR) has increased worldwide. However, the reasons are not well understood. One interesting observation is the differential prevalence of allergic diseases across geographic areas and populations. The reported prevalence of atopy is lower in rural areas than in urban areas.[1-3] Several studies suggest that farm children are less likely to develop AR and atopic sensitization.[4-6] For example, a population-based study in Mongolia[1] demonstrated that the prevalence of allergic sensitization increased significantly with increasing urbanization: 13.6% in villages, 25.3% in rural towns and 31.0% in the city. These and other data raise the possibility that allergic diseases may be related to lifestyle and degree of urbanization.

China is a developing country in the midst of rapid economic and cultural transition but the degree of economic development and urbanization varies tremendously across regions. The ISAAC revealed that the prevalence of allergic disease in China is lower than that in the US or Western Europe.[7] The prevalence of asthma and allergic disease in schoolchildren in Hong Kong, however, is higher than that in other parts of China and appears to be increasing.[8] A more recent study[9] used the ISAAC phase II protocol to determine the relationship of sensitization to individual allergens and the development of asthma and bronchial hyperresponsiveness in Chinese children. Atopy, defined as having ≥1 positive SPT, was found in 41.2% of Hong Kong children, 23.9% of Beijing children, and 30.8% of Guangzhou children. Leung et al[10] conducted a case-control study of asthmatic children in Hong Kong. Over 85% were sensitized to *D. pteronyssinus* or *D. farinae*. In addition, 33% were sensitized to cockroach (mixed American and German), 40% to cat dander, and 22% to dog dander.

Prior studies have generally focused on the prevalence of allergen sensitization among populations at increased risk for the development of allergic disease. To date, there is little published data on the prevalence of sensitization to foods in large unselected potentially low risk populations, such as rural communities. The purpose of this study was to determine the prevalence of sensitization to foods and aeroallergens in such a population in China and to determine the prevalence of allergic disease.

Methods

Study site and population

This study utilized an existing population cohort derived from a large-scale, community-based twin study in Anqing that was originally designed to examine environmental and genetic determinants of complex human diseases such as metabolic syndrome. Anqing is a prefecture-level municipality in southwestern Anhui province in the People's Republic of China. The average daily temperature is 60°F. Anqing, located 1048 km (651 miles) due south from Beijing

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and 431 km (268 miles) west of Shanghai, has 3 urban areas and 8 rural counties covering 15,000 km^2. The population was approximately 6.11 million in 2005 (The Government of Anqing, 2007). Anqing includes a farming community that raises cotton, rice, wheat, sweet potatoes, and vegetables. This homogeneous community is stable with little mobility; most residents have lived in this region their whole lives. However, consanguinity is not common.

The baseline study of the twins was carried out from 1998-2000 with follow-up beginning in 2005, when SPT was performed and allergy questionnaire data obtained. Eligible twins were ages 6-65 years upon enrollment and of the same sex. The majority of these twins lived in rural villages. Descriptions of the children[11, 12] and adults[13] of the twin cohort are published elsewhere. The study protocol was approved by the Institutional Review Boards of the Children's Memorial Hospital and the Anhui Medical University Biomedical Institute. Written informed consents were obtained from all study subjects.

Study population and ascertainment of twins and zygosity

This was a general population sample of rural Anhui Province, China. The analysis included 1059 twin pairs (n=2118) with an age range of 11-71 years. Zygosity was determined in 95% of our cohort by DNA fingerprinting, which has an accuracy rate exceeding 99%.[14] Of 1010 twin pairs (n=2020) in whom zygosity was determined, 65.8% (n=1328) were monozygotic.

Skin prick testing (SPT)

SPT was performed on the volar surface of the arms on normal skin using Multi-Test II (Lincoln Diagnostics, Decatur, IL). Subjects were tested to 14 allergens, including common indoor aeroallergens (house dust mite mix [equal parts mixture of *D. farinae* and *D. pteronyssinus*], cat hair, dog epithelia, cockroach mix [American and German cockroach] *Alternaria tenuis)* and 9 common food allergens (cow milk, egg white, soybean, wheat, peanut, English walnut, sesame seed, fish mix [cod, flounder, halibut, mackerel, tuna], and shellfish mix [clam, crab, oyster, scallops, shrimp]) plus negative (50% glycerinated saline) and positive (histamine, 1.0 mg/mL) controls (Greer, Lenoir, NC). The results were measured 15 minutes after application, and the mean wheal diameter was calculated and recorded. The test was considered positive if the mean wheal diameter was ≥3 mm than the saline control. Data was excluded if the saline control was ≥3 mm, the histamine control was <3 mm, or if the difference of histamine minus saline was <3 mm.

