

Skin prick tests and specific IgE in adults from three different areas of Sweden

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The aims of this part of the European Respiratory Health Survey were to estimate the prevalence of atopic sensitization to inhalant allergens among adults in three different areas of Sweden and to investigate the association between sensitization and certain risk factors. Randomly selected subjects aged 20–46 years from Göteborg, Uppsala, and Västerbotten were investigated with the skin prick test (SPT), analyses for specific IgE antibodies in serum (specific IgE) and total serum immunoglobulin E (total IgE), and a questionnaire. SPT was performed in 1572 subjects and analyses of specific IgE in 1470. One or more positive SPT were found in 35.6% and one or more positive specific IgE in 31.7% – approximately the same values in all three areas. Birch, grass, cat, and dog were the most frequent sensitizing agents and occurred at similar prevalences, i.e., around 15%, in all areas. The SPT to mite was positive in 14.1% in Göteborg, 7.4% in Uppsala, and 7.9% in Västerbotten. A positive SPT to pellitory of the wall (*Parietaria*), not described previously in Sweden, was found in 3.4% in Göteborg. Living in Göteborg was independently associated with a higher risk of a positive SPT to mite and *Parietaria*. Heredity, male sex, and low age were independently associated with atopy. Birth in the Scandinavian countries was independently associated with sensitization to cat, whereas birth in other countries was associated with sensitization to mite. The overall prevalence of atopy was similar in the three Swedish areas, but the sensitizing allergens varied. There is an indication that sensitization is increasing in the population, as low age was associated with sensitization. Sensitization to cat, but not to mite, appears to be particularly important in persons born in the Scandinavian countries.

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Atopy, the tendency to develop IgE antibodies to common allergens, is associated with asthma, allergic rhinoconjunctivitis, and eczema. Atopy is in part due to genetic susceptibility (1). Studies from several countries (2–9) reveal an increasing prevalence of atopic diseases, indicating that exposure to environmental factors plays an important role. Furthermore, some studies reveal a geographic variation in the occurrence of asthma (10–12). Åberg (11) and Åberg et al. (12) found higher prevalences in the north of Sweden than in the south. It is not known whether these regional differences are caused by a difference in the prevalence of atopic sensitization itself, or by an increasing and geographically variable susceptibility in sensitized persons to develop clinical disease.

In this study, the prevalence of atopic sensitization to inhalant allergens was estimated among adults in three Swedish areas which differ in climate and air pollution. There are no previous Swedish studies describing the prevalence of atopic sensitization among adults in random population samples from various parts of the country. Another objective was to investigate the relationship between sensitization and sex, age, some types of exposure during childhood, and smoking habits.

This study is included in the European Community Respiratory Health Survey (ECRHS), which estimates the variation in the prevalence of asthma, asthma-like symptoms, and bronchial lability in Europe and the variation of known or suspected risk factors for asthma (13).

Material and methods

Study design and population

The study was performed in accordance with the ECRHS protocol (14), i.e., a cross-sectional investigation of a random sample of the general population. A random sample of 1800 men and 1800 women aged 20–44 years was selected from each of these centers by means of the population registers. A postal questionnaire (the screening questionnaire) was sent to all subjects in December 1990. An analysis of the screening questionnaire has been published previously (15). With the aim of obtaining 600 subjects from each center, random subsamples of subjects (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. Participation in the different stages of the ECRHS investigation is shown in Fig. 1.

Of the 1859 subjects who agreed to participate, 234 persons were not investigated clinically because they agreed to be interviewed only by telephone. Nine underwent no SPT because of pregnancy or ongoing treatment with antihistamines, phenothiazines, or imipramine. Sixteen persons in whom the histamine positive control of the SPT was <3 mm and 11 persons in whom the negative control was ≥ 3 mm (dermatographic reactions) were not included in the analysis of SPT. Seventeen subjects refused SPT and 16 refused to give a blood sample, and in 139 subjects blood samples were not analyzed for technical reasons. In all, a SPT was analyzed in 1572 individuals, total and specific IgE were determined in 1470, and 1431 completed both investigations.

Areas of residence

Demographic data for the three areas are presented in Fig. 2.

