Prevalence of allergic sensitization in the United States: Results from the National Health and Nutrition Examination Survey (NHANES) 2005-2006

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Background: Allergic sensitization is an important risk factor for the development of atopic disease. The National Health and Nutrition Examination Survey (NHANES) 2005-2006 provides the most comprehensive information on IgE-mediated sensitization in the general US population.

Objective: We investigated clustering, sociodemographic, and regional patterns of allergic sensitization and examined risk factors associated with IgE-mediated sensitization.

Methods: Data for this cross-sectional analysis were obtained from NHANES 2005-2006. Participants aged 1 year or older (n = 9440) were tested for serum specific IgEs (sIgEs) to inhalant and food allergens; participants 6 years or older were tested for 19 sIgEs, and children aged 1 to 5 years were tested for 9 sIgEs. Serum samples were analyzed by using the ImmunoCAP System. Information on demographics and participants' characteristics was collected by means of questionnaire.

Results: Of the study population aged 6 years and older, 44.6% had detectable sIgEs, whereas 36.2% of children aged 1 to 5 years were sensitized to 1 or more allergens. Allergen-specific IgEs clustered into 7 groups that might have largely reflected biological cross-reactivity. Although sensitization to individual allergens and allergen types showed regional variation, the overall prevalence of sensitization did not differ across census regions, except in early childhood. In multivariate modeling young age, male sex, non-Hispanic black race/ethnicity, geographic location (census region), and reported pet avoidance measures were most consistently associated with IgE-mediated sensitization.

Conclusions: The overall prevalence of allergic sensitization does not vary across US census regions, except in early life, although allergen-specific sensitization differs based on sociodemographic and regional factors. Biological cross-reactivity might be an important but not the sole contributor to the clustering of allergen-specific IgEs. (J Allergy Clin Immunol 2014;134:350-9.)

Key words: *Allergen, allergy, allergic sensitization, serum IgE*

The increased prevalence of allergic diseases is a major public health concern worldwide.[1] In the United States millions of persons are affected by IgE-mediated diseases, which not only affect the quality of life but also place considerable economic burden on patients and society.[2,3]

The common hallmark of atopic disease is the production of serum specific IgE (sIgE) against allergens. Assessment of sIgE antibodies with *in vivo* skin test challenges or *in vitro* serologic analyses confirms allergic sensitization, whereas the patient's clinical history and physical examination remain important cornerstones of the diagnosis of atopic disease.[4] Monitoring the prevalence and patterns of IgE-mediated sensitization in populations over time is important because allergic sensitization is a significant risk factor for the development of atopic disease.[1] In the United States the prevalence of allergic sensitization in the general population has been estimated in 3 National Health and Nutrition Examination Surveys (NHANESs).[5-8] In NHANES II (1976-1980) and III (1988-1994) allergy testing was conducted by using skin prick tests, whereas NHANES 2005-2006 measured sIgE levels in serum. NHANES 2005-2006 provides the largest and most recent nationally representative data on IgE-mediated sensitization in the US population. Participants aged 6 years and older were tested for 19 sIgE antibodies, and those aged 1 to 5 years were tested for a subset of the antibodies (9 sIgEs). NHANES 2005-2006 not only tested a greater number of allergens across a wider age range than the prior studies, but also provided quantitative information on the extent of allergic sensitization.

This article provides a comprehensive report on clustering, sociodemographic, and regional patterns of allergic sensitization in the US population. Patterns of sensitization in NHANES 2005-2006 were compared with NHANES III data. We also identified factors independently associated with IgE-mediated sensitization in the general population.

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Abbreviations used
GM: Geometric mean
NCHS: National Center for Health Statistics
NHANES: National Health and Nutrition Examination Survey
SES: Socioeconomic status
sIgE: Serum specific IgE

METHODS

Data

Data were obtained from NHANES 2005-2006, which is designed to assess the health and nutritional status of the civilian, noninstitutionalized US population. NHANES 2005-2006, which includes 10,348 subjects, oversampled persons of low income, adolescents aged 12 to 19 years, persons 60 years of age and older, African Americans, and Mexican Americans to ensure adequate samples for subgroup analyses. All data analysis with restricted and not publicly available variables (census region, level of urbanization) was conducted at the National Center for Health Statistics (NCHS) Atlanta Research Data Center to protect participant confidentiality. The survey protocol was approved by the NCHS Ethics Review Board,[9] and written informed consent was obtained from all participants. A detailed description of the survey design and methods is available online at http://www.cdc.gov/nchs/nhanes/nhanes2005-2006/nhanes05_06.htm.[10] To examine sensitization patterns over time, we used NHANES III data for comparisons. Study procedures and methods for the NHANES III data have been previously described.[7]

