

The prevalence of allergic skin test reactivity to eight common aeroallergens in the U.S. population: Results from the second National Health and Nutrition Examination Survey

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Immediate hypersensitivity skin tests to eight select allergens were performed on a sample (N = 16,204) of the civilian noninstitutional population of the United States, 6 to 74 years of age, in the second National Health and Nutrition Examination Survey (NHANES II). The eight allergens were house dust, cat, dog, Alternaria, mixed giant/short ragweed, oak, perennial ryegrass, and Bermuda grass. Skin test reactivity was defined as a mean erythema diameter ≥ 10.5 mm at the 20-minute reading. Overall, 20.2% of the participants reacted to at least one allergen. Peak reactivity occurred in the 12 to 24-year-old age group. Reactivity was higher in blacks versus whites, but the difference did not reach statistical significance (23.2% versus 19.8%; $p > 0.05$). Male participants had an increased prevalence of reactivity versus female participants in whites (22.0% versus 17.6%), but not in blacks (23.2% versus 23.3%). Skin test reactivity increased in both whites and blacks with increasing income and education. The prevalence of skin test reactivity was higher in urban versus rural areas, but the difference was statistically significant only for whites (whites, 21.6% versus 16.4%; blacks, 23.8% versus 18.4%; $p > 0.05$). With logistic regression, the most important predictors of skin test reactivity in whites were age, sex, urban residence, and poverty status. In blacks, the most important predictors were age, urban residence, and poverty status. (J ALLERGY CLIN IMMUNOL 1987; 80:669-79.)

Allergic diseases (asthma, hay fever, allergic rhinitis, and atopic dermatitis) are important causes of morbidity. More than 14 million physician's office visits for asthma and allergic rhinitis were made in 1980,¹ and medication was prescribed in >90% of the visits.¹ Estimates of the prevalence of allergic diseases in the U.S. population fall in the range of 19% to 34%.²⁻⁵

The determination of whether a clinical syndrome may have an allergic etiology can be studied by the use of immediate hypersensitivity skin tests. This determination is important diagnostically because specific prophylactic and therapeutic interventions can be used once an allergic cause has been identified.

The size of the skin reaction, the dose of allergen

Abbreviations used

NHANES II: Second National Health and Nutrition Examination Survey
SES: Socioeconomic status
OR: Odds ratio

required to produce a given skin reaction size, and the number of positive skin tests are associated with laboratory and clinical indicators of immediate hypersensitivity. Skin test reactivity is positively correlated with total IgE^{6, 7} and specific serum IgE levels.^{8, 9} Skin test reactivity to an allergen is also highly correlated to both basophil sensitivity⁸ and tissue (bronchial)^{10, 11} and nasal¹² sensitivity to that allergen.

Clinically, the immediate hypersensitivity skin test has been demonstrated to have predictive diagnostic value. Subjects with a history of an allergic syndrome occurring during allergen exposure and with skin test reactivity at low doses of that allergen are at a very high risk of experiencing a recurrence of the allergic syndrome when they are reexposed to the aller-

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Received for publication Nov. 17, 1986.

Accepted for publication April 21, 1987.

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gen.⁸⁻¹³ The degree and number of positive skin tests to a battery of allergens have also been demonstrated to be positively associated with the reported prevalence of allergic diseases in the population.^{14, 15} Furthermore, asymptomatic subjects, who are skin test positive, are at a higher risk of developing an allergic syndrome, especially less than the age of 40 years,¹⁶ as compared to subjects who are skin test negative.¹⁷

Allergy skin testing is, therefore, a useful objective clinical method for evaluating the prevalence of immediate hypersensitivity to selected allergens. In addition, allergy skin tests are ideally suited for population surveys because multiple tests can be performed on a single participant within a short period of time (10 to 20 minutes for development of a response) with relative safety.

We used data from the NHANES II, which was conducted by the National Center for Health Statistics in 1976 to 1980, to investigate allergen reactivity in the United States. The results provide a comprehensive data base for assessing the prevalence and correlates of immediate hypersensitivity in the U.S. population. This survey offered the first opportunity to study skin test reactivity in a systematic way on a national sample of the civilian noninstitutional population of the United States.

METHODS

The survey

The NHANES II was a national sample of the civilian noninstitutional population of the United States conducted at 64 sampling sites during 1976 to 1980. It was based on a stratified multistage, probability cluster sample of households. When the appropriate sampling weights are used, the estimates from the sample represent the civilian noninstitutional population residing in the United States at the midpoint of the survey, March 1, 1978.

