

Association between atopic sensitization and asthma and bronchial hyperresponsiveness in Swedish adults: Pets, and not mites, are the most important allergens

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Background: Atopic sensitization is a well-known risk factor for asthma and bronchial hyperresponsiveness (BHR). Mites have been regarded as the most important allergens, but the prevalence of sensitization to mites is relatively low in Sweden.

Objective: The aim of the study was to investigate possible associations between sensitization to various allergens and asthma and BHR in adults.

Methods: A random sample of 1859 subjects, aged 20 to 46 years, was investigated in a cross-sectional study by using a questionnaire, skin prick tests (SPTs), specific and total IgE measurements, and methacholine bronchial challenge tests. Possible associations were analyzed univariately and by using multivariate logistic regression analysis and proportional hazard regression analysis.

Results: Positive SPT and specific IgE results were more common in subjects with asthma and BHR than in subjects without these conditions for all allergens. The independent associations between positive SPT responses and asthma and BHR are given as adjusted prevalence ratios (PRRs): pets and asthma, PRR = 3.6; pets and BHR, PRR = 2.0; grass and asthma, PRR = 2.0; grass and BHR, PRR = 1.7; mites and asthma, PRR = 1.4; and mites and BHR, PRR = 1.2. The use of specific IgE measurements instead of SPTs showed essentially similar results.

Conclusion: Cats and dogs were the sensitizing allergens most closely associated with asthma and BHR. The relationships with sensitization to grass and mites were less pronounced. (*J Allergy Clin Immunol* 1999;103:58-65.)

Key words: Atopy, cats, dogs, mites, asthma, bronchial hyperresponsiveness, skin test reactivity, specific IgE, total IgE, European Community Respiratory Health Survey

Atopic sensitization is a well-known risk factor for asthma and bronchial hyperresponsiveness (BHR), particularly in children.¹⁻⁷ The role of allergy has been more controversial in adult asthma, but some studies of adults have revealed associations between sensitization and asthma. Burrows et al⁸ found an association between asthma and elevated total IgE. Gergen et al⁹ found that asthma was associated with house dust and *Alternaria* spp. However, their study was conducted before modern standardized skin test extracts were available, and specific IgE was not used. In addition, the study included both young adults and children. The Spanish part of the European Community Respiratory Health Survey (ECRHS) found that asthma was associated with sensitization to both indoor and outdoor allergens.¹⁰ Cookson et al¹¹ found the risk of BHR was greater in subjects sensitized to house dust and molds than in those sensitized to grass. Two other ECRHS studies^{12,13} found an increased risk of BHR in subjects sensitized to indoor allergens or pollens.

Most previous studies were performed in countries with a high prevalence of sensitization to house dust mites (HDMs). In a study from Canada, Murray et al¹⁴ showed that sensitization to HDMs is rare in areas that are "dry," either as a result of a semiarid climate or a cold climate with a long heating season. Most parts of Sweden are typical examples of areas with a long heating season. Consequently, there is a relatively low occurrence of sensitization to HDMs. In contrast, the prevalence of sensitization to pollens and especially to pets is high.^{15,16}

The primary aim of this study was to investigate the relationships between sensitization to common inhaled allergens and asthma and BHR in adults from 3 areas of Sweden.

METHODS

Study design and population

The study was performed in accordance with the ECRHS protocol¹⁷ (ie, a cross-sectional investigation of a random sample of the general population). A random sample of 1800 men and 1800 women, aged 20 to 44 years, was selected from each of these cen-

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Abbreviations used

BHR:	Bronchial hyperresponsiveness
CI:	Confidence interval
ECRHS:	European Community Respiratory Health Survey
HDM:	House dust mite
OR:	Odds ratio
PAR:	Population attributable risk
PRR:	Prevalence ratio
SPT:	Skin prick test

ters by using the population registers. A postal questionnaire was sent to all subjects in December 1990¹⁸; the response rate was 86%. With the aim of obtaining 600 subjects from each center, random subsamples of individuals (950, 800, and 672 subjects from Göteborg, Uppsala, and Västerbotten, respectively) were selected for participation in the second stage of the study. The different numbers were due to differences in estimated participation rates between the centers. Only those who had previously answered the screening questionnaire were invited to participate. In all, 89.2% of the invited subjects agreed to participate. The clinical examinations were conducted between February 1991 and June 1992.