Laboratory testing

Total circulating eosinophil counts were assessed in 2107 subjects (99.5%) manually by a trained technician. Total serum IgE levels were examined in 399 subjects (18.8%). Sampling was independent of atopic status or sex. Elevated total serum IgE was defined as >333 kU/L as such elevations after 14 years of age are strongly associated with atopic disorders such as AR, extrinsic asthma, and AD.[15, 16] Total and specific IgE levels via ImmunoCAP technology were obtained (Phadia, Sweden).

Questionnaire data

Questionnaire data were obtained, including self-reported diagnoses of physician-diagnosed allergic disease: asthma, AR, eczema or atopic dermatitis (AD), and food allergy (FA). FA symptoms were gathered from the questionnaire-based interview. Clinical criteria for symptomatic food allergy were met if typical symptoms of an allergic reaction to a food with onset within 2 hours of ingestion were reported. Symptoms included any one of the following: skin (hives or angioedema); respiratory tract (difficulty breathing, shortness of breath, repetitive coughing, wheezing, chest tightness); oropharyngeal (throat tightness, choking, or difficulty swallowing; tongue swelling); cardiovascular (fainting, dizziness, light-headedness, or decreased level of consciousness); or gastrointestinal (vomiting).

The questionnaire was created by study investigators and was not validated, except for respiratory symptoms and diseases (asthma and AR), for which the ATS questionnaire was utilized. Participants were also asked about diet, environmental exposures, and history of personal and parental atopic disease. The questionnaire was translated into Chinese and then back translated into English by bilingual investigators in consultation with local physicians. The questionnaire was piloted in Anqing prior to initiation of the formal study and administered by trained field staff via a face-to-face interview. Literacy and level of education was also assessed by our questionnaire.

Statistical analysis

Subjects were stratified into 2 age groups: 11-17 years (children) and ≥18 years (adults). The sex-specific prevalence of sensitization was calculated for each food and environmental allergen. For categorical values, chi-square test was used to test sex differences within each age group and age differences within each sex. The prevalence of sensitization between twin A (1st born twin) and twin B (2nd born twin) within each biological pair was also assessed, stratified by age and sex. Multivariate logistic regression models of potential risk factors for sensitization to foods and aeroallergens were also performed with and without being stratified by age and sex. Since these associations were not modified by age and sex, only the full models (with age and sex included as exposure variables) are presented. Generalized estimating equations were applied in all regression models. .

Results

This study included 2118 participants aged 11-71 years from a population-based twin cohort. Characteristics of the subjects are shown in Table 1. Approximately half of the cohort was <18 years. Farming was a common occupation among adults (36.2%). Among 596 twin pairs with complete occupational data, 70.8% had the same occupation.

Overall prevalence of atopy

Atopy was observed in 47.2% (n=999) of subjects, of whom 63.6% were sensitized to ≥2 allergens (Table 2). A higher percentage of children were atopic compared to adults (51.7% vs. 43.8%, p<0.01). Overall, more males were atopic than females (50.4% vs. 42.8%, p<0.01).

Sensitization to food allergens

Among 918 children, 29.7% had positive SPT at least one food. Among 1200 adults, 21.9% were sensitized to at least one food (Table 2). Overall, the most common sensitizing food allergens were shellfish (16.7%) and peanut (12.3%) (Table 3). Generally, wheal sizes were small (range 3.5-3.8 mm). Only one participant (32 year-old male) had a skin prick test ≥8 mm, which was to peanut, but he did not report peanut allergy.

Sensitization to aeroallergens

Among children, 41.1% were sensitized to ≥1 aeroallergen while 36.5% of adults were sensitized (Table 2). The most common sensitizing aeroallergens were dust mites (30.6%) and cockroach (25.2%), with a higher prevalence in males (p<0.01 for both allergens) (Table 3). Sensitization to dog and cat was uncommon. The median wheal size for each aeroallergen ranged from 3.5-4.3 mm (Table 4).