Both interview and examination procedures were used to collect a broad spectrum of health data on participants in NHANES II. To ensure that all procedures were conducted in a standardized controlled environment across the country and throughout the survey, the interviewers, technicians, and mobile examination centers were moved to each of the 64 sites.

All interviews were by trained interviewers using structured questionnaires. Brief interviews were first conducted in each household selected in the sample to obtain information about the household and to select, in a systematic fashion, the individual participants. Longer interviews were then conducted with selected individuals (or with caretakers if the sample person was a child) to obtain detailed medical and other information. The selected individuals were then invited to participate in the examination. All examinations were by trained technicians in mobile examination centers.

Details of the NHANES II design, sample selection, operational plan, and quality control have been published previously.¹⁸

Response rates

Of the 25,286 people, aged 6 months through 74 years, who were selected in the sample and interviewed in the household, 80.4% accepted the invitation to participate in the examination. Information on the nonrespondents was analyzed, and no evidence of a significant bias to the examination phase of the study was observed.¹⁹

All 16,204 participants in the examination who were 6 through 74 years of age were eligible to receive allergy skin testing. There were 14,164 whites and 2040 blacks scheduled to receive allergy skin testing. All eight allergen and histamine skin tests were administered to 89.0% of the whites and 86.3% of the blacks who participated in the examination. Participation of the examinees in the allergy skin test varied little by sex, age, income, or urban/rural residence for either race. The participants not receiving skin testing reported higher prevalences of allergies than participants who underwent skin testing (35.8% versus 20.1%; $p < 0.001$). This was somewhat by design. Examinees with histories of significant allergies were selectively excluded to minimize the risk to the participants in the survey. This nonparticipation will cause the prevalences of skin test reactivity reported here to be lower than they would have been if the high-risk subjects had been included.

Allergens and definitions of reactivity

Eight unstandardized allergens licensed by the Food and Drug Administration were applied to the forearm by the prick-puncture procedure with a 25-gauge needle.²⁰ The extracts used included indoor allergens (house dust, cat, and dog) and outdoor allergens (*Alternaria*, mixed giant/short ragweed, oak, perennial ryegrass, and Bermuda grass). Two complete batteries of extracts, identical in type but differing in both method of manufacture and the manufacturer, were used during the course of the survey. Both were 1:20 wt/vol, but the first was in 50% glycerol, and the second was freeze-dried and reconstituted in 50% glycerol. The change in allergen manufacture did not bias the survey results, since the use of the two batteries of extracts was approximately equivalent over all subgroups.²¹ A negative control (50% glycerol) and a positive control (histamine diphosphate) skin test were also applied. The sizes of the resulting wheal and erythema were recorded at 10 and 20 minutes. The length recorded was the largest diameter parallel to the length of the arm. The width was defined as the diameter perpendicular to the length at the midpoint. The mean size of the wheal and erythema was defined as the mean of the length and width. The analyses reported here are based on the 20-minute reading of the mean erythema size.²¹

Two concentrations of histamine were used during the course of the survey. Although the recommended histamine base concentration for skin puncture testing is 1 mg/ml,²² this was used only in the last 16 sites of the survey. Therefore, only data from the last part of the survey are included in analyses of histamine reactions.²¹

A positive allergy skin test is defined as an erythema reaction with a mean diameter ≥ 10.5 mm.²¹ A participant was considered to be a positive reactor with at least one positive skin test.

Definitions

The participant's race was assigned by the interviewer. Although detailed information on race was obtained in NHANES II, only two categories, white and black, were used in this study. Subjects of all other racial categories (2.0% of the participants in the allergen testing) are included with whites.

The large sample size of the NHANES II allowed us to examine both races separately. Few studies have been published on skin test reactivity in blacks.

Education was defined by the education of the head of the household for participants less than 20 years of age, and by the participant's own education for those aged 20 and older.

Family income was defined by the participant's (or adult caretaker's) own responses to a series of questions to obtain the total income of family members living in the household. The poverty level was derived from total household income and family size.²³

Residence was defined as urban or rural based on the 1970 census. Urban areas were, in general, towns with >2500 population size. Skin test reactivity was also evaluated by region of the country.¹⁸

Statistical methods

All results presented in this article are based on statistical methods that incorporate the sampling weights and the complex survey design of the NHANES II. The sampling weights include adjustments for nonresponse and after stratification to population estimates furnished by the U.S. Bureau of the Census. The use of the weights allows national estimates to be made. The complex sample design affects the variances and tests of significance. In general, the variances will be larger from a clustered sample than from a simple random sample.