The study was approved by the ethics committees at the universities in the 3 areas and by the Swedish Data Protection Board.

Areas of residence

Göteborg (Gothenburg) is Sweden's second largest city. Compared with the other areas, the climate is warmer and more humid because of Göteborg's location near the sea in the southern part of Sweden. Uppsala is a university city, 60 km northwest of Stockholm in the interior part of the country. Västerbotten is a large county in northern Sweden. The climate is subarctic, with short summers and long, cold winters.

Questionnaires

The screening questionnaire was the ECRHS-modified version of the International Union Against Tuberculosis and Lung Disease questionnaire, and the main questionnaire was developed from preexisting questionnaires.^{19,20} It included questions on symptoms, medical history, occupational and social status, smoking habits, home environment, medication use, and use of services.²⁰ The questionnaire was administered by interviewers trained at a joint workshop.

Definitions of asthma and atopy

The criterion for asthma was a positive answer to the questions "Have you ever had asthma?" and "Was it diagnosed by a physician?" and a positive answer to at least 1 of 5 questions about asthma symptoms during the past 12 months (questions 1 to 5 in the main questionnaire).²¹

Atopy was defined as a positive skin prick test (SPT) response to one or more allergens.

Allergic sensitization

Sensitization to various allergens was estimated by using 2 different methods: SPTs and CAP-RAST analyses for specific IgE (RAST).

SPTs were carried out by using Phazets (Pharmacia Diagnostics, Uppsala, Sweden), stainless-steel lancets precoated with lyophilized standardized allergen extracts.²² SPTs were performed as single tests and in accordance with the European Academy of Allergology and Clinical Immunology position paper.²³ All the fieldworkers were trained to perform the SPTs in a standardized

manner.^{15,17} The following ECRHS panel of allergens was used: cat, HDM (*Dermatophagoides pteronyssinus*), timothy grass, birch, *Cladosporium herbarum*, *Alternaria alternata*, olive, common ragweed, and *Parietaria judaica*. In addition, 2 common Swedish allergens, dog and mugwort, were added. A histamine-coated Phazet was used as the positive control, and an uncoated Phazet was used as the negative control. A mean wheal diameter of 3 mm or more was regarded as positive.²³ SPTs to olive and common ragweed were not included in this presentation because of the very low occurrence of these allergens in Sweden.¹⁸

SPT responses to pets were defined as a positive response to cats, dogs, or both. To avoid colinearity in the multivariate analysis because of the close association between sensitization to cats and dogs,²⁴ pets were included as an independent variable instead of using cats and dogs as separate variables. SPT responses to molds were defined as positive to *C herbarum*, *A alternata*, or both. Because of the low number of cases, SPTs to molds were used in the multivariate analysis instead of using *C herbarum* and *A alternata* as separate variables. SPTs to *P judaica* were not included in the multivariate analyses because of the low number of cases of sensitization.

Total serum IgE and specific IgE toward cats, HDMs (*D pteronyssinus*), grass, birch and *C herbarum* were measured (Pharmacia CAP systems, Pharmacia Diagnostics).²⁵ RAST results were categorized into class 0 (specific IgE <0.35 kU/L), class 1 (specific IgE ≥0.35 kU/L), class 2 (specific IgE ≥0.7 kU/L), class 3 (specific IgE ≥3.5 kU/L), and class 4 or more (specific IgE ≥17.5 kU/L). A RAST class of at least 2 was regarded as positive.

Bronchial methacholine challenge

The methacholine challenge test was performed according to the ECRHS protocol.²⁰ The Mefar MB3 dosimeter (Mefar Ele H2O; Medicali, Brescia, Italy) was used. After inhaling the diluent, methacholine in cumulative doses from 0.0039 mg to 2 mg was inhaled. FEV₁ was measured before and during the methacholine challenge test 2 minutes after the delivery of each dose. The Spiro Medics computerized dry rolling seal spirometer system 2130 (Sensor Medics, Anaheim, Calif) was used. BHR was defined as a decline in FEV₁ of 20% or greater compared with the postdiluent value after inhalation of a cumulative dose of methacholine of 2 mg or less.