Göteborg (Gothenburg) is Sweden's second largest city. The study area comprised only the island of Hisingen, constituting the northern part of the city – a predominantly urban environment. Here the annual average income is lower, the numbers of immigrants and smokers are higher, and the general health status of the population is lower than in the other areas. Because of the nearness to

the sea, the climate is characterized by moderately warm and humid summers and, by Scandinavian standards, mild winters. Pollution levels from motor vehicles and factories are higher than in the other two areas. There are two substantial pollen seasons with high pollen levels: birch from the end of April to the beginning of June, and grass from the beginning of June until the beginning of August. In addition, there is a mugwort pollen season from the middle of July until the end of August, but the pollen levels are much lower than in the first two seasons (16).

Uppsala is a university city 60 km northwest of Stockholm in the interior of the country. The study area comprised the municipality of Uppsala, including participants both from the city itself (74%) and from the surrounding countryside (26%). The climate is colder and the winters are longer than in Göteborg. Pollution from industrial sources is low. The pollen seasons are similar to those in Göteborg.

Västerbotten is a large county in northern Sweden. The study comprised the southern and western parts (the Umeå and Lycksele health-care districts) – an area as large as The Netherlands. The area included participants from an urban area, Umeå (50%), and from rural areas (50%). The climate is subarctic with short, hot summers and long, cold winters. Generally, air pollution from industry and motor vehicles is low, but considerable local variations exist. The birch and grass pollen seasons are equal to those in the other study areas, but the pollen levels in the mugwort season are lower.

Season

In Göteborg, 64% of the participants were investigated in the winter from October to March, and 36% were examined in the summer from April to September. In Uppsala, the corresponding percentages were 36% and 64%, and in Västerbotten they were 55% and 45%.

Country of birth

The participants were categorized into two groups by country of birth. One group included subjects born in the three northern European countries, Sweden ($n = 1401$), Finland ($n = 50$), and Norway ($n = 13$), a total of 1464. The other group included 107 subjects from 30 different countries (59 from other European countries; 29 from the Middle East and North Africa; 15 from Latin America, tropical Africa, and Asia; and four from the USA and Canada). The country of birth was not registered in one subject.

STUDY FLOW

PARTICIPATION

	TOTAL	(Göteborg — Uppsala — Västerbotten)
Stage 1, random sample	$n = 10800$	(3600 — 3600 — 3600)
↓	↓	↓
Answering questionnaire	$n = 9281$	(2885 — 3144 — 3252)
As percentage of sample	85.9	
↓	↓	↓
Stage 2, random subsample	$n = 2422$	(950 — 800 — 672)
↓	↓	↓
Invited to stage II (random subsample plus answer to stage 1)	$n = 2084$	(772 — 707 — 605)
↓	↓	↓
Participated in stage 2	$n = 1859$	(682 — 625 — 552)
As percentage of those invited	89.2	
As percentage of subsample	76.8	
↓	↓	↓
Participated in SPT	$n = 1572$	(589 — 527 — 456)
As percentage of those invited	75.4%	
Participated in IgE test	$n = 1470$	(574 — 472 — 424)
As percentage of those invited	70.5%	
Participated in both tests	$n = 1431$	(564 — 454 — 413)
As percentage of those invited	68.7%	

Fig. 1. Study flow and participation from three areas: Göteborg, Uppsala, and Västerbotten.

The questionnaires

The screening questionnaire was the ECRHS modified version of the International Union Against

Tuberculosis and Lung Disease (IUATLD) questionnaire, and the main questionnaire was also developed from pre-existing questionnaires (17, 18). It included questions on symptoms, med-

