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Degree and clinical relevance of sensitization to common allergens among adults: a population study in Helsinki, Finland

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Summary

Background We aimed to assess the prevalence of allergic sensitization and multiple sensitization, risk factors, and the clinical impact of being sensitized in the adult population of Helsinki, Finland.

Methods As a part of the FinEsS study, a population-based random sample of 498 adults aged 26–60 years were tested for 15 common aeroallergens with skin prick tests (SPTs) and interviewed on respiratory symptoms and diseases, including respiratory irritants and childhood environment.

Results The prevalence of at least one positive prick test was 46.9%. A large difference by age was found: 56.8% were sensitized among those aged 26–39 years, 49.2% in the age group 40–49 years, and 35.6% in the age group 50–60 years ($P < 0.001$). Sensitization to multiple allergens was common among young subjects with 42% of the sensitized responding to at least four allergens, while this proportion was only 16% of the sensitized among those aged 50–60 years. The prevalence of physician-diagnosed asthma, allergic rhinitis (AR) or conjunctivitis, and wheeze increased significantly with increasing number of positive responses to SPTs. Having a family history of AR or conjunctivitis was a significant risk factor for allergic sensitization and for sensitization to any of the pollens. Further, urban living in childhood yielded an increased risk for pollen sensitization.

Conclusions The prevalence of allergic sensitization was high in the urban adult population of Helsinki. More than half of those aged 26–39 years was sensitized and 24% was sensitized to at least four allergens. Sensitization to multiple allergens was associated with a high prevalence of asthma, AR or conjunctivitis, and wheeze.

Keywords allergic rhinitis, asthma, multiple sensitization, sensitization, skin prick test

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Introduction

Allergies have become a common burden in westernized countries. Wide variation in the prevalence of allergic sensitization measured by specific IgE to common airborne allergens was shown in the European Community Respiratory Health Survey (ECRHS) ranging from 16% in Spain to 45% in New Zealand [1]. A comparison of Eastern Finland with a neighbouring district of Russia showed a higher prevalence of sensitization in Finland, where 34% had at least one positive prick test reaction compared with 22% in Russia [2]. The most common allergens were dog and cat in Finland, while mugwort and cockroach

were most common in Russia. It is unclear how allergen exposure differs between these countries. Similarly, cockroach was the most common allergen, followed by mugwort in a recent population-based study of subjects aged 17–66 years from Tallinn, Estonia [3]. The prevalence of allergic sensitization was 35% in total, while 46% of the subjects aged 17–24 years were sensitized [3].

Allergic sensitization is a well-known risk factor for asthma among adults [4], and the most important risk factor among children [5]. Sensitization to more than one indoor allergen is common, 36%, among atopic children in the USA [6]. Young adults with multiple sensitization are at high risk for bronchial hyper-responsiveness [7].

Further, high specific IgE is strongly related to clinical allergy [8].

There is strong evidence of a high prevalence of allergic sensitization among young adults in many westernized countries, but there are less studies assessing the degree of sensitization and its impact on health. The prevalence of asthma and hayfever increase with increasing number of positive skin prick tests (SPTs) in children [9]. We aimed to assess the prevalence of allergic sensitization, multiple sensitization, and their association to allergic diseases in adults. Further aims were to evaluate risk factors for sensitization and multiple sensitization in an urban population-based sample of adults for the first time in Finland.

Material and methods

Study population

The present study reports the results of allergy testing in Helsinki as a part of a large epidemiological study on obstructive airway diseases and allergy, the FinEsS study, which is in progress in Finland, Estonia, and Sweden. The original study population was obtained from the population register designed to be representative for the general population of Helsinki, the capital of Finland, in the age range of 20–69 years. The first part of the study, a postal questionnaire survey, was performed in 1996 [10]. A random sample of those who participated in the postal questionnaire was invited to the second part of the study performed in 2001–2003. Of the 1200 invited, 643 (54%) participated in this second part. SPTs were performed on those less than 61 years of age, which made 503 eligible subjects. Five subjects were excluded because of pregnancy or regular use of antihistamines, and altogether 498 SPTs were performed. After omitting 29 subjects with dermatographism and four subjects with no weal in response to the positive control, 465 valid test results were obtained.