Statistical analysis

The chi-square test was used when analyzing differences between groups. The chi-square test for trends was used to test for a possible increase in the trend in prevalence according to RAST class. Multivariate logistic regression analysis was performed to estimate the adjusted odds ratios (ORs) when taking several independent variables into account. The OR may be a biased estimate of the relative risk, especially with common disorders. Therefore an adjusted prevalence ratio (PRR) was also calculated by using proportional hazard regression.^{26,27} Differences between total IgE values were tested by using an unpaired *t* test after logarithmic transformation. The statistical analysis was performed with the Statistica 4.0 (StatSoft Inc, Tulsa, Okla) software package. The adjusted PRR was calculated by using the SAS statistical package, procedure PHREG (SAS Institute, Cary, NC). Probability (*P*) values of less than .05 (2-tailed test) and ORs with 95% confidence intervals (CIs) excluding 1.0 were regarded as statistically significant. Unless otherwise specified, the multivariate analysis included sex, age, area of residence, smoking status, and sensitization to specific allergens as independent variables. When possible associations with BHR were studied, FEV₁ was included as an independent variable.²⁸ The proportion of asthma and BHR in the population that could be attributed to atopy and specific sensitization was calculated as the population attributable risk (PAR) by using the point estimate of the

TABLE I. Basic characteristics of subjects with or without asthma and bronchial BHR

	Asthma		BHR	
	No (n = 1488)	Yes (n = 84)	No (n = 1194)	Yes (n = 218)
Female, %	49.9	63.1*	45.8	58.3†
Mean age (SD), y	33 (7.3)	32 (7.6)	33 (7.4)	33 (7.4)
Living in Göteborg, %	37.6	34.5	38.3	33.5
Living in Uppsala, %	33.6	32.1	34.5	33.0
Living in Västerbotten, %	28.8	33.3	27.2	33.5
Smokers, %	29.2	23.8	27.6	39.0†
Cat/dog at home, %	30.1	22.1	28.7	31.3
Cat/dog as a child, %	67.5	71.2	67.2	67.4

* $P < .05$.† $P < .001$.

adjusted PRR. The association between sensitization to cat and dog allergens was described by Cohen's kappa statistic (κ).²⁹

RESULTS

Study participation

The questionnaire was answered by 1859 of the 2084 subjects invited to participate. SPTs were performed on 1572 individuals, IgE tests in 1470, and bronchial methacholine challenges in 1450. In all, 1412 subjects participated in SPTs and tests for BHR, and 1318 participated in IgE tests and tests for BHR. When comparing participants with nonparticipants by using the data from the stage 1 screening questionnaire, there was no difference regarding self-reported asthma attacks or current smoking, but nonparticipants had a slightly lower mean age, a slightly lower prevalence of wheezing, and comprised a slightly higher proportion of males.

Univariate analysis

The prevalence of asthma was 5.6%, and the prevalence of BHR was 15%. The basic characteristics of subjects with or without asthma and BHR are shown in Table I. Asthma and BHR were more common among women than men. The mean age was the same in subjects with and without asthma and BHR. There was no statistically significant difference between areas in the prevalence of asthma and BHR, but a tendency toward a higher prevalence was seen in Västerbotten than in the other 2 areas. There were more smokers among subjects with BHR. There was no difference in the occurrence of present domestic pets or pets in childhood between subjects with or without asthma or with or without BHR.

Positive SPT responses and positive RAST results were more prevalent in subjects with asthma and BHR than in subjects without these conditions for all allergens (Table II). Only a few subjects were sensitized to *P. judaica* and to the 2 molds. Atopy was found twice as frequently among subjects with asthma and more than 50% more frequently in persons with BHR compared with subjects without these conditions. Similarly, one or more

positive RAST results were found two and a half times as often among subjects with asthma and nearly twice as often in persons with BHR compared with subjects without BHR. Total IgE was higher in subjects with asthma and in subjects with BHR compared with persons without these conditions. In subjects without asthma, there were similar, but somewhat less pronounced, differences between subjects with BHR and subjects without BHR.

The occurrence of asthma and BHR increased as the RAST classes increased, particularly when it came to cats (Figs 1 and 2).

SPT responses to cats were closely associated with SPT responses to dogs ($\kappa = 0.6$ in the population, 0.55 in nonasthmatic subjects, and 0.7 in asthmatic subjects).