Assessment of allergen-specific IgEs and atopy

Participants aged 1 year and older were eligible for serum IgE testing. Blood samples were analyzed with the Pharmacia Diagnostics ImmunoCAP 1000 System (Kalamazoo, Mich), now known as Thermo Scientific ImmunoCAP Specific IgE. Participants aged 6 years and older were tested for allergen-specific IgE antibodies to 15 inhalant (ie, indoor and outdoor) allergens (*Alternaria alternata*, *Aspergillus fumigatus*, Bermuda grass *[Cynodon dactylon]*, birch *[Betula verrucosa]*, cat dander, cockroach *[Blatella germanica]*, dog dander, dust mite [*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*], mouse urine proteins, oak *[Quercus alba]*, ragweed *[Ambrosia elatior]*, rat urine proteins, Russian thistle *[Salsola kali]*, and rye grass *[Lolium perenne]*) and 4 food allergens (egg white, cow's milk, peanut *[Arachis hypogaea]*, and shrimp *[Pandalus borealis]*). Because of smaller quantities of serum, the IgE panel for children less than 6 years of age was limited to 9 allergens (*Alternaria alternata*, cat dander, cockroach *[Blatella germanica]*, dog dander, dust mite [*D farinae* and *D pteronyssinus*], egg white, cow's milk, and peanut *[Arachis hypogaea]*). Of the participants 6 years of age and older (n = 8086), 89.9% (n = 7268) had data for all 19 specific IgEs, and of the children aged 1 to 5 years, 63.2% (n = 856) had complete data for the partial IgE panel.

The threshold for a positive test result, which was considered indicative of sensitization, was the level of detection (≥0.35 kU_A/L). Subjects with at least 1 positive sIgE result were considered atopic. A detailed description of the laboratory procedures is presented elsewhere.[11,12]

Statistical analyses

Descriptive analyses and predictive modeling were performed with SAS (version 9.2; SAS Institute, Cary, NC) and SUDAAN (version 10.0; RTI International, Research Triangle Park, NC). Cluster analysis was conducted with the R system for statistical computing (version 2.10.1). To account for the complex survey design, survey nonresponse, and poststratification, sampling weights and design variables were applied to all analyses (NHANES 2005-2006, NHANES III) to obtain unbiased national prevalence and variance estimates.

Participants aged 6 years and older and those aged 1 to 5 years were analyzed separately because of the differences in IgE panels. Differences in the prevalence of positive allergen-specific IgE test results by general population characteristics were tested with χ^2 statistics. Among atopic subjects, we used F statistics to test differences in geometric mean (GM) concentrations of sIgEs across population characteristic categories. When evaluating racial/ethnic differences, we focused on the 3 main groups: non-Hispanic white, non-Hispanic black, and Mexican American subjects, excluding the group "others" because of racial/ethnic heterogeneity. To examine clustering of sIgEs, we used different statistical methods, including hierarchic clustering, factor analysis, and multidimensional scaling.

We used logistic regression analysis to identify predictors of specific IgE positivity (ie, sensitization) in the general population. For the predictor modeling, we used sociodemographic and other characteristics associated with skin test positivity in NHANES III.[7] We also included reported pet avoidance measures because avoidance, removal, or both of pets because of allergy or asthma was strongly associated with the overall prevalence of sensitization (data not shown). In the full model we included age, sex, race/ethnicity, poverty/income ratio, education, serum cotinine level, body mass index, year of home construction, census region, level of urbanization, number of household members, household crowding, presence of cats and/or dogs in the home, and reported pet avoidance and used backward elimination for model selection. All of the remaining predictors in the final model had *P* values of .05 or less. We also evaluated potential 2-way interactions between age, sex, and race/ethnicity, but no strong evidence for effect modification was found.

Sensitivity analyses were conducted to determine whether the modeling results were influenced by using a different cut point for a positive serum IgE test result. We also investigated whether similar risk factors were associated with increased sIgE levels among atopic subjects. We considered specific IgE levels to be increased if any of the sIgE concentrations exceeded 17.5 kU_A/L among subjects aged 6 years and older and 3.5 kU_A/L among the 1- to 5-year-old subjects. The cutoffs were not based on clinical relevance; however, they distinguished those with the highest sIgE levels (<10%) among the atopic subjects. Because the additional analyses resulted in similar results (data not shown), we present results only from the logistic regression using the cutoff of 0.35 kU_A/L for a positive test result.

RESULTS

Prevalence and distributions of allergen-specific IgEs

Among the US population aged 6 years and older, 44.6% had positive test results to at least 1 of the 19 allergens, and 36.2% of children aged 1 to 5 years were sensitized to at least 1 of the 9 allergens tested. The median number of positive test results was 3 among those 6 years and older and 2 among those aged 1 to 5 years.

Fig 1 shows the prevalence of positive test results and distributions of sIgE concentrations in the US population. Among those aged 6 years and older, the prevalence of a positive IgE test result varied from 1.1% (mouse) to 19.5% (rye grass). Sensitization to any indoor and any outdoor allergens was equally common (30%) and more prevalent than sensitization to foods (16.2%, see Table E1 in this article's Online Repository at www.jacionline.org). The prevalence of food sensitization (28%) was significantly higher among children younger than 6 years than in older age groups, as previously reported.[13] Detailed data on sIgEs, including prevalences and GMs, are presented in Tables E1 to E4 in this article's Online Repository at www.jacionline.org.

Clustering of positive IgE test results

We previously reported in abstract form that the 19 specific IgEs group into clusters[14]; Fig 2 shows details from the cluster