The representativity of the study population was tested by comparing the results of the participants in the original postal questionnaire to the results of those participating in SPTs in relevant ages, and no statistically significant differences were found in reported prevalence of physician-diagnosed asthma, allergic rhinitis (AR) or conjunctivitis, wheeze, attacks of shortness of breath, and longstanding cough. The Ethical Committee of Helsinki, University Central Hospital approved the study.

Interview and skin prick tests

All subjects underwent a structured interview by a physician involved in the study. This interview consisted of questions about respiratory symptoms and diseases, smoking habits, childhood environment, airway irritants, occupational history, and asthma medication. SPTs with

15 allergens were performed by three trained nurses on the volar surface of the forearm using separate sterile lancets and standardized allergen extracts according to the recommendations of the European Academy of Allergy and Clinical Immunology, but as single tests on one arm [11]. The allergens consisted of cat (10 HEP), dog (10 HEP), cow (1 : 100 w/v), horse (10 HEP), birch (10 HEP), timothy (10 HEP), mugwort (10 HEP), the moulds *Alternaria alternata* (100 bu/mL) and *Cladosporium herbarum* (1 : 20 w/v), the house dust mites (HDMs) *Dermatophagoides pteronyssinus* (10 HEP) and *D. farinae* (10 HEP), the storage mites *Acarus siro* (1 : 100 w/v) and *Lepidoglyphus destructor* (100 bu/mL), Cockroach (1 : 100 w/v), and latex (100 IR/mL). All extracts were provided by ALK-Abelló (Hørsholm, Denmark) except latex, which came from Stallergenes Laboratories (Antony, France). Histamine dihydrochloride 10 mg/mL was used as the positive control, and the solvent (glycerin) as the negative control. After 15 min the weal size was measured in millimeters in two perpendicular directions including the longest diameter, and their mean was recorded as the response. A response of at least 3 mm was regarded as positive.

Definitions

Allergic sensitization was defined as at least one positive SPT reaction.

Multiple sensitization refers to at least four positive reactions in the prick tests.

The following definitions were based on questions asked at the interview:

Physician-diagnosed asthma: 'Have you by a physician been diagnosed as having asthma?'

AR or conjunctivitis: 'Do you have or have you had hayfever or AR or conjunctivitis?'

Wheeze: 'Have you had wheezing or whistling in your chest at any time in the last 12 months?'

Attacks of shortness of breath: 'Have you had any attacks of shortness of breath during the last 12 months?'

Longstanding cough: 'Have you had longstanding cough during the last years?'

Statistical analyses

Statistical analyses were performed with SPSS, version 11.0. χ^2 -test, Fisher's exact test, and analysis of variance were used calculating bivariate analyses and testing for trend. A *P*-value < 0.05 was considered statistically significant. Multiple logistic regression analysis was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for sensitization. As independent variables were chosen significant variables from the bivariate analyses; gender, age, family history of allergic rhinoconjunctivitis,

and area of domicile at age 0–5 years. Sensitization to any pollen, any animal, any allergen, and multiple sensitization were selected as outcome variables.

Results

Allergic sensitization

The prevalence of allergic sensitization was 46.9%, while it was 45.9% if cockroach was not taken into account, 44.3% without storage mites, and 42.2% if both cockroach and storage mites were omitted. The most common positive SPTs were to dog and cat, followed by birch, timothy, and mugwort (Table 1). Only 5–6% reacted to HDMs, and 2% to moulds. The prick test responses for the dominant allergens were generally larger than for the less common allergens. The median weal sizes for positive SPT to HDMs and moulds varied from 3 to 3.5 mm, while it was 5 mm for birch pollen, and 5.5 mm for cat. Reactions to timothy, *D. pteronyssinus*, and mites as a group were significantly more common among men than women, otherwise no gender differences were found. Allergic sensitization was most common among young subjects aged 26–39 years with 56.8% having at least one positive prick reaction, while the corresponding figures were 49.2% among those aged 40–49 years and 35.6% in the age group 50–60 years ($P < 0.001$).