The direct method was used for age adjustment. The reference population was the civilian noninstitutional population of the United States at the midpoint of the survey, March 1, 1978. Age-adjusted prevalence estimates and the standard errors were calculated with the computer programs SURREGR,²⁴ a regression program taking the complex survey design into account, and GENCAT,²⁵ a program for generalized least-squares categorical data analysis. Statistical testing was performed with a Wald statistic, which is analogous to a chi-square statistic, generated by GENCAT.

The use of multivariate modeling in this study allowed the determination of the "best" set of predictors of skin test reactivity. To avoid bias, a standardized technique was needed. A categorical data technique that is analogous to stepwise regression was used for each race.²⁶ In essence, variables were selected in the order of their chi-square statistic (assuming simple random sampling) divided by the number of degrees of freedom.

Sample-size considerations constrained us to four variables for whites and three variables for blacks.

Age, residence, poverty level, and sex were selected for inclusion in the model for whites. Age was divided into four groups (6 to 17, 18 to 29, 30 to 44, and 45 to 74 years of age). Since sex was an important variable in all prior

TABLE I. Prevalence of positive skin test reactivity to selected allergens in examinees aged 6 to 74 years in the United States 1976 to 80

Allergen	% Positive*
One or more positive	20.2 (0.83)†
Total indoor aeroallergens	7.6 (0.62)
House dust	6.2 (0.66)
Cat	2.3 (0.26)
Dog	2.3 (0.25)
Total outdoor aeroallergens	17.7 (0.74)
Ryegrass	10.2 (0.56)
Ragweed	10.1 (0.57)
Oak	4.7 (0.36)
Bermuda grass	4.4 (0.42)
<i>Alternaria</i>	3.6 (0.26)

*Mean erythema diameter ≥ 10.5 mm.

†Standard error presented in parentheses.

analyses, separate models were fit for male and female subjects. For each sex, the effect of urban or rural residence and being above or below the poverty level was investigated within each age group.

Age, residence, and poverty level were selected for inclusion in the model for blacks. Age was divided into only two groups (6 to 29 and 30 to 74 years of age). A single main effect model was created for blacks because of the smaller sample size.

For the logistic models, the prevalence estimates and the variance-covariance matrix were first calculated with SURREGR.²⁴ These were then used in GENCAT²⁵ to calculate the ORs and 95% confidence intervals and to test for statistical significance. The full model was created by eliminating those differences that were not statistically significant. Only the final parsimonious models that demonstrate statistically significant differences are presented in the tables.

RESULTS

Allergen and histamine reactivity

Overall, 20.2% of the population, aged 6 to 74 years, had at least one positive skin test (Table I). Rates of reactivity varied greatly among the eight allergens. Ryegrass and ragweed elicited the most positive reactions with about 10% of the population reacting to each allergen. Reactivity to house dust, oak, Bermuda grass, *Alternaria*, cat, and dog ranged from 6.2% to 2.3%. Outdoor aeroallergens in general caused a higher rate of reactivity than indoor aeroallergens (17.7% versus 7.6%; $p < 0.001$).

An examination of the percent distribution of the number of positive skin tests revealed a rapid drop-off as the number of positive skin tests increased: 9.0% reacted to only one allergen and 0.9% reacted

TABLE II. Percent distribution of examinees and mean size of positive skin test and histamine reactions by the number of positive skin tests for examinees aged 6 to 74 years in the United States 1976 to 80

	No. positive skin tests*						
	0	1	2	3	4	5	6-8
% Distribution							
Estimate	79.8 (0.83) [†]	9.0 (0.37)	4.7 (0.24)	2.6 (0.21)	1.8 (0.15)	1.2 (0.16)	0.9 (0.13)
Mean size of positive allergen reaction (mm)*							
Estimate	— —	22.6 (0.39)	24.0 (0.32)	24.2 (0.43)	25.7 (0.45)	27.3 (0.56)	26.6 (0.56)
Mean size histamine reaction (mm) [‡]							
Estimate	18.1 (0.70)	19.5 (0.69)	20.2 (0.84)	18.6 (0.89)	19.1 (0.82)	22.2 (0.87)	22.3 (2.48)

*Mean erythema diameter ≥ 10.5 mm[†]Standard error presented in parentheses.[‡]Mean erythema diameter > 0 mm.

§Data from 16 sites with 1 mg/ml of histamine base as the positive control.

to 6 to 8 allergens (Table II). The percent distribution of the number of positive skin tests did not change when dermatographism was controlled by eliminating all sample persons who reacted to the saline control.

A positive relationship was found between the number of positive skin tests and the mean size of the allergic reaction. The mean size of the positive reaction ranged from 22.6 mm for subjects reacting to just one skin test to 26.6 mm for subjects reacting to 6 to 8 skin tests ($p < 0.05$).

