

Age Effects on Objective Measures of Atopy in Adult Asthma and Rhinitis

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ABSTRACT

A cross-sectional survey of 132 adult men referred to the outpatient allergy clinic at the West Los Angeles Veterans Affairs Medical Center was performed to assess age effects on allergic disease in the elderly. Total serum immunoglobulin E (IgE), immediate hypersensitivity skin testing, and serum eosinophil count were measured in all subjects. Subjects were stratified by age into one of five groups for comparison. In asthma, prevalence of allergy skin test reactivity and mean total serum IgE levels did not decline with advancing age, suggesting that IgE-dependent mechanisms continue to be significant in elderly patients with asthma. In subjects with rhinitis, prevalence of allergy skin test reactivity and mean total serum IgE did decline among elderly subjects relative to younger subjects. However, the prevalence of allergic rhinitis did not decline in the elderly. This suggests that although allergic rhinitis is common in elderly patients, nonallergic causes of rhinitis may become more prevalent with advancing age. (Allergy and Asthma Proc 25:175–179, 2004)

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Airway dysfunction affecting the nose and the lungs is an important cause of morbidity and mortality in the elderly. Although nasal and pulmonary symptoms in young adults often can be readily attributed to allergic asthma and allergic rhinitis, age-associated physiological changes and comorbidities often complicate these diagnoses in older adults. In fact, the relative significance of allergic inflammation in the pathogenesis of nasal and respiratory symptoms generally has been felt to diminish with aging. This concept is being challenged by several studies that point to the continued importance of allergic inflammation in elderly patients with asthma.

To address the potential importance of allergic causes of airway dysfunction in the elderly, we performed a cross-sectional survey of adults referred to our outpatient allergy clinic. Total serum immunoglobulin E (IgE) levels and allergy skin test reactivity were assessed in relationship to age and the clinical diagnoses of asthma and rhinitis.

SUBJECTS AND METHODS

One hundred thirty-two consecutive male patients referred to the outpatient allergy clinic at the West Los Angeles Veterans Affairs (VA) Medical Center were enrolled in the study. The referrals were made by general and subspecialty medical and surgical services within the VA.

Presence of asthma and/or rhinitis was determined by a detailed medical history and physical exam performed or supervised by an attending allergist. Immediate hypersensitivity skin testing was performed on all subjects. Subjects were tested with 13 common aeroallergens including selected trees, grasses, weeds, molds, and dust-mite antigens. Presence of immediate hypersensitivity skin test reactivity (skin test reactivity) was defined as a positive prick or intradermal reaction to 1 or more of the 13 aeroallergens tested. A positive prick or intradermal reaction was defined as a wheal reaction 5 mm greater than control. Allergic

TABLE I

Prevalence of Asthma and Rhinitis					
Age Group (yr)	Total Subjects	Subjects with Asthma	Subjects with Rhinitis	Prevalence of Asthma	Prevalence of Rhinitis
25-34	8	4	4	0.5	0.5
35-44	26	13	16	0.5	0.62
45-54	21	10	11	0.48	0.52
55-64	39	21	21	0.54	0.54
65-74	38	13	27	0.34	0.71

rhinitis was defined as skin test reactivity in the presence of a clinical diagnosis of rhinitis. Total serum IgE was determined by the paper radioimmunosorbent test. Absolute eosinophil count was performed with an automated cell counter.

Total serum IgE values (IU/mL) and eosinophil count (cells/ μ L) were converted to base 10 logarithms before statistical analysis to account for their log normal distribution in the general population. Statistical comparison of group means was by Student's *t*-test. Comparison of prevalence was by *z*-test for two proportions. Ninety-five percent confidence intervals were calculated.

RESULTS

The age range of the study population was 25–75 years with a mean of 54.95 years. Subjects were stratified by age into one of six groups for comparison (Table I).