Allergic sensitization in relation to airway diseases and symptoms

AR or conjunctivitis and wheezing were significantly more common among those with at least one positive SPT response than those without any reaction, while asthma did not reach statistical significance (Table 2). AR or conjunctivitis was also strongly correlated with sensitization to any pollen, any animal, any mite, and any mould ($P < 0.001$). Among those who reported physician-diagnosed asthma, 56.3% had positive prick test reactions. Physician-diagnosed asthma was significantly correlated with sensitization to pollens ($P = 0.023$). Further, asthma was significantly associated with sensitization to dogs ($P = 0.025$) and to cats ($P = 0.020$). Wheezing was significantly correlated with sensitization to both pollens and animals.

Multiple sensitization

The subjects in the oldest age group were most often sensitized to a single allergen, with only 16% of the sensitized reacted to at least four allergens (Fig. 1). On the contrary, 42% of those sensitized in the youngest age group reacted to at least four allergens, corresponding to 24% of all subjects aged 26–39 years. The prevalence of asthma was 18.2%, and of AR or conjunctivitis 80.3% among those sensitized to at least four allergens (Table 3).

Table 1. Prevalence (%) of positive skin prick tests (SPTs) to various allergens, groups of allergens, and any positive reaction in SPT by age groups and gender in descending order by frequency.

Allergen	26–39 years (<i>n</i> = 169)	40–49 years (<i>n</i> = 122)	50–60 years (<i>n</i> = 174)	<i>P</i> -value	Men (<i>n</i> = 200)	Women (<i>n</i> = 265)	<i>P</i> -value	Total (<i>n</i> = 465)
1. Dog	30.2	26.2	12.1	< 0.001	25.0	20.4	0.236	22.4
2. Cat	31.4	17.2	10.3	< 0.001	23.0	17.4	0.131	19.8
3. Birch	27.8	17.2	10.9	< 0.001	18.0	19.2	0.733	18.7
4. Timothy	26.6	18.0	10.3	< 0.001	22.5	15.1	0.041	18.3
5. Mugwort	13.0	11.5	9.2	0.529	10.0	12.1	0.482	11.2
6. Cockroach	8.9	13.1	8.6	0.380	12.5	7.9	0.102	9.9
7. <i>Lepidoglyphus destructor</i>	8.3	10.7	8.0	0.704	11.0	7.2	0.149	8.8
8. <i>Dermatophagoides farinae</i>	8.3	9.0	1.7	0.010	8.0	4.5	0.119	6.0
9. Horse	11.2	4.1	0.6	< 0.001	5.0	5.7	0.755	5.4
10. <i>D. pteronyssinus</i>	7.1	4.9	2.3	0.111	7.0	3.0	0.045	4.7
11. <i>Acarus siro</i>	4.7	6.6	2.3	0.194	6.0	3.0	0.117	4.3
12. Cow	4.7	2.5	1.1	0.127	3.5	2.3	0.423	2.8
13. <i>Cladosporium herbarum</i>	0.6	6.6	1.1	0.002	2.0	2.6	0.652	2.4
14. <i>Alternaria alternata</i>	2.4	1.6	0.6	0.391	1.0	1.9	0.437	1.5
15. Latex	1.8	0.8	0.6	0.5317	1.0	1.1	0.891	1.1
Any pollen (3, 4, 5)	41.4	33.6	23.0	0.001	36.0	29.8	0.158	32.5
Any animal (1,2,9,12)	40.2	31.1	14.9	< 0.001	32.5	25.3	0.087	28.4
Any mite (7,8,10,11)	16.0	17.2	10.3	0.176	19.0	10.6	0.010	14.2
Any mould (13,14)	3.0	6.6	1.7	0.073	2.5	4.2	0.334	3.4
Any allergen	56.8	49.2	35.6	< 0.001	50.5	44.2	0.174	46.9

Difference (*P*-value) by age groups and gender.