A positive relationship was also found between the number of positive skin tests and the mean size of the histamine reaction. The size of the histamine reaction ranged from 18.1 mm for subjects with no positive skin tests to 22.3 mm for subjects with 6 to 8 positive skin tests ($p < 0.05$). However, after controlling for the number of positive skin test reactions, the sizes of the allergen and histamine reactions were not related.

Overall reactivity to one or more allergens

The variation of skin test reactivity to at least one allergen was examined across the sociodemographic variables recorded in the NHANES II. The use of overall reactivity allowed us to evaluate whites and blacks separately.

Reactivity to at least one allergen differed markedly with age for both races (Fig. 1). Rates were highest among adolescents and young adults and lowest

among older people. Although several of the age-specific estimates for blacks were unstable because of the small number of blacks in each age group, the data suggest that differences in reactivity with age were similar in whites and blacks.

Because of the strong association between age and allergy skin test reactivity, all the prevalence estimates for other characteristics were age adjusted.

The age-adjusted prevalence of reactivity to at least one allergen was higher in blacks (23.2%) as compared to whites (19.8%), but the difference was not statistically significant.

Among whites, male examinees had higher rates of reactivity than female examinees (22.0% versus 17.6%; $p < 0.01$), whereas among blacks, male and female examinees had equivalent rates of reactivity (23.3% versus 23.3%).

For both races, rates of reactivity were generally higher at higher SES. People living at or above the poverty level had significantly higher rates of reactivity than individuals living below the poverty level (Table III). Rates of skin test reactivity were also significantly higher at higher levels of family income; the slight increase in the reactivity rate in the highest income group of blacks was not statistically significant. Rates of reactivity were also higher at higher levels of education.

Skin test reactivity varied by residence. The prevalence of skin test reactivity was higher among urban

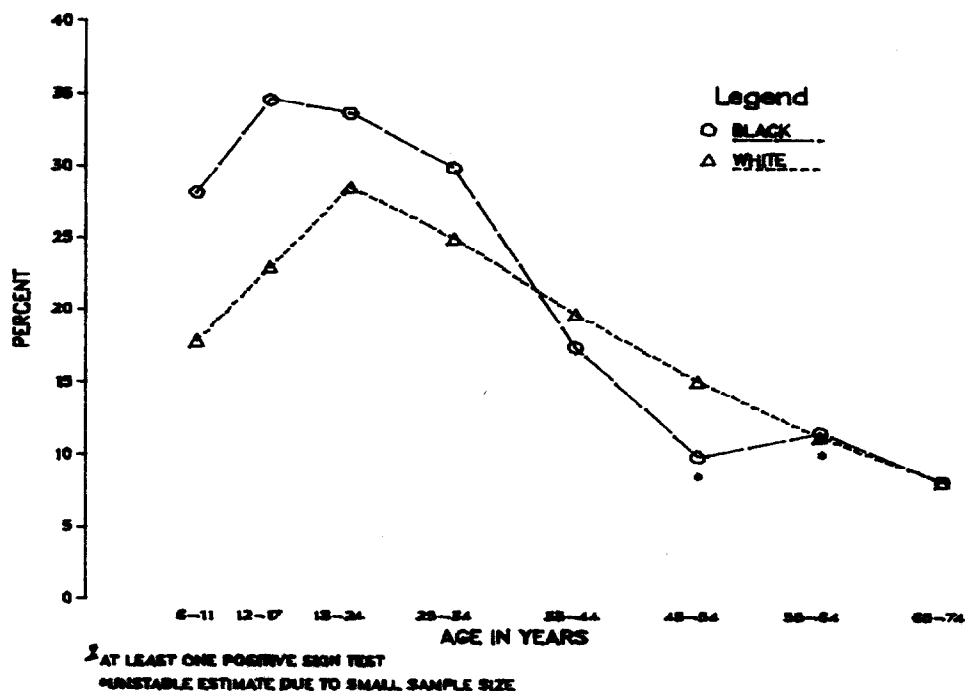


FIG. 1. Prevalence of overall allergen skin test reactivity¹ to eight common aeroallergens by race, aged 6 to 74 years, in the U.S. population 1976 to 1980.

than among rural dwellers, but this difference only attained statistical significance in whites. Geographic location also appeared to be associated with allergy skin test reactivity, but again, only in whites. The Northeast (25.6%) had the highest prevalence of skin test reactivity, whereas the South (12.5%) had the lowest.

Multivariate analysis

The odds ratios for whites in Table IV illustrate the contrast of people in the three younger age groups with people aged 45 to 74 years, and then the specified contrast within each age group.