Co-existing sensitization to foods and aeroallergens

Notably, among subjects sensitized to allergens containing tropomyosin, the proportion of co-existing sensitization to each of the other allergens was quite high (Table 4). The prevalence of sensitization to soy was much lower than that for peanut despite the fact both are legumes (Table 3). Among those sensitized to peanut, only 16.1% (n=42) was also co-sensitized to soy.

Prevalence of sensitization by twin birth order

The prevalence of sensitization to each allergen between twin A and twin B of each pair was assessed by age (11-17 years vs. ≥18 years) and sex (data not shown). There were no statistically significant differences in the prevalence of sensitization between twin A and twin B among male children. Among the other groups (female children, male adults, and female adults), there was only one allergen in each group (*Alternaria tenuis*, wheat, and peanut, respectively) that was found to be dissimilar statistically between twin A and twin B ($p<0.05$).

Prevalence of sensitization by zygosity

Stratified by age and sex, the prevalence of sensitization to each allergen among MZ twins as a group was similar to that among DZ twins. However, concordance rates for skin test positivity were slightly higher among MZ twins than DZ twins for almost all groups. (Table E1).

Correlations of sensitization with self-reported allergic disease

Seventy-four subjects (3.5%) reported FA of which 41.9% (n=31) were children. Of these 74 subjects, 14 individuals were twin pairs (6 MZ twin pairs and 1 pair with missing zygosity data). Seven subjects (9.5%) (including one twin pair) claimed peanut allergy, of which only one had a positive skin test to peanut (female, 14.4 years old). This subject, along with 2 others, failed to report any symptoms with peanut ingestion. Of the 4 who reported symptoms with peanut ingestion, 2 subjects reported lip itching/tingling and 2 reported diarrhea.

Of the 28 subjects (3 MZ twin pairs) who reported shellfish allergy, 21 reported symptoms with ingestion and 7 had missing data. Six (21.4%) subjects had positive SPTs to shellfish mix, and the mean wheal size was 4.2 mm (SD 0.9). Of these six, 5 reported symptoms, and 1 had missing data. The majority of subjects reporting shellfish allergy were adults (64.3%, n=18).

The other reported FA included fish (10 including 1 MZ twin pair), egg (9), fruit (5 including 1 MZ twin pair), wheat (4), bean (3), milk (1), and food additives (1). Six subjects did not specify the allergen.

Based on questionnaire data, only 16 subjects (0.8%) indicated current or prior asthma, including one MZ twin pair. Three people (0.1%) reported a pet allergy. Thirty-five subjects (1.7%), including 4 twin pairs (2 MZ, 1 DZ, 1 unknown), reported current or prior diagnosis of AR. Of these 35 subjects, less than half (n=15, including 1 DZ twin pair, or 42.9%) had positive SPTs to at least one aeroallergen. Two hundred eighty subjects (13.3%), including 59 twin pairs (43 MZ, 15 DZ, 1 unknown), reported current or prior AD: 83 (29.6%), including 14 twin pairs (11 MZ, 3 DZ), had positive SPTs to at least one food and 124 (44.3%), including 21 twin pairs (17 MZ, 4 DZ), had positive SPTs to at least one aeroallergen.

Other markers of allergic disease

Eosinophil counts were also ascertained, but only 0.24% of our cohort had an absolute eosinophil count (AEC) of >400 cells/μl. This may indicate a low likelihood of parasitic disease. None of the 5 participants with an AEC>400 reported any allergic disease diagnoses within the previous year.

Total IgE was obtained in <20% of the cohort.. The range for total IgE was 2.01-4338.00 (median 93.80 kU/L). Elevated IgE (>333 kU/L) was observed in 14.8% (n=59, median 342.00 kU/L). The association between total IgE (>333 kU/L vs ≤333 kU/L [reference group]) and self-reported allergic disease was not significant (OR=2.0, 95%CI 0.7-6.1, p=0.21, adjusted for age and sex). However, this was insufficiently powered as only 21 subjects (among those with total IgE data) reported current or past allergic disease. The correlation between elevated total IgE and SPT positivity was moderate but similar between males and females in both children and adults (Table E2). SPTs are also compared to specific IgE values in Table E3. Overall, there was good agreement between SPT and specific IgE levels.