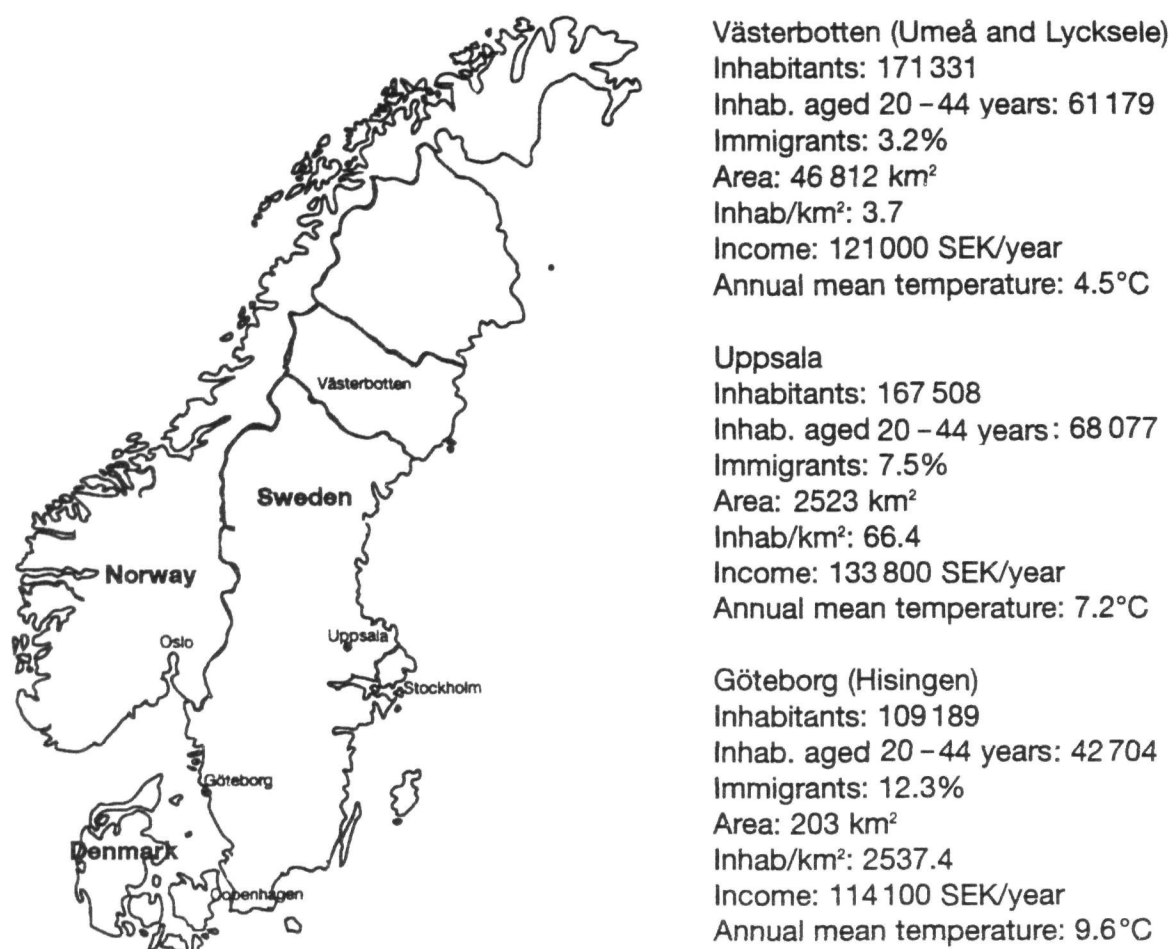


Fig. 2. Geography and demographic data from three investigated areas.

ical history, occupational and social status, smoking habits, and home environment as well as questions on medication and use of services. The exact wording of all the questions is published in the ECRHS protocol (14). The questionnaire was administered by interviewers trained at a joint workshop.

Skin prick test (SPT)

Skin prick testing was done with Phazets® (Pharmacia Diagnostics, Uppsala, Sweden), stainless-steel lancets precoated with lyophilized, standardized allergen extracts (19). SPT was performed as single tests and in accordance with the EAACI position paper (20). All the fieldworkers were trained to perform the SPT in a standardized manner (13, 14). The common ECRHS panel of allergens was used: cat (e1), mite (*Dermatophagoides pteronyssinus*, d1), timothy grass (g6), birch (t3) *Cladosporium herbarum* (m2), *Alternaria alternata* (m6), olive (t9), common ragweed (w1), and *Parietaria judaica* (w21). In addition, two common Swedish allergens were added: dog (e5) and mugwort (w6). A histamine-coated Phazet was used as the positive control and an uncoated one as the negative control. A mean wheal diameter of 3 mm or more was regarded as positive (20).