For both white male and female subjects, the odds of a positive skin test reaction were significantly higher for each of the younger age groups as compared with subjects aged 45 years and older. For white male examinees in each of the younger age groups, the odds were significantly higher if they lived in an urban area, and for adolescents aged 12 to 17 years, the odds were also higher if the family was at or above the poverty level. For white female subjects aged 6 to 17 and 30 to 44 years, the odds for positive skin test reactivity were higher for both residence in an urban area and living in a family with an income above the poverty level. Thus, in general, the odds for positive skin test reactivity were higher if the person was less than age 45 years. Within the age group 6 to 44 years, the odds

were generally higher in urban than in rural areas. Within the age group 12 to 17 years, the odds were higher if the adolescent lived in a family above the poverty level.

The number of blacks in the sample was too small to allow as detailed an analyses as in whites. The final logistic model for blacks demonstrated that three factors were associated with increased skin test reactivity: age less than 30 years (OR = 2.99), at or above the poverty level (OR = 1.74), and urban residence (OR = 1.45) (Table V).

COMMENT

The overall prevalence of skin reactivity is 20.2% to one or more of the eight allergens used in this sample of the U.S. population. The NHANES II estimate probably underestimates the true prevalence of immediate hypersensitivity for a number of reasons. A conservative cutoff point was used to define a skin test positive reaction.²¹ Unstandardized allergenic extracts, which may have been of low potency, were used to test the population.²¹ Approximately 11% of the eligible sample participants in NHANES II did not receive all eight allergen skin tests and histamine for a variety of reasons, including past history of allergies, a history of previous allergy shots, use of allergy medication, patient refusal, etc. These nontested individuals, some of whom were deliberately excluded, did

TABLE III. Age-adjusted prevalence of overall skin test reactivity by selected demographic characteristics of examinees 6 to 74 years of age according to race in the United States 1976 to 80

Characteristic	% With positive reaction	
	White	Black
Total	19.8 (0.78)*	23.2 (2.52)
Sex†		
M	22.0 (1.01)	23.2 (3.10)
F	17.6 (0.81)	23.3 (2.84)
Poverty level‡		
Below	14.7 (1.49)	18.7 (2.92)
At or above	20.4 (0.81)	25.8 (2.46)
Family income‡		
\$0-5,999	14.1 (1.29)	17.9 (3.19)
\$6,000-9,999	17.6 (1.20)	19.7 (3.41)
\$10,000-19,999	18.5 (0.92)	30.2 (2.10)
\$20,000 or more	24.1 (0.97)	26.1 (3.37)
Education level‡		
0-8 yr	12.2 (1.22)	16.0 (3.00)
9-12 yr	17.2 (0.84)	21.5 (3.24)
13 yr or more	25.0 (1.11)	32.3 (3.41)
Residence†		
Urban	21.6 (0.99)	23.8 (2.63)
Rural	16.4 (1.14)	18.4 (3.99)
Region†		
Northeast	25.6 (1.58)	22.2 (1.66)
Midwest	19.6 (1.60)	26.7 (4.93)
South	12.5 (2.03)	21.3 (5.07)
West	20.4 (1.16)	21.3 (3.31)

*Standard error presented in parentheses.

†Significant at $p < 0.01$ for white; not significant at $p < 0.05$ for black.‡Significant at $p < 0.01$.

report a higher rate of any allergies than the skin tested individuals (35.8% versus 20.1%; $p < 0.001$).

Prevalence estimates of skin test reactivity reported in the literature can be divided into two groups based on whether the sample studied was from a general population or an allergic population. Studies on a variety of populations, consisting of either random samples of communities or nonallergic subjects, are summarized in Table VI. A wide range of skin test reactivity prevalence (5% to 64%) has been reported. Studies conducted on allergic populations are summarized in Table VII. The range of prevalence estimates is 27% to 95%, with the estimated rates of reactivity higher than in the nonallergic populations. For both allergic and nonallergic populations, the rates of reactivity reported in studies from outside of the United States are higher than rates reported in U.S.