Table 2. Prevalence (%) of physician-diagnosed asthma, allergic rhinitis or conjunctivitis, and respiratory symptoms among those with negative skin prick test (SPT) and positive SPT to any allergen and groups of allergens.

Condition	Negative prick (n = 247)	Any allergen (n = 218)	Any pollen (n = 151)	Any animal (n = 132)	P-value	Any mite (n = 66)	P-value	Any mould (n = 16)	P-value
Physician-diagnosed asthma	5.7	8.3	11.9	10.6	0.023	4.5	0.074	12.5	0.270
Allergic rhinitis or conjunctivitis	25.1	61.0	70.2	72.7	< 0.001	50.0	< 0.001	81.3	< 0.001
Wheeze	18.6	26.6	32.5	31.1	0.002	27.3	0.006	37.5	0.066
Longstanding cough	19.8	19.3	18.5	17.4	0.751	25.8	0.568	12.5	0.472
Attacks of shortness of breath	17.0	19.3	18.5	17.4	0.709	22.7	0.291	25.0	0.419

Difference (P-value) calculated comparing to those with negative prick reaction.

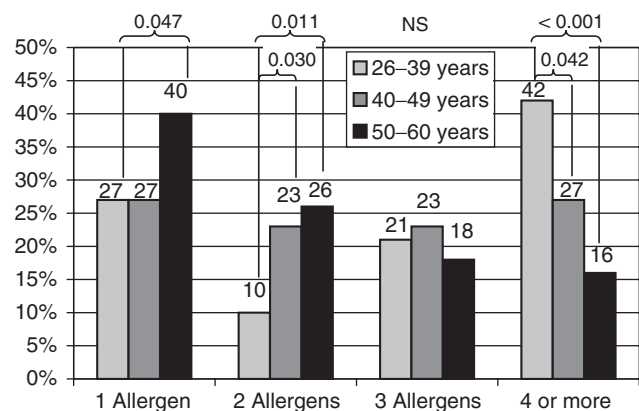


Fig. 1. Proportions of sensitization to 1, 2, 3, and 4 or more allergens in different age groups. Statistically significant differences between the age groups given as P-values

The prevalence of both asthma and AR or conjunctivitis increased significantly with increasing number of positive SPT responses ($P < 0.001$) (Fig. 2). Moreover, wheezing was significantly related to the degree of sensitization: 42.4% of the multisensitized, 19.4% of those sensitized to a single allergen, and 18.6% of non-sensitized reported wheezing.

Multivariate relationships

Belonging to the youngest age group was the strongest risk factor for being sensitized to any allergen, to any of the pollens, any animal, as well as to multiple sensitization, with an OR of 2.06–4.29 (Table 4). Having a family history of AR or conjunctivitis was a significant risk factor for being sensitized to any allergen, OR 1.59 (95% CI 1.07–2.37), and to any pollen, OR 2.13 (95% CI 1.40–3.26), and a strong trend for multiple sensitization, OR 1.73 (95% CI 0.99–3.02). Urban living during the first 5 years in childhood was a significant risk factor for sensitization to any pollen. In bivariate analyses, severe respiratory infections in childhood, having furred pets in childhood, number of siblings, and smoking habits were not significantly associated with allergic sensitization and were thus not included in the multivariate analyses.

Discussion

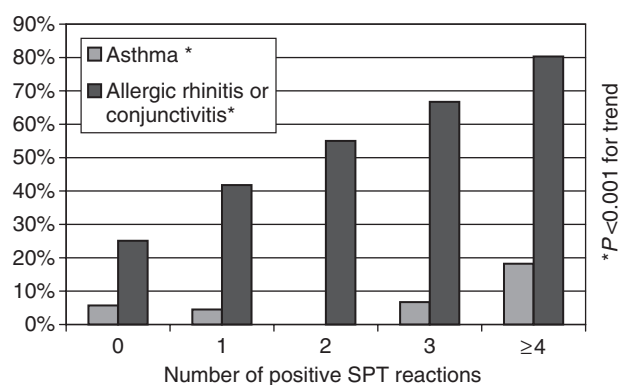
In the present study, allergic sensitization was strongly age dependent. More than half, 57%, of the young adults aged 26–39 years were sensitized to at least one airborne allergen, and 42% of these sensitized subjects reacted to at least four allergens. This multiple sensitization was associated with a high prevalence of asthma, wheezing, and AR or conjunctivitis.