Multivariate analyses

Table 5 reveals the multivariate logistic regression model of potential risk factors for sensitization to foods or aeroallergens. Sensitization to at least one food was associated only with younger age (11-17 years). All other factors (gender, pets, farm animals, mice, cockroaches, breastfeeding, or tobacco exposure) were not found to be significantly associated with food sensitization. Similarly, sensitization to at least one aeroallergen was associated only with male gender. Family history of atopy (parent with asthma, AD, AR, or FA) was reported only by 69 subjects (3.3%). There was no association between having a family history of atopy and sensitization to a food or aeroallergen (data not shown). Education and occupation (but not socioeconomic status) were included in the analysis, but neither were significantly associated with atopy in this cohort. This in part may be due to the fact that this was a relatively homogeneous population sample in terms of observed variables.

Discussion

This study has several interesting findings. First, we found evidence of sensitization to foods or aeroallergens in nearly half of this unselected rural Chinese cohort of twins. The prevalence of sensitization may have been even higher if regional pollens, such as trees and grass, had been included. Moreover, food allergy is more common among children than adults and is most prevalent among children in the first few years of life. The children in our study were older (>10 years). Therefore, the rate of food sensitization may have been even higher in this population if younger children had been studied. In contrast to findings among the general population[17-20], birth order within each twin pair did not have a significant effect on the rates of sensitization to the vast majority of allergens tested. This may be partly explained by the common prenatal environment that each twin pair shared, regardless of whether the twins were MZ or DZ.

The prevalence of atopy in our cohort is unexpected based on our hypothesis, and much higher than that found in other rural populations in Europe.[21-23] Since 1999, almost all of the 15 studies performed in rural areas in Europe[21] have reported a lower prevalence of atopic sensitization among farm children compared with non-farm children.[22] Growing up on a farm has been found to have a protective effect on atopic sensitization as well as allergic disease. In the PARSIFAL[23] study, atopic sensitization (using *in vitro* methods) was identified in 22.7% of farm children, which was lower than our findings. It has been postulated that the protective farm effect is due, at least in part, to exposure to livestock and farm animals. However, in our multivariate logistic regression, the presence of farm animals was not protective for atopic sensitization. However, this may be accounted for by the pervasive exposure (≥75%) to farm animals. We cannot adequately assess rural vs. urban differences among this cohort. Other proxies for microbial exposures, including exposure to pets, mice, and cockroaches, were also not found to be protective factors for atopic sensitization. We did not, however, explore whether our study subjects had these same exposures in early childhood. We hypothesize that they may have, given the limited mobility of this population.

The reasons for the high prevalence of sensitization may in part be due to the presence of a pan-allergen. Of the four most common sensitizing allergens, three share a homologous protein: tropomyosin. This could explain the high prevalence of sensitization to these particular allergens. Cockroaches are commonly found in homes worldwide but specific allergen levels within mainland China are not well documented in the literature. Studies have previously established detectable levels of house dust mite allergen in Hong Kong,[24] Taiwan,[25] and mainland China.[26] However, only 6.5% of participants (n=138) were sensitized to all three allergens (shellfish, cockroach, and dust mite) in our study. There are likely to be other reasons that are yet to be determined.

Second, in this study cohort, the most common sensitizing food allergens were shellfish (16.7%) and peanut (12.3%), with prevalence higher in children than adults ($p<0.001$ for both allergens). This is consistent with previous literature. The common food allergens in China are fish, shrimp, and crab.[27, 28] One retrospective review of anaphylaxis within a Hong Kong emergency department (in a predominantly ethnic Chinese community) reports that 71% of all food-related reactions were due to seafood.[29] However, the prevalence of seafood allergy in mainland China is less well defined. In our cohort, shellfish mix (clam, crab, oyster, scallops, and shrimp) was the most commonly sensitizing food extract. In contrast, sensitization to fish mix (cod, flounder, halibut, mackerel, and tuna) was much less common (2.0%). It is possible that these types of fish are not the most commonly ingested fish among this population.

In general, MZ twins had higher concordance rates than DZ twins. However, we did not find a substantial difference between MZ and DZ twins with regard to atopy or atopic disease. Our findings suggest that zygosity itself is not a risk factor. This is supported by Strachan et al[30] who previously demonstrated that genetically identical twins are often discordant in their expression of atopy.