TABLE IV. Odds ratios for final logistic models of skin test reactivity for white male and female examinees aged 6 to 74 years in the United States 1976 to 80

Comparisons	ORs	95% Confidence limits
Male examinees		
Age		
6-17 vs 45-74 yr	1.47	1.20-1.81
18-29 vs 45-74 yr	2.00	1.58-2.55
30-44 vs 45-74 yr	1.45	1.21-1.74
6-17 yr		
Urban vs rural residence	1.41	1.14-1.74
At/above vs below poverty	1.82	1.28-2.63
18-29 yr		
Urban vs rural residence	1.55	1.18-2.04
30-44 yr		
Urban vs rural residence	1.32	1.01-1.72
Female examinees		
Age		
6-17 vs 45-74 yr	1.61	1.29-2.02
18-29 vs 45-74 yr	2.39	2.00-2.85
30-44 vs 45-74 yr	1.67	1.17-2.37
6-17 yr		
Urban vs rural residence	1.44	1.08-1.92
At/above vs below poverty	1.52	1.08-2.13
30-44 yr		
Urban vs rural residence	1.57	1.17-2.11
At/above vs below poverty	2.26	1.12-4.58

studies. This difference may be due to the allergens used, varying criteria for positivity, or true differences in reactivity. The overall prevalence rate of 20.2%, found in this study, is approximately equal to the mean value found in Table VI for U.S. studies on nonallergic populations.

Despite the lack of comparability among studies, the variation of reactivity rates over selected demographic variables reported in this study are comparable, since they reflect internal comparisons from the same study. No previous study attempted to use multivariate techniques when skin test reactivity was evaluated; therefore, the results of our model can only be discussed in respect to the univariate findings of the other studies.

Blacks demonstrated a consistently higher rate of allergic skin reactivity than whites, although the differences were not statistically significant. Few studies have compared racial differences in skin test reactivity in the United States. Lindblad and Farr²⁸ found no difference between the races. Freidhoff et al.²⁹ found blacks more reactive than whites; however, the difference reached statistical significance only in

women reporting allergies. Findings of an increased prevalence of immediate hypersensitivity reactions in blacks are consistent with the observed higher total IgE levels of blacks versus whites in the United States.³⁸

Higher reactivity to allergens in blacks was discordant with the tendency for a lower degree of skin reactivity to histamine observed in blacks (83.6% versus 92.9%; not significant). If the lower rates of histamine reactivity in blacks represent an underreading of the skin test reactions secondary to skin color, then the rates of allergen skin test reactivity observed in blacks may be conservative estimates of the true prevalence. Thus, the true black-white difference in skin test reactivity may be even greater than observed in this study. Other possibilities that might account for the discordance between allergen and histamine skin reactivity may be end organ unresponsiveness to histamine (one of many inflammatory mediator released in the allergic reaction) or racial differences in the release, metabolism, or proportion of allergic vasoactive mediators. Interestingly, despite the differences in reactivity rates, the SES and residency correlates of skin test reactivity were the same in both blacks and whites.

Age was associated with immediate hypersensitivity reactions. In general, the 12 to 24-year-old age group demonstrated peak reactivity to all allergens used in this study. Age remained an important indicator of reactivity in all multivariate analyses. However, these data are cross-sectional and cannot by themselves be used to indicate a change with age. Several other studies have reported decreased prevalence of skin reactivity with age.^{37, 39} Peak skin test reactivity has previously been reported to be highest in the 15- to 30-year-old age group,⁴⁰ 20- to 34-year-old age group,³⁹ the first half of the third decade,³⁰ and in subjects less than 40 years of age.³⁷

Diminished end organ responsiveness in infants⁴¹ and elderly individuals⁴² to inflammatory mediators appears to be one contributory mechanism for decreased prevalence of allergen skin test reactivity at the extremes of age. There is an age-associated loss of vascular bed (50% reduction of mast cells and 35% reduction of venular cross-sections) and a reduction in histamine release observed in the skin of older adults.⁴² In addition, a decrease in skin response to mast cell degranulating agents has been reported in infants.⁴³

However, the overall effect of age on allergen reactivity is not explained by the inability of the skin to respond to histamine. There is little or no decrease in the prevalence of reactivity to histamine with age until after the age of 55 years, thus implicating differences

TABLE V. Odds ratios for final logistic model of skin test reactivity for black examinees aged 6 to 74 years in the United States 1976 to 80

Comparisons	ORs	95% Confidence limits
Aged 6-29 vs 30-74 yr	2.99	2.34-3.82
At/above vs below poverty	1.74	1.41-2.15
Urban vs rural residence	1.45	1.01-2.10

in allergen exposure with age, immunologic responsiveness, or tissue differences responsible for the age-related differences in prevalence.²¹

Age differences observed in skin test reactivity parallel the differences observed in IgE levels. The highest total IgE levels are noted in male examinees between 6 to 24 years of age and in female examinees 6 to 14 years of age with a gradual decrease thereafter.⁴⁴ Similarly, the highest allergen-specific IgE levels are found between 12 and 20 years of age.⁴⁵ The increase in IgE antibody levels during these years may reflect the higher number and proliferative capacity of clonable T and B cells observed during ages 24 to 35 years, which decline in later years.⁴⁶