The study population for this part of the study was obtained in a random manner from the participants in the

Table 3. Prevalence (%) of physician-diagnosed asthma, allergic rhinitis or conjunctivitis, and respiratory symptoms by number of positive reactions in prick test

Condition	Number of positive reactions in prick test				P-value
	1 (n = 67)	2 (n = 40)	3 (n = 45)	4 or more (n = 66)	
Physician-diagnosed asthma	4.5	0	6.7	18.2	< 0.001
Allergic rhinitis or conjunctivitis	41.8	55.0	66.7	80.3	< 0.001
Wheeze	19.4	17.5	22.2	42.4	0.007
Attacks of shortness of breath	19.4	20.0	13.3	22.7	0.098
Longstanding cough	16.4	20.0	17.8	22.7	0.195

Difference (P-value) between groups calculated by one-way ANOVA.

**Fig. 2.** Prevalence of physician-diagnosed asthma and allergic rhinitis (AR) or conjunctivitis by number of positive skin prick test (SPT) reactions.

earlier phase, in which the participation rate was 76% [10]. The original sample was designed to be representative of the population in Helsinki from age 20–69 years. The prevalence of asthma, AR, and asthma related symptoms did not differ from the results of the original study population in relevant ages. Thus, the results can be generalized to the urban adult population of Helsinki.

Allergic sensitization in our study (47%) was more common than in the ECRHS results from Sweden among subjects aged 20–44 years (36%) [12], and in results from Denmark [13]. A high prevalence of allergic sensitization, 49%, among Finnish adolescents was already shown by Haahetela et al. [14]. Similarly, 53% of young adults were sensitized in Australia in 1992 [15]. Our results represent a larger and older age group from 26 to 60 years, and the very high prevalence particularly among young adults may indicate an increase of allergic sensitization. A Danish study found a significant increase in the prevalence of positive SPT reaction to one or more of ten common allergens from 28% to 34% among adults from 1990 to 1998 [13]. No previous urban population-based study from Finland is available, thus no detailed comparisons about the trend of allergic sensitization in Finland can be made.

The distribution of prick test reactions to different allergens was similar to previous findings in Finland: dog, cat, and pollens being the most common allergens,

while mites and moulds were less common [2, 16]. In the neighbouring countries Russia and Estonia, however, the proportion of those sensitized to cat, dog, birch, and timothy has been considerably lower, while mugwort, cockroach, and mites were the most common sensitizers [2, 17]. In Sweden, the distribution of sensitization to allergens has been similar to our findings, with the role of HDMs being more pronounced in the southern areas of Sweden [12, 17]. In a study from Northern Sweden, HDMs were not present in dust samples from schools and homes [18], and allergy to mites was rare [19].

Cockroach sensitization of nearly 10% was a surprise, but prevalence estimates up to 7.5% have been reported from eastern Finland [2], from Norway [20], with even higher rates from Tallinn, Estonia [3]. However, in contrast to Estonia, sensitization to cockroach and storage mites did not increase the total prevalence of allergic sensitization in Helsinki more than with a few percent units. In a study from New York City, sensitization to cockroach was associated with a more severe asthma, and it was the most common allergen among hospitalized asthma patients [21]. Similarly, sensitization to indoor allergens, cat and HDMs, has been related to a lower lung function in asthmatics in the ECRHS [22]. It is not known how common mites and cockroaches are in Finnish homes, but this would be worth of studying owing to the profile of sensitization in our study.