Finally, and most interestingly, we found a dramatic dissociation between skin test positivity and prevalence of allergic disease among this rural Chinese cohort. A recently published ISAAC study[31] found that the link between atopy and asthma symptoms is strongest among populations with increased economic development. The average annual net income of Anqing farmers in 2006 was 2970 Chinese Yuan per person (~US$407) while in the urban Anqing population, it was 9483 Chinese Yuan per person (~US$1299). Overall, Anqing (both rural and urban) has experienced economic growth at a rate of over 10% annually. Compare this to the gross national income per capita for Hong Kong, which is approximately US$25,000. [31] Hong Kong is a highly westernized city with a subtropical climate. In contrast, Anqing consists of rural farming communities and is located 943 km (586 miles) north of Hong Kong. Despite the high rate of atopic sensitization in our cohort, the prevalence of self-reported physician-diagnosed allergic disease was quite low, as expected for the region.

In contrast to the high rates of sensitization to foods (nearly 30% of children and over 20% of adults), only 3.5% reported a history of FA. Prior studies in Western populations have established that self-reports of FA generally overestimate (by up to 4 times) the true prevalence,[32, 33] indicating that the true prevalence of FA in this Chinese cohort is likely to be even lower. Also it has been reported that the diagnostic capacity of SPTs to foods is highly variable.[34, 35] Food challenges were not performed to confirm the diagnosis in our study. However, when specific food allergens were examined, for example, peanut and shellfish, only a small minority of subjects with self-reported FA to these allergens had symptoms in addition to positive skin test results. Therefore, despite relatively high sensitization rates to foods, the rate of disease (based on self-report combined with positive skin test) was comparatively quite low (<1%), thereby further indicating that skin testing to foods has a relatively high false positive rate. We do not believe that parasitic disease accounts for the dissociations, based on lack of peripheral eosinophilia, a crude marker for parasitosis.

Although this cohort was tested to only 5 aeroallergens, the rate of sensitization was quite high (38.5%) in contrast to a low prevalence of reported asthma (current or past) of <1% in this unselected Chinese rural population. The clinical significance of wheal sizes of positive SPTs to aeroallergens is unclear. The rates of allergic rhinitis, hay fever, and pet allergy were comparable to that of asthma.

This study is limited because only sensitization was evaluated and the prevalence of allergic disease in this cohort was not confirmed, particularly for FA. However, food challenges would have been impractical and costly in such a large cohort. The Multi-Test II device has been shown to produce larger wheal sizes than the ALK lancet for example[36] and may have the potential to increase the rate of falsely positive results.[37] Overall, the wheal sizes were small for the foods and aeroallergens tested in our study. The Multi-Test II is easy to administer and the technique has greater potential to be consistent among multiple operators across various locations and allows for the application of multiple extracts with one application.

In conclusion, this is the one of the largest unselected cohorts of children and adults in China to be assessed for sensitization to both foods and aeroallergens. Sensitization was common in this agricultural Chinese population, particularly to shellfish, peanut, dust mites, and cockroach. Atopy was observed in nearly half the total number of subjects. The prevalence of atopic sensitization varied by age and by sex. While sensitization was common, the prevalence of allergic disease was comparatively quite low. It remains to be determined if the rate of allergic disease will increase in this rural community with expanding urbanization and lifestyle changes that become more akin to those in westernized countries.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AD, atopic dermatitis; AR, allergic rhinitis; ATS, American Thoracic Society; DZ, dizygotic; FA, food allergy; ISAAC, International Study of Asthma and Allergies in Childhood; MZ, monozygotic; SPT, skin prick tests or skin prick testing.

