

Dissociation between the prevalence of atopy and allergic disease in rural China among children and adults

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

Objective: We sought to describe patterns of sensitization and allergic disease in an unselected agricultural Chinese population.

Methods: The data were derived from a community-based twin study in Anqing, China. Skin prick tests were performed to foods and aeroallergens. Atopy was defined as sensitization to 1 or more allergens. Allergic disease was ascertained by means of 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 to 71 years, and 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 that risk factors for sensitization include age for foods and sex for aeroallergens. The rates of food allergy and asthma were estimated to be less than 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. (*J Allergy Clin Immunol* 2008;122: 929-35.)

Key words: Aeroallergens, rural, farming community, Chinese, food allergens, prevalence, sensitization, skin prick tests

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 have AR and atopic sensitization.⁴⁻⁶ For example, a population-based study in Mongolia¹ 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 might 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 International Study of Asthma and Allergies in Childhood (ISAAC) revealed that the prevalence of allergic disease in China is lower than that in the United States 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 study⁹ 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 or more positive skin prick test (SPT) responses, was found in 41.2% of Hong Kong children, 23.9% of Beijing children, and 30.8% of Guangzhou children. Leung et al¹⁰ conducted a case-control study of asthmatic children in Hong Kong. More than 85% were sensitized to *Dermatophagoides pteronyssinus* or *Dermatophagoides 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 are few 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 used 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,

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Abbreviations used

AD: Atopic dermatitis
 AR: Allergic rhinitis
 DZ: Dizygotic
 FA: Food allergy
 ISAAC: International Study of Asthma and Allergies in Childhood
 MZ: Monozygotic
 SPT: Skin prick test

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 and 431 km (268 miles) west of Shanghai, has 3 urban areas and 8 rural counties covering 15,000 km². 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 to 2000, with follow-up beginning in 2005, when SPTs were performed and allergy questionnaire data were obtained. Eligible twins were ages 6 to 65 years on enrollment and of the same sex. The majority of these twins lived in rural villages. Descriptions of the children^{11,12} and adults¹³ 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 consent was 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 to 71 years. Zygosity was determined in 95% of our cohort by means of 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 (MZ).

SPTs

SPTs were performed on the volar surface of the arms on normal skin with the Multi-Test II (Lincoln Diagnostics, Decatur, Ill). 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], and *Alternaria tenuis*) and 9 common food allergens (cow's milk, egg white, soybean, wheat, peanut, English walnut, sesame seed, fish mix [cod, flounder, halibut, mackerel, and tuna], and shellfish mix [clam, crab, oyster, scallops, and 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 result was considered positive if the mean wheal diameter was 3 mm larger than that elicited by the saline control. Data were excluded if the saline control was larger than 3 mm, the histamine control was less than 3 mm, or the difference of histamine minus saline was less than 3 mm.

Laboratory testing

Total circulating eosinophil counts were assessed in 2107 (99.5%) subjects manually by a trained technician. Total serum IgE levels were examined in 399 (18.8%) subjects. Sampling was independent of atopic status or sex. Increased total serum IgE levels were defined as greater than 333 kU/L because such increases after 14 years of age are strongly associated with atopic disorders,

such as AR, extrinsic asthma, and atopic dermatitis (AD).^{15,16} Total and specific IgE levels were obtained by using ImmunoCAP technology (Phadia, Uppsala, Sweden).

Questionnaire data

Questionnaire data were obtained, including self-reported diagnoses of physician-diagnosed allergic disease: asthma, AR, eczema or AD, and food allergy (FA). FA symptoms were gathered from the questionnaire-based interview. Clinical criteria for symptomatic FA 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, or chest tightness); oropharyngeal (throat tightness, choking, difficulty swallowing, or 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 American Thoracic Society questionnaire was used. 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 before initiation of the formal study and administered by trained field staff in a face-to-face interview. Literacy and level of education were also assessed by using our questionnaire.

Statistical analysis

Subjects were stratified into 2 age groups: 11 to 17 years (children) and 18 years or older (adults). The sex-specific prevalence of sensitization was calculated for each food and environmental allergen. For categorical values, the χ^2 test was used to test sex differences within each age group and age differences within each sex. The prevalence of sensitization between twin A (first-born twin) and twin B (second-born twin) within each biologic pair was also assessed and 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. Because 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 to 71 years from a population-based twin cohort. Characteristics of the subjects are shown in Table I. Approximately half of the cohort was younger than 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 the subjects, of whom 63.6% were sensitized to 2 or more allergens (Table II). A higher percentage of children were atopic compared with adults (51.7% vs 43.8%, *P* < .01). Overall, more male subjects were atopic than female subjects (50.4% vs 42.8%, *P* < .01).

Sensitization to food allergens

Among 918 children, 29.7% had positive SPT responses to at least 1 food. Among 1200 adults, 21.9% were sensitized to at least 1 food (Table II). Overall, the most common sensitizing food

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