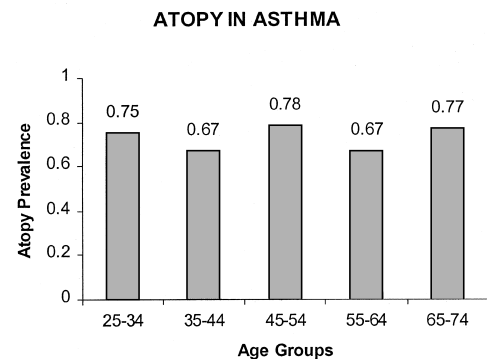
In our adult subjects with an asthma diagnosis, there is no evidence of an age-related difference in objective measures of atopy. Prevalence of skin test reactivity was almost identical in the youngest and oldest age groups (Fig. 1 A). Total serum IgE showed a slight tendency to increase with advancing age (Fig. 1 B).

A difference was noted when examining age effects on atopic measures in subjects with rhinitis. Prevalence of skin test reactivity and total serum IgE were both relatively decreased in older rhinitis patients (Fig. 2, A and B).

The likelihood of an asthma diagnosis in our allergy referrals varied little with age except for a relative decline in asthma prevalence in the oldest age group (Table I). This decline contrasts with a relative increase in the likelihood of a rhinitis diagnosis in the oldest subjects (Table I).

In analyzing the study population as a whole without regard to diagnosis, our allergy referrals showed slight trends toward decreasing skin test reactivity, total serum IgE, and serum eosinophilia with advancing age. Presence of skin test reactivity was associated with a higher mean total serum IgE in all age groups (Fig. 3). None of the observed age group differences in the study was significant to a level of $p < 0.05$.

A



B

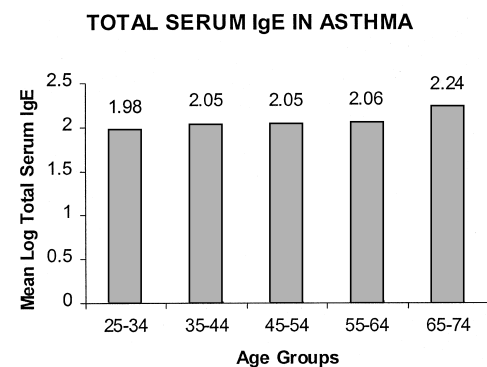


Figure 1. These graphs show (A) the prevalence of allergy skin test reactivity (atopy) by age group in subjects with asthma and (B) the mean log total serum IgE (IU/mL) by age group in subjects with asthma.

DISCUSSION

The importance of allergic inflammation in airway dysfunction historically has been thought to decline among the elderly; perhaps this concept was based on reported declining skin test reactivity and total serum IgE with aging. However, our finding of undiminished atopy in elderly subjects with asthma is in line with a growing body of evidence supporting the continued importance of an allergic etiology for pulmonary symptoms in older adults. Huss *et al.* found 74.7% of their elderly patients with asthma were atopic.¹

The mean total serum IgE of elderly asthma patients has been shown to be significantly elevated relative to age and