Specific and total IgE

Venous blood samples were frozen at –70°C pending analysis for total serum immunoglobulin E (total IgE) and specific serum immunoglobulin E antibodies (specific IgE) against cat (e1), *D. pteronyssinus* (d1), grass (g6), birch (t3), and *Cladosporium* (m2). All the analyses were performed at the same laboratory (Pharmacia CAP systems, Pharmacia Diagnostics, Uppsala, Sweden) (21). A specific IgE of 0.35 kU/l or more was regarded as positive.

Definition of atopy and sensitization

Atopy was defined as one or more positive SPT or as one or more positive specific IgE. Sensitization was defined as a positive SPT or as a positive specific IgE.

Statistics

The chi-square test was used when analyzing differences between groups. The chi-square test for trends was used to test an increasing or decreasing trend according to age. As total IgE distribution is skewed, the geometric mean values are presented. Differences between total IgE values were tested with an unpaired *t*-test after logarithmic transfor-

mation. Multivariate logistic regression analysis was performed to estimate the adjusted odds ratios (OR) when taking several independent variables into account. A linear multiple regression analysis was used to estimate the influence of some covariates on total IgE. The differences between the coefficients and zero were tested with the *t*-test. The statistical analysis was performed with the StatView 4.0 (Abacus Concepts, Berkeley, CA, USA), Epi Info 5.00 (WHO), and Statistica 4.0 (StatSoft, Tulsa, OK, USA) software packages. *P* values < 0.05 (two-tailed test) and OR with the 95% confidence intervals (CI) excluding 1.0 were regarded as statistically significant.

The study was approved by the local ethics committees in the three areas and by the Swedish Data Protection Board.

Results

Study participation

Participation rates were similar in the three areas; i.e., about 75% of those invited to participate did so (Fig. 1). Subjects who participated in the skin test (*n* = 1572) were compared with the nonresponders from the random sample (*n* = 338) in terms of area, age, and sex. They were also compared with those who answered the screening questionnaire (*n* = 512) on smoking habits, rhinitis, and asthma, but did not participate in the SPT. Nonresponders had a lower mean age and were more often male. Nonparticipants had a slightly lower mean age, included a higher proportion of men, and had a lower prevalence of self-reported allergic rhinitis, but there were no differences in asthma medication or attacks of asthma. Nonparticipants included a lower proportion of men (*P* < 0.05), a slightly higher proportion of smokers (NS), and a lower proportion of previous smokers (*P* < 0.05) (Table 1).

The prevalence of atopic sensitization

The overall prevalence of atopic sensitization was 35.6% when measured with SPT, 31.7% when measured with specific IgE, and 41.0% when measured with both SPT and specific IgE. Birch, grass, cat, and dog were the most common offending allergens with positive SPT of 16.3, 16.2, 15.3, and 13.9%, respectively. The prevalences of positive SPT and specific IgE to all the allergens which were used are shown in Table 2.

Sensitization and areas of residence

In the univariate analysis (Table 2), the prevalence of atopic sensitization and the geometric mean

values of total IgE were similar in the three areas. Persons living in Göteborg had a higher prevalence of sensitization to mite, mugwort, and *Parietaria*, while sensitization to ragweed was less frequent in Göteborg than in the other areas. Positive SPT to *Cladosporium* was most common in Västerbotten. There were fewer subjects with positive SPT to dog in Uppsala than in Göteborg and Västerbotten. A logistic multivariate analysis including atopic heredity, sex, age, area of residence, country of birth, and day-care attendance before the age of 5 years revealed that area of residence was not associated with atopic sensitization or with sensitization to grass and birch pollen (Tables 3 and 4). Living in Göteborg was associated with higher risk of positive SPT to mite (Table 5) and *Parietaria* (OR = 19.9, CI: 2.7–149) and lower risk of sensitization to ragweed (OR = 0.06, CI: 0.01–0.5). Subjects living in Göteborg or Västerbotten had higher risk of positive SPT to dog (OR = 1.7, CI: 1.2–2.5). Living in Västerbotten was a risk factor for positive SPT to *Cladosporium* (OR = 4.6, CI: 1.6–13.1).