Sex differences in the prevalence of skin reactivity were noted for whites in NHANES II. White male examinees demonstrated a higher prevalence of reactivity than white female examinees. However, white female examinees had slightly higher rates of reactivity to 1 mg/ml of histamine base than male examinees, but not to a statistically significant degree (92.7% versus 91.6%; not significant). Thus, the lower allergenic reactivity in white female examinees does not appear to be due to decreased end organ reactivity to histamine. Other studies have also reported the tendency for male subjects to have larger skin reactions at lower²⁸ or equal³³ concentrations of allergen or to have significantly more positive skin tests or a higher rate of reactivity to the allergens tested than female subjects.^{33, 47} The lack of sex difference in U.S. blacks is noteworthy and requires further study.

The male predominance in allergen skin test reactivity is in keeping with the higher levels of total IgE in men as compared to women⁴⁷ and earlier manifestations of allergic syndromes in male subjects, with the prevalence for female subjects not equaling the prevalences of male subjects until the third or fourth decade of life.⁴⁸⁻⁵¹

Residency in urban areas was an indicator for increased reactivity in all multivariate analyses. Other studies tend to support this association. Linna⁵² found

TABLE VI. Skin test reactivity in community samples or nonallergic populations

Author	Location	Subjects	Age (yr)	No. of extracts	Type of test	% Positive
U.S. studies						
Curran and Goldman ²⁷	Boston	100 Nonallergic	16-60 +	9	Scratch	5
Hagy ⁵	Providence	765 Nonallergic	16-20	14	Scratch	17.4
Lindblad and Farr ²⁸	Pittsburgh	100 Nonallergic	16-81	5	Intradermal	24*
Freidhoff et al. ²⁹	Baltimore	115 Subjects in an industrial plant	18-55	7	Prick	24.3
Barbee et al. ³⁰	Tucson	3012 Community sample	3-75 +	5	Prick	34
Studies outside U.S.						
Bandelet al. ³¹	Nigeria	100 Nonallergic	10-60	22	Not stated	10
Tan and Teoh ³²	Singapore	50 Nonallergic	10-73	21	Prick	12
Haahtela et al. ³³	Finland	708 Sample of ninth graders	15-17	16	Prick	49
Herxheimer et al. ³⁴	London	100 Nonallergic	5-75	12	Prick	50
Haahtela and Jokela ³⁵	Finland	295 Nonallergic army conscripts	18-19	16	Prick	50
Cserhati et al. ³⁶	Hungary	300 Nonallergic	2-16	16	Prick	64

*Results from 1:10 concentration

TABLE VII. Skin test reactivity in allergic populations

Author	Location	Subjects	Age (yr)	No. of extracts	Type of tests	% Positive
U.S. studies						
Freidhoff et al. ²⁹	Baltimore	262 Reporting allergies	18-55	7	Prick	55
Hagy ⁵	Providence	478 Reporting allergies	16-20	15	Scratch	63.9* 26.7†
Studies outside U.S.						
Bandelet al. ³¹	Nigeria	221 With asthma	10-60	22	Not stated	67
Tan and Teoh ³²	Singapore	138 With asthma	10-73	21	Prick	69
Hendrick et al. ³⁷	London	656 With asthma	<10-30 +	22	Prick	84
Haahtela et al. ¹⁵	Finland	292 Reporting allergies	15-17	16	Prick	87‡ 83§ 69
Herxheimer et al. ³⁴	London	300 With respiratory allergies	5-75	12	Prick	95

*Asthma, hay fever, and/or nonseasonal allergic rhinitis.

†Other allergies.

‡Subjects with asthma.

§Allergic rhinitis.

||Atopic dermatitis.

reactivity to tree pollens increased in urban blue-collar dwellers, but house dust-mite reactivity was more common in rural blue-collar dwellers. No differences in skin reactivity were found between white-collar workers in urban versus rural settings. Rhyne, as

quoted by Smith et al.,⁵³ reported significantly more skin reactivity to ragweed and grass in urban children. Similarly, comparative studies of rural and urban populations suggest "the same or lower incidence" for rural populations.⁵³

The reason for an increased prevalence of reactivity in urban populations is not apparent but may be related to pollutants in the urban environment, urban clustering of families with positive allergic histories, or cultural differences between urban and rural groups that may impact on the development of immediate hypersensitivity.

Skin test reactivity varied by geographic region of the country in the univariate analyses for whites. Region did not, however, remain in the final multivariate model for either whites or blacks. Thus, it appears that the variation observed between regions is explained by the other variables in the model.