Multivariate analysis

The relationship between sensitization to allergens and asthma is presented as ORs and PRRs in Table III. Of all allergens, pets were most strongly associated with asthma. Sensitization to grass and HDMs was associated with asthma to a smaller degree, whereas sensitization to birch, mugwort, and molds was not independently associated with asthma. The results were essentially the same whether SPTs or RASTs were used to estimate sensitization and whether adjusted ORs or adjusted PRRs were used to estimate the associations. PAR for atopy was 26%. PAR for a positive SPT response to pets was 14%, for a positive SPT response to grass was 8%, and for a positive SPT response to HDMs was 3%.

Female sex was associated with asthma (OR = 1.9, CI = 1.2-3; PRR = 1.8, CI = 1.2-2.8), whereas age, area of residence, and smoking status were not related to asthma.

To control for the influence of atopy itself, a multivariate logistic regression analysis, including only the atopic subjects in the population ($n = 560$), was performed. SPT responses to pets (OR = 3.5, CI = 1.7-7.1) and grass (OR = 2.0, CI = 1.1-3.6) were still associated with asthma. To control for the influence of the general tendency to produce IgE, a multivariate logistic regression analysis, including log total IgE as an independent variable together with RAST, sex, age, area of residence, and smoking status, was performed. RAST results to cats were still associated with asthma (OR = 3.5, CI = 2.0-6.0).

Of all allergens, pets were most strongly associated with BHR (Table IV). Sensitization to grass was more weakly associated with BHR. Sensitization to HDMs, birch, mugwort, and molds was not independently associated with BHR. The results were essentially the same whether SPTs or RASTs were used to estimate sensitization and whether adjusted PRRs or adjusted ORs were used to estimate the association. PAR for atopy was 19%. PAR for positive SPT responses to pets was 10%, for grass was 7%, and for HDMs was 2%.

Smoking was associated with BHR (PRR = 1.5, CI = 1.1-2.9). Sex, age, and area of residence were not related to BHR.

In addition to control for the influence of atopy itself, a multivariate logistic regression analysis, including only

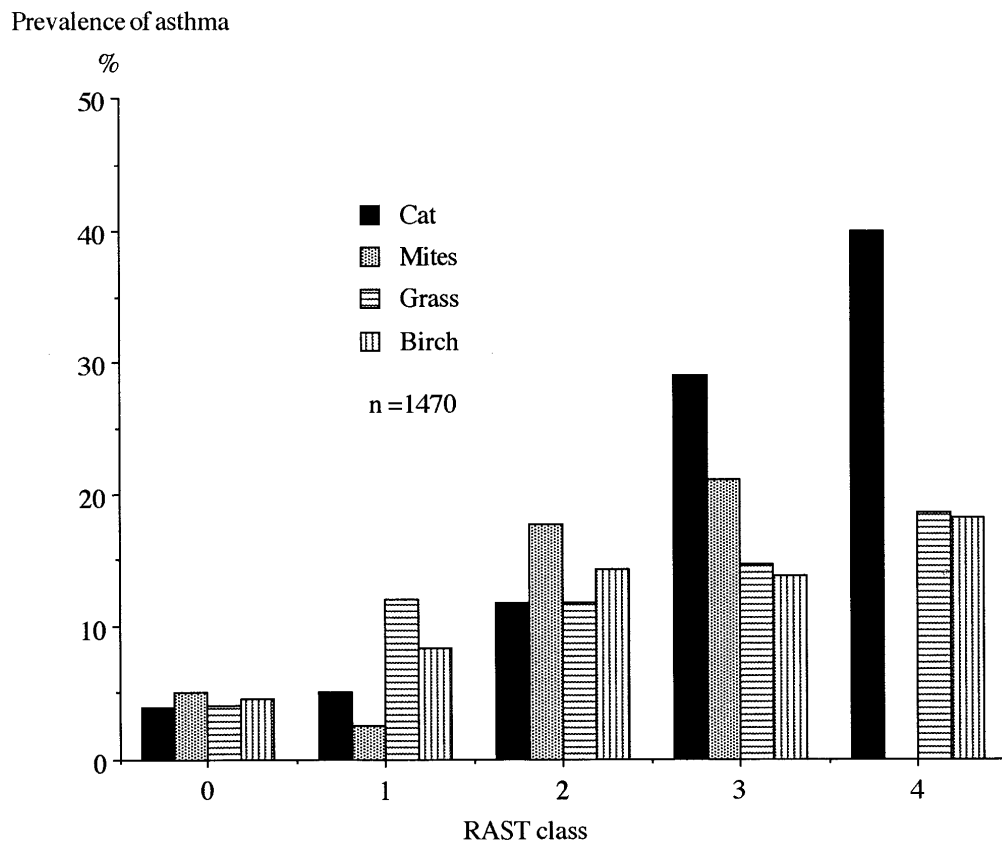


FIG 1. Prevalence of asthma by RAST class.