Sensitization and season

Of subjects investigated in the winter, 11.9% had positive SPT to mite compared to 8.0% of persons tested during the summer (*P* < 0.01). The corresponding values for specific IgE were 11.0% and 7.3% (*P* < 0.05). There was no difference in the prevalence of sensitization to grass, birch, cat, dog, or molds or to the frequency of one or more positive SPT or specific IgE. In a logistic multivariate analysis, including season of investigation, atopic heredity, sex, age, area of residence, country of birth, and day-care attendance before the age of 5 years, season was not associated with atopic sensitization or sensitization to single allergens. Total IgE did not vary with season.

Sensitization, sex, and age

The prevalence of one or more positive SPT was 37.8% in men and 33.5% in women (NS). The prevalence of one or more specific IgE was 36.1% in men and 27.5% in women (*P* < 0.001). The geometric mean of total IgE was 28.4 kU/l in men and 21.4 kU/l in women (*P* < 0.001). In the logistic multivariate analysis, male sex was significantly associated with atopic sensitization and with sensitization to grass (Tables 3 and 4). Sensitization to mite and birch appeared to be more common in men, but the findings were not statistically significant for SPT (Tables 4 and 5). Total IgE, adjusted for age and smoking, was higher in men (*P* < 0.001).

The prevalence of atopic sensitization decreased with age (Tables 3 and 6). Correspondingly, the

Table 1. Age, sex, smoking habits, and allergic symptoms in participants and nonparticipants and age and sex in nonresponders to screening questionnaire

	Participants	Nonparticipants	Nonresponders
<i>n</i>	1572	512	338
Mean age (years) (SD)	32.1 (7.3)	31.2 (7.2)**	31.0 (7.3)**
Sex (% male)	49.4	53.7*	59.6***
Current smokers (%)	35.0	37.8	—
Previous smokers (%)	24.0	18.4*	—
Hay fever/allergic rhinitis (%)	24.4	17.1***	—
Attacks of asthma last 12 months (%)	2.9	3.1	—
Asthma medication last 12 months (%)	5.9	6.0	—

Nonparticipants and nonresponders are compared to participants: **P* < 0.05; ***P* < 0.01; ****P* < 0.001.

Table 2. Distribution by area of positive skin prick test, specific IgE, and total IgE. Values are given in percentage. Total IgE is presented as geometric mean in kU/l

Area	Skin prick test			Specific IgE		
	Göteborg	Uppsala	Västerbotten	Göteborg	Uppsala	Västerbotten
<i>n</i>	589	527	456	574	472	424
Cat (%)	14.1	13.9	18.4	13.1	14.8	13.7
Dog (%)	15.3	10.3 ^a	16.2	—	—	—
Mite (%)	14.1 ^b	7.4	7.9	12.0 ^b	8.3	6.6
Grass (%)	16.6	16.7	14.9	17.4	17.8	16.8
Birch (%)	15.6	16.3	17.1	15.0	15.7	13.4
Mugwort (%)	7.3 ^c	5.9	3.3	—	—	—
<i>Parietaria</i> (%)	3.4 ^d	0.2	0.7	—	—	—
Olive (%)	2.6	1.1	2.2	—	—	—
Ragweed (%)	0.2 ^e	2.3	1.8	—	—	—
<i>Alternaria</i> (%)	1.5	1.9	2.4	—	—	—
<i>Cladosporium</i> (%)	1.4	1.0	3.5 ^f	2.3	2.3	2.8
One or more SPT (%)	37.2	34.2	35.3	—	—	—
One or more specific IgE (%)				31.7	32.8	30.4
Total IgE, geometric mean (kU/l)				25.3	24.7	23.3

Three areas are compared: ^alower value in Uppsala than in Göteborg (*P* < 0.05) and Västerbotten (*P* < 0.01), ^bhigher value for SPT and specific IgE in Göteborg than in Västerbotten (*P* < 0.01) and in Uppsala (*P* < 0.01 in terms of SPT and *P* < 0.05 in terms of specific IgE), ^chigher value in Göteborg than in Västerbotten (*P* < 0.01), ^d higher value in Göteborg (*P* < 0.01) than in both other areas, ^elower value in Göteborg than in both other areas (*P* < 0.01), ^fhigher value for STP in Västerbotten (*P* < 0.05) than in both other areas.

prevalence of sensitization to the most common allergens, apart from mite, decreased with age (Tables 4 and 5). Total IgE did not vary with age.