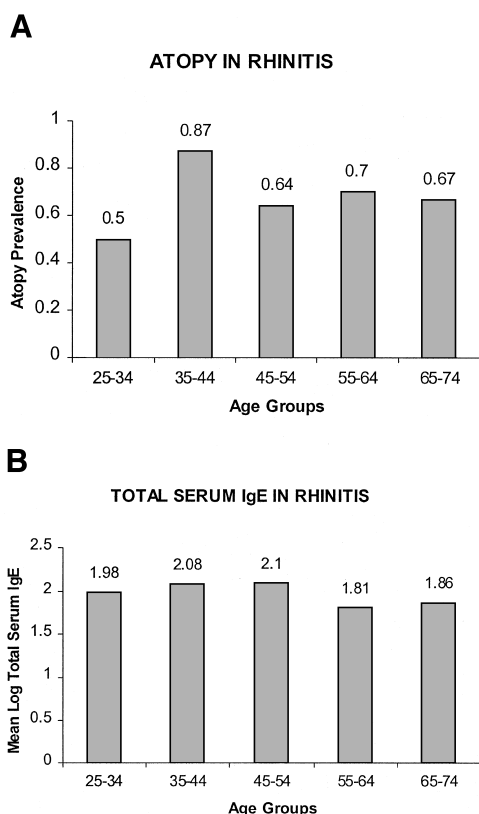


Figure 2. These graphs show (A) the prevalence of allergy skin test reactivity (atopy) by age group in subjects with rhinitis and (B) the mean log total serum IgE (IU/mL) by age group in subjects with rhinitis.

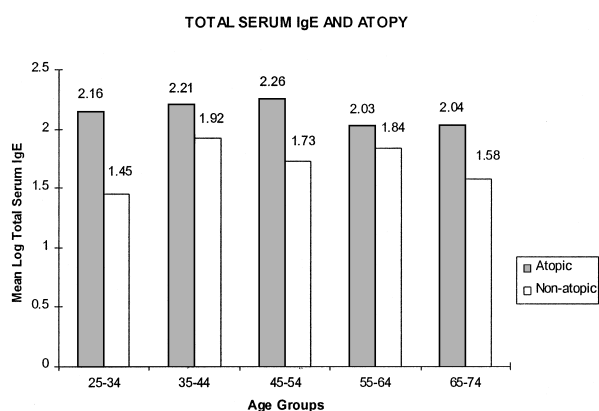


Figure 3. Log total serum IgE in subjects with and without atopy. Shaded bars represent subjects with positive reactions to allergy skin testing. Open bars represent subjects who did not react to allergy skin testing.

sex-matched patients without asthma.² Prevalence of asthma in both young and old adults is associated closely with age/sex-adjusted total serum IgE levels, suggesting that IgE-mediated processes are important in the elderly as well as younger asthma patients.³ The finding of increased skin test reactivity in elderly onset asthma as compared with

young adult-onset asthma underscores the significance of allergic (extrinsic) causes of asthma in the elderly.⁴

Several other observations in the literature point to allergic inflammation as a cause of pulmonary symptoms in older adults. A survey of adult skin test-positive asthma patients in Japan found no age-related decline in total serum IgE, bronchial and conjunctival responsiveness, or antigen-triggered histamine release from peripheral leukocytes.⁵ The same study found a decline in prevalence of skin test reactivity to house dust, dust mites, Japanese cedar, and *Alternaria* antigens in elderly patients with asthma but no age-related decrease in prevalence of skin test reactivity to the *Candida* antigen. Presence of skin test reactivity independently predicts a subsequent decline of lung function in middle-aged and older men with no history of respiratory disease.⁶ In adults with an asthma diagnosis, bronchial responsiveness to methacholine and bronchodilators does not diminish with aging.⁷ Another study found that patients with late-onset asthma (asthma diagnosed after the age of 65 years) had a 72% incidence of atopy with higher radioallergosorbent test and skin test scores than those of younger asthma patients.⁸

In view of the wide-ranging evidence for the persistence of allergic inflammation in elderly patients with pulmonary symptoms, anti-inflammatory medications and immunotherapy should be emphasized as front-line therapy for older adults just as they are for younger adults. At first glance, the relatively lower percentage of skin test reactivity in our elderly subjects with rhinitis would seem to suggest that nasal allergic inflammation becomes less important with aging. A closer look at the data reveals that in light of the relatively higher prevalence of rhinitis in our oldest subjects (Table I), the prevalence of allergic rhinitis (clinical rhinitis with positive allergy skin testing) does not decrease with advancing age (Fig. 2 A). Our findings do support the suggestion that nonallergic causes of rhinitis become more prominent in the elderly.