TABLE II. SPTs, RASTs, and total IgE measurements in subjects with or without asthma, with or without BHR, and without asthma (with or without BHR)

	Asthma		BHR		BHR in subjects without asthma	
	No (n = 1488)	Yes (n = 84)	No (n = 1194)	Yes (n = 218)	No (n = 1167)	Yes (n = 180)
SPT						
Cats, %	13.5	46.4 [‡]	12.5	29.4 [‡]	11.9	23.3 [‡]
Dogs, %	12.1	45.2 [‡]	10.8	29.4 [‡]	10.1	25.0 [‡]
Pets, %	17.8	53.6 [‡]	16.5	35.8 [‡]	15.7	30.6 [‡]
Mites, %	9.5	20.2 [†]	9.5	15.1 [*]	9.4	13.3
Timothy grass, %	14.8	40.5 [‡]	13.7	28.0 [‡]	13.3	23.9 [‡]
Birch, %	15.5	31.0 [†]	14.6	25.2 [‡]	14.3	23.9 [†]
Mugwort, %	5.4	10.7 [*]	5.4	7.3	5.4	6.1
<i>P judaica</i> , %	1.4	3.6	1.4	2.8	1.5	1.7
Molds, %	3.2	6.0	2.9	5.5 [*]	2.9	4.4
Atopy, %	33.9	66.7 [‡]	32.3	54.1 [‡]	31.7	49.4 [‡]
RAST						
Cats, %	9.4	40.0 [‡]	7.9	26.0 [‡]	7.3	20.4 [‡]
Mites, %	5.8	18.8 [‡]	5.7	13.0 [‡]	5.6	10.1 [*]
Grass, %	12.6	35.3 [‡]	11.8	22.6 [‡]	10.9	20.8 [‡]
Birch, %	10.4	29.4 [‡]	10.3	18.3 [‡]	9.6	17.3 [†]
<i>C herbarum</i> , %	1	3.5 [*]	0.7	2.9 [†]	0.7	1.8
Any RAST, %	23.8	62.4 [‡]	22.6	41.4 [‡]	—	41.4 [‡]
Total IgE, kU	23.1	66.8 [‡]	22.5	40.6 [‡]	21.8	35.7 [‡]
(geometric mean)						

* $P < .05$.

[†] $P < .01$.

[‡] $P < .001$.