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Table 1

Participant characteristics

	11-17 years		18+ years	
	Male (n=510)	**Female (n=408)**	**Male (n=710)**	**Female (n=490)**
Mean ± SD				
Age (years)	15.4±1.3	15.5±1.2	38.9±15.1	34.5±11.7***
Height (cm)	158.2±8.8	151.7±5.6***	162.5±5.9	152.2±5.6***
Weight (kg)	45.7±8.3	44.2±6.6**	56.2±8.0	50.8±6.5***
BMI (kg/m^2)	18.1±2.1	19.2±2.3***	21.3±2.5	21.9±2.6***
n (%)				
Education				
Illiterate	1(0.2)	0(0.0)	64(9.1)	123(25.2)
Primary school	77(15.1)	51(12.5)	228(32.2)	161(32.9)
Junior middle school	311(61.0)	275(67.4)	261(36.9)	146(29.9)
High school & above	121(23.7)	82(20.1)	154(21.8)	59(12.1)***
Occupation	n (%)			
Student	445(87.3)	339(83.3)	78(11.0)	37(7.6)
Farmer	6(1.2)	2(0.5)	245(34.7)	189(38.7)
Others	59(11.6)	66(16.2)	384(54.3)	263(53.8)
Pet, yes	324(63.5)	218(53.4)**	339(48.0)	219(44.8)
Farm animal, yes	411(83.2)	318(81.7)	545(79.3)	362(75.1)
Mice in house				
No	130(25.5)	112(27.5)	218(30.8)	173(35.3)
Yes, occasionally	258(50.7)	203(49.8)	327(46.3)	225(45.9)
Yes, some or many	121(23.8)	93(22.8)	162(22.9)	92(18.8)
Cockroach				
No	297(58.5)	258(63.2)	392(55.4)	287(58.7)
Yes, occasionally	160(31.5)	124(30.4)	250(35.4)	173(35.4)
Yes, some or many	51(10.0)	26(6.4)	65(9.2)	29(5.9)
Breast feeding, yes	273(54.0)	257(63.1)**	409(58.2)	274(56.0)
Current smoking, yes	18(3.6)	0(0.0)***	395(55.9)	17(3.5)***
Passive smoking	359(71.2)	273(69.8)	322(46.3)	345(71.0)***

Sex differences within same age stratum

(Two-sided p-value: t-test for continuous variables and chi-square test or Fisher’s exact test for frequency)

* $p<0.05$

** $p<0.01$

*** $p<0.001$

Table 2

Prevalence and degree of atopy as defined by skin prick tests to foods and environmental allergens stratified by age and sex

Age (years)	11-17			18+			Total		
	Male (n=510)	Female (n=408)	Total (n=918)	Male (n=710)	Female (n=490)	Total (n=1200)	Male (n=1220)	Female (n=898)	Total (n=2118)
Food									
None	352(69.0)	293(71.8)	645(70.3)	553(77.9)	384(78.4)	937(78.1)	905(74.2)	677(75.4)	1582(74.7)
One	92(18.0)	59(14.5)	151(16.4)	98(13.8)	74(15.1)	172(14.3)	190(15.6)	133(14.8)	323(15.3)
Two or more	66(12.9)	56(13.7)	122(13.3)	59(8.3)**	32(6.5)**	91(7.6)***	125(10.2)	88(9.8)	213(10.1)
Environmental									
None	292(57.3)	249(61.0)	541(58.9)	417(58.7)	345(70.4)	762(63.5)	709(58.1)	594(66.1)	1303(61.5)
One	98(19.2)	68(16.7)	166(18.1)	115(16.2)	69(14.1)	184(15.3)	213(17.5)	137(15.3)	350(16.5)
Two or more	120(23.5)	91(22.3)	211(23.0)	78(25.1)†††	76(15.5)**	254(21.2)	298(24.4)†††	167(18.6)	465(22.0)
Any									
None	232(45.5)	212(52.0)	444(48.4)	373(52.5)	302(61.6)	675(56.3)	605(49.6)	514(57.2)	1119(52.8)
One	109(21.4)	67(16.4)	176(19.2)	114(16.1)	74(15.1)	188(15.7)	223(18.3)	141(15.7)	364(17.2)
Two or more	169(33.1)	129(31.6)	298(32.5)	223(31.4)* ††	114(23.3)**	337(28.1)**	392(32.1)††	243(27.1)	635(30.0)

Age difference within same gender

(Two-sided p-values: chi square test for frequency difference of each variable between two age groups for same gender or combined)

Gender difference within same age group

(Two-sided p-values: chi square test for frequency difference of each variable between male and female in each age stratum)

* p<0.05

** p<0.01

*** p<0.001

† p<0.05

†† p<0.01

††† p<0.001

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Table 3

Prevalence of sensitization and wheal diameter distribution of positive SPTs to foods and environmental allergens (mm)[†]