SES factors were positively associated with the prevalence of skin test reactivity. Reactivity was greater in both whites and blacks living at or above versus below the poverty income ratio. In addition, overall reactivity was higher at higher levels of education or family income. Barbee et al.³⁰ found increasing skin test reactivity with increasing income levels. Linna⁵² found statistically significant increases in reactivity in white-collar versus blue-collar children for grass pollens (in urban dwellers) and tree pollens (in urban and rural dwellers).

The inclusion of both high SES and residence in urban areas in the multivariate analyses leads to the postulation that the development of cutaneous hypersensitivity may be dependent on life-style. It is possible that by growing up in an upper SES urbanized environment, exposure to the aeroallergens used for testing in this survey is reduced and tolerance is not developed, as it would be in a lower SES environment. It has been noted in animals and humans that exposure to an antigen early in life will promote the development of tolerance to this antigen.^{54, 55} By contrast, there may be some environmental factor that is associated with the upper SES life-style that causes individuals to be more susceptible to the development of hypersensitivity. Further research is needed to investigate these issues.

The number of positive skin tests and the size of the histamine reaction were found to be associated in this study. This suggests that multiple positive allergy skin tests are required to influence histamine reaction size. Prior studies found no association between histamine and allergen reactivity.^{30, 56} Local skin interactions, caused by the proximity and intensity of positive allergen reactions, may cause an artifactual increase in the histamine skin reactions nearby.^{57, 58} This issue needs to be further explored.

The total number of positive skin tests appears to be associated with the degree of immune responsiveness, since a positive relationship was found between the number of positive skin tests and the size of the

allergic response. This assumption is supported by the finding that allergic persons with multiple positive allergen skin tests and/or larger skin reactions have higher total⁶ and specific¹² IgE levels, another indicator of immune hypersensitivity. In contrast, no significant association exists between histamine skin reaction size and total IgE in skin test positive allergic patients.¹²

In addition to defining the prevalence of percutaneous immediate hypersensitivity in the civilian non-institutional U.S. population, the results of NHANES II reveal intriguing variations in skin test reactivity related to age, sex, race, residency, and SES. Elucidation of these associations will lead to a fuller understanding of the immunologic, social, and cultural factors involved in the acquisition and maintenance of the immediate hypersensitivity state and, thus, to a better understanding and appreciation of the allergic disease state.

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Heat-labile neutrophil chemotactic activity in subjects with asthma after allergen inhalation: Relation to the late asthmatic reaction and effects of asthma medication

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*Neutrophil chemotactic activity (NCA) in serum is raised in subjects with asthma after inhalation of an allergen. Two kinds of NCA have been demonstrated, heat-stable and heat-labile. In addition, inhibitory activity is generated after inhalation challenge. In the present study we have investigated the relationship of heat-labile NCA to the development of the late asthmatic reaction (LAR) in 13 subjects with asthma after allergen challenge and the effects of asthma medication on the formation of this activity. Heat-labile NCA peaked 120 to 240 minutes after challenge and demonstrated at this time significant ($p < 0.001$) quantitative relationships to the ensuing LAR. The inhalant corticosteroid, budesonide, significantly inhibited ($p < 0.001$) the generation of heat-labile NCA and the development of LAR both after a single dose and after 4 weeks of pretreatment. Single-dose disodium cromoglycate pretreatment, initially, slightly enhanced ($p < 0.05$) heat-labile NCA but, after 120 minutes, slightly inhibited ($p < 0.05$) the activity. Disodium cromoglycate also slightly abrogated the development of LAR. Single-dose pretreatment with the β_2 -agonist, terbutaline, inhibited generation of heat-labile NCA ($p < 0.001$) but was without effect on LAR. It is concluded that the generation of heat-labile NCA is related to the development of the LAR and may be of importance for the attraction of inflammatory cells to the lung in the development of the inflammatory reaction probably responsible for LAR. However, the pharmacologic control of heat-labile NCA indicates that the process is multifactorial and not solely dependent on the generation of NCAs detected in serum. (*J ALLERGY CLIN IMMUNOL* 1987;80:679-88.)*

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Supported by grants from the Swedish Medical Research Council, AB Draco, Lund (subsidiary of ASTRA), and the University of Uppsala.

Received for publication Nov. 6, 1985.

Accepted for publication April 21, 1987.

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The presence in serum of NCA has been demonstrated in individuals with asthma after provocation with allergens^{1,3} or unspecific stimuli such as exercise.⁴ Basically, the activity may be divided into heat-stable, high-molecular-weight activity, and heat-labile activity with a molecular weight of 120 to 300 kd.⁵ The origin of these activities is uncertain, although some indirect data would indicate the mast cell as the origin in the case of the heat-stable, high-molecular-