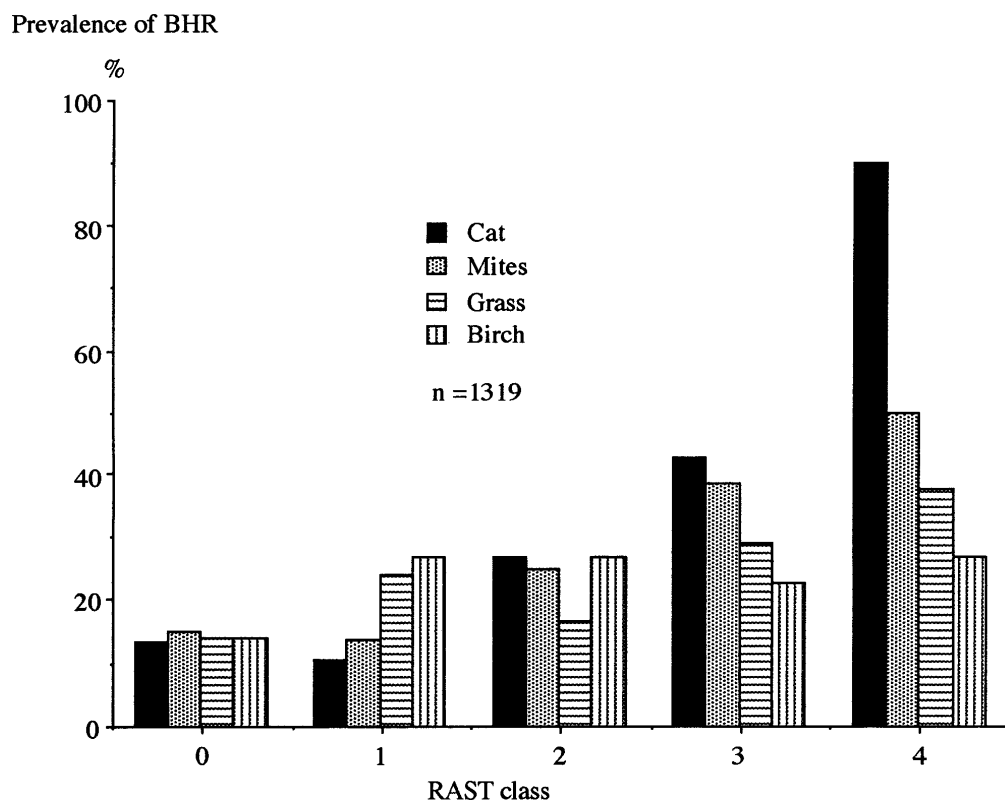


FIG 2. Prevalence of BHR by RAST class.

TABLE III. The association between sensitization and asthma presented as ORs and PRRs

	OR (CI) crude	OR (CI) adjusted*	PRR (CI) crude	PRR (CI) adjusted*
SPTs				
Cats	5.5 (3.5-8.7)	—	4.8 (3.2-7.2)	—
Dogs	6.0 (3.8-9.5)	—	5.1 (3.4-7.7)	—
Pets	5.3 (3.4-8.3)	4.0 (2.3-7.1)	4.7 (3.1-7.1)	3.6 (2.1-6.3)
Mites	2.4 (1.4-4.2)	1.5 (0.8-2.7)	2.3 (1.4-3.8)	1.4 (0.8-2.5)
Grass	3.9 (2.5-6.2)	2.2 (1.2-3.9)	3.5 (2.3-5.3)	2.0 (1.1-3.5)
Birch	2.5 (1.5-4.0)	0.8 (0.5-1.5)	2.3 (1.5-3.6)	0.9 (0.5-1.5)
Mugwort	2.1 (1.0-4.0)	1.3 (0.7-2.4)	2.0 (1.0-3.9)	0.9 (0.4-1.8)
Molds	1.9 (0.8-5.0)	0.8 (0.3-2.1)	1.9 (0.8-4.4)	0.8 (0.3-2.0)
Atopy	3.9 (2.5-6.2)	4.0 (2.5-6.5)	3.6 (2.3-5.6)	3.7 (2.3-5.8)
RASTs				
Cats	6.4 (4.0-10.3)	4.2 (2.4-7.3)	5.3 (3.6-7.9)	3.5 (2.1-5.9)
Mites	3.8 (2.1-6.8)	2.3 (1.2-4.5)	3.3 (2.0-5.5)	1.9 (1.1-3.5)
Grass	3.8 (2.4-6.0)	2.1 (1.1-3.9)	3.4 (2.2-5.1)	1.9 (1.1-3.4)
Birch	3.6 (2.2-5.9)	1.3 (0.7-2.4)	3.2 (2.1-5.0)	1.3 (0.7-2.2)
<i>C herbarum</i>	3.6 (1.0-12.7)	0.8 (0.2-3.1)	3.1 (1.1-8.9)	0.8 (0.2-2.7)
Any allergen	5.3 (3.4-8.4)	5.8 (3.7-9.3)	4.7 (3.1-7.2)	5.0 (3.2-7.8)

*Adjusted for sex, age, area of residence, smoking status, and sensitization to other allergens. Atopy was adjusted for sex, age, area of residence, and smoking status.

the atopic subjects in the population ($n = 503$), was conducted. SPT responses to pets ($OR = 1.9$, $CI = 1.2-3.0$) were still associated with BHR. To control for the influence of the general tendency to produce IgE, a multivariate logistic regression analysis, including log total IgE as an independent variable together with RAST results, sex, age, area of residence, smoking status, and FEV_1 , was

conducted. RAST results to cats were still most strongly associated with BHR ($OR = 3.2$, $CI = 2.0-4.9$).