Similarly, to other studies from the Nordic countries [13, 19, 23], asthma was related to sensitization to cat and dog, and also pollen. Wheezing was related to animal sensitization besides pollens, but not to mites or moulds. The fact that allergic sensitization was related to wheezing more consistently than to physician diagnosed asthma suggests an under-diagnosis of allergic asthma, which may happen if symptoms occur only when exposed to allergens. As expected, there were 32 (6.9%) asthmatics among the 465 subjects. However, the relatively small number of asthmatics limits the conclusions concerning asthma. Of those with physician-diagnosed asthma 56.3% were sensitized, which was less than the proportions in the ECRHS varying from 62.7% to 80.6% [24]. The subjects in the ECRHS were younger than in our study, which may in part explain this difference.

Table 4. Risk factors (odds ratio (OR)) for any of the allergens, groups of pollens and animals, and for multiple sensitization (4 or more allergens)

Independent variables	Dependent variables								
		Any pollen		Any animal		Any allergen		Multiple sensitization	
Variables	Categories	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Sex	Female	1.0		1.0		1.0		1.0	
	Male	1.53	(1.00–2.33)	1.49	(0.96–2.30)	1.40	(0.95–2.07)	1.41	(0.80–2.46)
Age (years)	50–60	1.0		1.0		1.0		1.0	
	40–49	1.66	(0.98–2.83)	2.57	(1.45–4.57)	1.74	(1.07–2.81)	2.35	(1.02–5.44)
	26–39	2.06	(1.24–3.41)	3.65	(2.11–6.31)	2.15	(1.35–3.43)	4.29	(2.00–9.20)
Family history of allergic rhinoconjunctivitis	No	1.0		1.0		1.0		1.0	
	Yes	2.13	(1.40–3.26)	1.39	(0.90–2.17)	1.59	(1.07–2.37)	1.73	(0.99–3.02)
Area of domicile at age 0–5 years	Countryside	1.0		1.0		1.0		1.0	
	Suburban	1.22	(0.65–2.23)	1.07	(0.56–2.04)	1.11	(0.63–1.97)	1.61	(0.68–3.80)
	Urban	1.69	(1.02–2.79)	1.40	(0.82–2.37)	1.42	(0.90–2.23)	1.59	(0.75–3.36)

Statistically significant values with $P < 0.05$ in bold.

AR or conjunctivitis was strongly related to all sensitization, which is in accordance to current knowledge [5, 13, 25]. Sensitization to multiple allergens was significantly related to high prevalence of asthma, AR or conjunctivitis, and wheeze compared with those with fewer positive responses in prick tests, which was consistent with recent Dutch results [7]. The prevalence of asthma was as high as 18.2% among those sensitized to multiple allergens, while no significant difference in prevalence of asthma could be found comparing those without any reaction in SPTs to those with at least one positive reaction. This points out that strong allergic sensitization is closely linked to asthma. However, there are also other than IgE-mediated causes of asthma particularly among middle-aged and elderly [26].

Belonging to the youngest age group was the most consistent demographic risk factor for sensitization. The Tucson studies showed the sum of positive responses to SPTs to be highest at ages 20–45 years, and to decrease in older ages [27]. Subjects with symptoms may have been more likely to participate, which may contribute to the high prevalence of allergic sensitization among young subjects, while the decreased skin reactivity with age may influence the results among elderly. Having a family history of AR or conjunctivitis was significantly related to having at least one positive prick test reaction and sensitization to pollen. Urban residence in childhood yielded higher ORs for sensitization compared with countryside or suburban residence, but reached statistical significance only for sensitization to pollens in our study. One third of the subjects had been living in countryside during the first 5 years of life, but living on a farm was not specified in the questionnaire. In a study on university students in Finland, farm environment in childhood was associated with a decreased risk for AR and conjunctivitis in early adulthood [28], and similar results were found in Estonia [3]. In the ECRHS, living on a farm in childhood

yielded a decreased risk for allergic sensitization in adulthood, OR 0.76 [29]. Further, rural residence was associated with a lower risk for allergic sensitization among schoolchildren in Sweden [5].

In conclusion, more than half of the young adults less than 40 years of age were sensitized to at least one allergen, and multiple sensitization was surprisingly common. Multiple sensitization was strongly associated with asthma, wheezing, and allergic rhinoconjunctivitis. We suggest that the degree of sensitization should be assessed when evaluating the impact of allergic sensitization.

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