	N (%)	25th %tile	median	75th %tile	max	n ≥8mm (%)
Shellfish	354(16.7)	3.3	3.5	4.3	7.0	0
Peanut	261(12.3)	3.3	3.5	4.3	8.8	1 (0.4)
Egg white	83(3.9)	3.4	3.8	4.3	6.5	0
Soy	78(3.7)	3.3	3.5	4.0	5.5	0
Walnut	54(2.5)	3.3	3.5	4.0	5.5	0
Sesame	50(2.4)	3.3	3.8	4.2	6.1	0
Fish	42(2.0)	3.2	3.5	3.9	5.0	0
Wheat	26(1.2)	3.4	3.6	4.0	5.5	0
Milk	22(1.0)	3.3	3.8	4.0	5.0	0
Dust mite	648(30.6)	3.5	4.3	5.0	16.9	15 (2.3)
Cockroach	533(25.2)	3.5	4.3	5.0	10.0	10 (1.9)
Alternaria tenius	159(7.5)	3.3	3.8	4.3	7.0	0
Dog epithelia	44(2.1)	3.1	3.5	4.0	6.5	0
Cat hair	34(1.6)	3.5	3.8	4.0	8.8	1 (2.9)

Histamine: median wheal size 7.25 mm (range 3.5-13.0) with interquartile range of 1.5 mm

Saline: median wheal size 0 mm with interquartile range of 0 mm

[†]Mean wheal diameter equals the average of the longest perpendicular diameters

Table 4

Co-existing sensitization to allergens containing tropomyosin

Sensitized allergen	Shellfish	Cockroach	Dust mite
# cases (11-17 years)	192	228	302
Shellfish (n [%])		78 (34.2)	113 (37.4)
Cockroach (n [%])	78 (40.6)		184 (60.9)
Dust mite (n [%])	113 (58.9)	184 (80.7)	
# cases (18+ years)	162	305	346
Shellfish (n [%])		78 (25.6)	93 (26.9)
Cockroach (n [%])	78 (48.1)		229 (66.2)
Dust mite (n [%])	93 (57.4)	229 (75.1)	

Table 5

Multivariate logistic regression models of potential risk factors for sensitization to foods or aeroallergens (n=1995)

	Sensitization to at least one food			Sensitization to at least one aeroallergen		
	OR	**%95_CI**	**p value**	**OR**	**%95_CI**	**p value**
Age (years)						
11-17	1			1		
>=18	0.67	0.51,0.89	0.005	0.88	0.69,1.13	0.317
Sex						
male	1			1		
female	0.94	0.72,1.21	0.623	0.7	0.56,0.89	0.003
Education						
Primary school & lower	1			1		
Junior middle school	0.85	0.64,1.13	0.269	1.12	0.87,1.45	0.390
High school & above	0.93	0.65,1.33	0.701	1.30	0.94,1.79	0.114
Occupation						
Farmer	1			1		
Others	1.06	0.76,1.49	0.729	1.05	0.78,1.41	0.734
pet						
No	1			1		
Yes	1.14	0.90,1.43	0.285	1.04	0.84,1.29	0.734
Farm animal						
No	1			1		
Yes	0.93	0.69,1.25	0.637	1.02	0.78,1.33	0.903
Mice in house						
No	1			1		
Yes, occasionally	1.11	0.85,1.46	0.428	1.10	0.87,1.41	0.425
Yes, some or many	0.97	0.70,1.36	0.862	1.11	0.82,1.51	0.484
Cockroach						
No	1			1		
Yes, occasionally	1.08	0.85,1.38	0.514	0.88	0.71,1.10	0.267
Yes, some or many	1.13	0.73,1.76	0.584	0.90	0.61,1.33	0.604
Breast feeding						

	Sensitization to at least one food			Sensitization to at least one aeroallergen		
	OR	**%95_CI**	**p value**	**OR**	**%95_CI**	**p value**
No	1			1		
Yes	1.01	0.81,1.26	0.932	1.03	0.85,1.26	0.743
Current smoking						
No	1			1		
Yes	0.85	0.60,1.20	0.351	0.99	0.73,1.34	0.924
Passive smoking						
No	1			1		
Yes	0.82	0.65,1.04	0.101	1.07	0.87,1.32	0.534

Sample size for this analysis is decreased (from 2118 to 1995) for this analysis due to missing data for some covariates.

Age and sex were not found to modify these associations