Possible associations between sensitization and BHR were studied separately in subjects without asthma ($n = 1346$) in a similar multivariate logistic regression analysis. The results were essentially the same as those of the main analysis. SPT responses to pets were independent-

TABLE IV. Association between sensitization and BHR presented as ORs and PRRs

	OR (CI) crude	OR (CI) adjusted*	PRR (CI) crude	PRR (CI) adjusted*
SPTs				
Cats	2.9 (2.1-4.1)	—	4.8 (3.2-7.2)	—
Dogs	3.4 (2.4-4.8)	—	5.1 (3.4-7.7)	—
Pets	2.8 (2.1-3.9)	2.4 (1.5-3.6)	4.7 (3.1-7.1)	2.0 (1.4-2.8)
Mites	1.7 (1.1-2.6)	1.2 (0.8-1.9)	2.3 (1.4-3.8)	1.2 (0.8-1.7)
Grass	2.4 (1.7-3.4)	1.9 (1.2-3.0)	3.5 (2.3-5.3)	1.7 (1.1-2.4)
Birch	2.0 (1.4-2.8)	1.1 (0.7-1.7)	2.3 (1.5-3.6)	1.1 (0.7-1.6)
Mugwort	1.4 (0.8-2.4)	0.7 (0.4-1.4)	2.0 (1.0-3.9)	0.7 (0.4-1.3)
Molds	2.0 (1.0-3.9)	1.0 (0.5-2.1)	1.7 (1.0-2.9)	0.7 (0.4-1.4)
Atopy	2.4 (1.8-3.3)	2.8 (2.1-3.8)	3.6 (2.3-5.6)	2.2 (1.7-2.9)
RASTs				
Cats	4.1 (2.8-6.0)	3.5 (2.2-5.5)	2.9 (2.2-3.8)	2.5 (1.7-3.7)
Mites	2.5 (1.5-4.0)	1.5 (0.9-2.6)	2.0 (1.4-2.9)	1.2 (0.8-1.9)
Grass	2.2 (1.5-3.2)	1.6 (1.0-2.6)	1.9 (1.4-2.5)	1.4 (1.0-2.2)
Birch	2.0 (1.3-2.9)	0.9 (0.5-1.5)	1.7 (1.3-2.3)	0.9 (0.6-1.5)
<i>C herbarum</i>	4.1 (1.4-11.9)	1.8 (0.6-6.1)	2.8 (1.5-5.1)	1.5 (0.6-3.5)
Any allergen	2.4 (1.8-3.3)	2.6 (1.9-3.6)	2.1 (1.6-2.6)	2.1 (1.6-2.7)

*Adjusted for sex, age, area of residence, smoking status, FEV₁, and sensitization to other allergens. Atopy was adjusted for sex, age, area of residence, FEV₁, and smoking status.

ly associated with BHR (OR = 2.1, CI = 1.3-3.3), whereas SPT responses to HDMs were not statistically significantly associated with BHR (OR = 1.2, CI = 0.7-1.9). Similarly, when RAST analysis was used, cat was the allergen most closely associated with BHR (OR = 2.7, CI = 1.6-4.7).

Local results

Each center was analyzed separately by using multivariate logistic regression analysis. In Göteborg, sensitization to HDMs was also associated with BHR (OR = 2.2, CI = 1.4-4.3 when SPTs were used; OR = 3.1, CI = 1.4-6.9 when RASTs were used). The separate analysis of each center produced no other results that differed from the common study.

DISCUSSION

Asthma and BHR were both associated with sensitization to pets and, to a smaller degree, with sensitization to grass. Asthma was additionally, but to a less pronounced degree, associated with sensitization to HDMs. Our finding of a strong association between sensitization to pets and asthma was underlined by the increase in asthma prevalence as the RAST class increased. More than 30% of the subjects with a RAST class of 3 or more to cats had asthma.