Textbook descriptions of allergic rhinitis suggest that the condition improves in middle age and is seldom a problem in the elderly.⁹ However, few published surveys address this issue, and the significance of their findings is not clear. A British study describes a sharp drop-off in consultation rates for allergic rhinitis in a general practice after the age of 25–44 years but minimal declines thereafter.¹⁰ By contrast, a survey of the general population in Tecumseh, MI noted no such sharp drop-off in the prevalence of allergic rhinitis after the age of 25–44 years and only minimal declines after the age of 55–64 years.¹¹ To our knowledge, no published study has performed allergy skin testing in combination with clinical diagnosis to rigorously address the natural history of allergic rhinitis in adulthood. In our study, the high prevalence of atopic disease (*i.e.*, asthma or allergic rhinitis) in our patient population may be a function of the referral pattern to an allergy clinic. Our data suggest that elderly patients presenting with nasal symptoms and/or

wheezing have a high probability of atopy and thus warrant allergy skin testing and appropriate therapy.

Without regard to diagnosis, an analysis of our overall study population reveals slight trends toward declining skin test reactivity and total serum IgE with advancing age. Although the findings in our selected population of allergy patients can not be generalized to the population as a whole, most cross-sectional surveys of normal populations have reported statistically significant^{12–13} or statistically nonsignificant^{14–17} age-related declines in total serum IgE. Other cross-sectional studies of total IgE and aging show an age-related decline only in women¹⁸ or in atopic subjects¹⁹ or have failed to show any age-related decline.^{20,21} In an unselected population of 889 men, there was no significant difference in total IgE found between different age groups.²² A large, community-based, 20-year longitudinal study of the Tucson area residents found no significant change in total IgE after the age of 40 years.²³

Cross-sectional studies must be interpreted carefully because of the difficulty in determining whether age-group differences represent true age effects rather than differences between cohorts. This caveat is particularly important when addressing measures of atopy because of the potential importance of environmental and infectious disease exposures in influencing the immune system toward a TH1- or TH2-type response.^{24,25} In fact, the prevalence of “atopic asthma” (defined as asthma symptoms coexisting with allergic rhinitis symptoms) increased twofold in a survey of 45- to 54-year-old adults done in Scotland in 1996 when compared with a survey of 45- to 54-year-old adults done in 1972–1976.²⁶

Prevalence of allergy skin test reactivity has been found to decline with aging in cross-sectional surveys^{27–29} and in a longitudinal study of the Tucson cohort.³⁰ Controversy exists as to whether this age-related decrease in skin test reactivity truly reflects diminished allergic activity of the immune system or merely shows a change in target organ response. In fact, skin reactivity to both histamine and histamine-releasing factors has been shown to decline with aging.³¹

How can one reconcile the apparent age-related decline in objective measures of atopy in the general population with mounting evidence that allergic causes of airway dysfunction retain significance in the elderly? It remains unclear whether published studies supporting age-related declines in skin test reactivity and total serum IgE are truly an accurate reflection of the natural history of allergic inflammation. Even if aging does induce a decrease in IgE production, it is possible that molecular mechanisms exist in older adults, which tend to up-regulate other aspects of allergic inflammation, thereby counteracting the effect of lowered IgE production. One such proposed mechanism, derived from a mouse model, involves a “double negative” effect whereby an age-induced decrease in the expression of the negative regulator $F_\epsilon\gamma RII B$ produces increased degranulation of mast cells.⁴ Additional research based on both epidemiological

and molecular approaches is needed to improve our understanding of the natural history of allergic disease.

CONCLUSION

Asthma and rhinitis are diagnosed frequently even in subjects presenting at an advanced age in our VA allergy clinic. In asthma, prevalence of skin test reactivity and mean total serum IgE did not decrease with advancing age, suggesting that IgE-dependent mechanisms are important in the pathogenesis of respiratory symptoms in the elderly. Although evidence of allergic inflammation is common in elderly subjects with rhinitis, nonallergic causes of nasal symptoms become more prevalent with advancing age. Additional studies are needed to further our understanding of the natural history of allergic disease in the elderly.

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