Several indoor allergens are recognized as playing a significant role in asthma. Other studies from areas with a high prevalence of sensitization to pets have revealed an association between asthma and sensitization to pets,³⁰⁻³² but most attention has been paid to HDMs.³³ However, Åberg³⁴⁻³⁶ found the highest increase in asthma in the north of Sweden, where mite levels are the lowest. Nor did we find a higher prevalence of asthma in Göteborg, where mite sensitization is more common than in the other Swedish centers. The number of household

pets has increased in Sweden during the last decades.³⁷ In addition, there are changes in lifestyle that have resulted in pets currently living indoors in close contact with human beings, which is in contrast to the outdoor lifestyle of farmers' cats and dogs in previous societies. In our study 73% of the population were present or former pet owners, and 83% of pet owners allowed their pets in the bedroom, whereas only 2.6% kept their pets outdoors. Pet allergen exposure is not limited to pet owners. The allergens are easily transported and can be found at various public places, such as schools and day care centers, and in homes without pets.³⁸⁻⁴² Exposure to pets early in life is a risk factor for sensitization.⁴³⁻⁴⁵ A possible partial explanation of the increase in asthma prevalence could therefore be increased exposure to pets and exposure starting earlier in life. Asthma was also associated with sensitization to HDMs (only statistically significant when RAST was used) and grass pollen.

BHR is associated with asthma, but they are far from synonymous. Previous studies have found a relationship between BHR and sensitization to both HDMs and other allergens.^{3,4,6,11-13} As in asthma, we found a particular increase in the prevalence of BHR as the RAST class to cats increased, thereby underlining the importance of this allergen in Sweden. BHR was significantly associated with RASTs to HDMs only in Göteborg, where the prevalence of sensitization to mites is higher than in the other Swedish centers. In the Spanish ECRHS,¹³ BHR was associated with sensitization to pollens and HDMs, but not to cats, probably because of the low prevalence of domestic cats. However, the PAR of atopy for BHR was the same as in our study. It thus appears that BHR, like asthma, is associated with sensitization to different allergens in different areas.

Our results support the theory that repeated allergen exposure induces bronchial inflammation and an associated increase in BHR in the sensitized subject. In addi-

tion, allergen exposure can trigger attacks of bronchial obstruction (ie, clinical asthma).⁴⁶

The proportion of asthma and BHR explained by the atopic sensitization itself was relatively low. This reflects that although two thirds of the asthmatic subjects were atopic and more than 50% were sensitized to pets, most of the sensitized population did not have asthma. Consequently, other factors, such as the degree of allergen exposure, genetic determinants,⁴⁷ infections, and irritant exposure, play an important role in the development of these conditions.

Nonresponse was low compared with similar studies. The small differences between responders and nonresponders in terms of sex and age are not likely to result in any significant bias.

Physician-diagnosed asthma combined with current symptoms is a criterion for asthma with a higher specificity and a lower sensitivity compared with self-reported asthma or a diagnosis only based on asthma-like symptoms. When risk factors are studied, it is favorable to use criteria with the highest specificity to avoid the dilution of possible relationships.⁴⁸

Bronchial responsiveness is a continuous variable, and there is no definite cut-off point between normal responsiveness and hyperresponsiveness. The use of the dose-response slope would probably have produced similar results.¹²

A mean diameter of 3 mm as the cut-off point for skin test positivity is a limit commonly used in clinical practice and recommended in the European Position Paper.²³ When it came to specific IgE, we investigated the results by using different RAST classes and found that a positive RAST class of at least 2 produced the strongest associations with asthma and BHR. The essentially similar findings with the 2 methods increase the validity of the results.

Because cat and dog sensitivity were so closely related,²⁴ we chose to present sensitization to pets (ie, cats, dogs, or both) in the multivariate analysis. There was no difference between cats and dogs in terms of the degree of association between skin test sensitivity and asthma and BHR in the univariate analysis, and both were independently associated with asthma and BHR when additional multivariate analyses were performed.

The use of an adjusted OR might lead to an overestimation of the relationship between sensitization and asthma and BHR.^{26,27} However, adjusted PRRs showed only slightly lower values and no qualitatively different results.

In conclusion, atopic sensitization is independently associated with both asthma and BHR. In contrast to many earlier publications, which have emphasized mites as the most important allergen, we conclude that cats and dogs are the most important allergens in terms of asthma and BHR in Sweden. Domestic pets are popular in modern society and may contribute to the increase in asthma prevalence. The possibility of sensitization to pets should be taken into consideration in the prophylaxis, diagnosis, and treatment of adult asthma.

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