Sensitization and country of birth

The prevalence of atopic sensitization was the same among Scandinavian born subjects and those not born in the Scandinavian countries (Fig. 3). Scandinavian born persons had a higher prevalence of positive SPT to cat, dog, grass, and birch pollen. Subjects born in other countries had a higher prevalence of positive SPT to mite. Analyses of specific IgE revealed corresponding statistically significant differences for cat and mite. The logistic

multivariate analysis showed that birth in a Scandinavian country was independently associated with a higher frequency of positive SPT to birch (Table 4) and an increased sensitization to cat (Table 5). In contrast, birth in a Scandinavian country was negatively associated with sensitization to mite (Table 5), to ragweed (OR = 0.2, CI: 0.06–0.87), and to *Cladosporium* (OR = 0.3, CI: 0.08–0.82). The results were similar even when smoking habits were included in the logistic multivariate analysis.

Persons not born in Scandinavian countries had a mean resident time of 10.5 years with a standard deviation of 8.0. Scandinavian born subjects more frequently had cats at home at the time of the study (20.2% versus 9.6%, *P* < 0.01).

Table 3. Risk factors for one or more positive skin prick test and for one or more positive specific IgE. Results are presented as adjusted odds ratios (OR) with 95% confidence intervals in parentheses

	One or more skin prick test	One or more specific IgE
Living in Göteborg	1.2 (0.92–1.52)	1.0 (0.76–1.29)
Living in Västerbotten	1.1 (0.83–1.43)	0.9 (0.71–1.26)
Male sex	1.3 (1.03–1.58)	1.6* (1.26–1.97)
Age (10 years' difference)	0.8* (0.67–0.93)	0.8 (0.71–0.98)
Birth in Scandinavian country	0.9 (0.57–1.31)	1.0 (0.65–1.53)
Day care before age 5 years	1.1 (0.85–1.44)	1.3 (1.02–1.78)
Atopic heredity	1.4* (1.34–1.74)	1.4* (1.13–1.781)

Multivariate analysis includes atopic heredity, sex, age, area of residence (Uppsala OR = 1), birth in Scandinavian country, and attendance at day-care center before age of 5 years. * $P < 0.01$.

Table 4. Risk factors for positive skin prick test and specific IgE to grass and birch. Results are presented as adjusted odds ratios with 95% confidence intervals in parentheses

	Grass		Birch	
	Skin prick test	Specific IgE	Skin prick test	Specific IgE
Living in Göteborg	0.9 (0.63–1.27)	1.1 (0.78–1.51)	1.0 (0.74–1.41)	1.0 (0.72–1.43)
Living in Västerbotten	0.9 (0.63–1.27)	1.0 (0.68–1.40)	1.0 (0.74–1.46)	0.9 (0.60–1.29)
Male sex	1.7* (1.25–2.19)	1.8* (1.37–2.41)	1.2 (0.94–1.62)	1.5* (1.15–2.08)
Age (10 years' difference)	0.6* (0.52–0.77)	0.6* (0.50–0.76)	0.7* (0.61–0.91)	0.8 (0.62–0.94)
Birth in Scandinavian country	1.1 (0.79–1.50)	1.8 (0.87–3.66)	3.7* (1.50–9.36)	1.2 (0.64–2.40)
Day care before age of 5 years	1.1 (0.79–1.55)	1.3 (0.92–1.80)	1.1 (0.75–1.48)	1.2 (0.85–1.74)
Atopic heredity	1.6* (1.19–2.06)	1.8* (1.33–2.34)	1.3 (0.98–1.69)	1.6* (1.17–2.11)

Logistic multivariate analysis includes atopic heredity, sex, age, area of residence (Uppsala, OR = 1), birth in Scandinavian country, and attendance at day-care center before age of 5 years. * $P < 0.01$.

Table 5. Risk factors for positive skin prick test and specific IgE to cat and mite. Results are presented as adjusted odds ratios (OR) with 95% confidence intervals in parentheses

	Cat		Mite	
	Skin prick test	Specific IgE	Skin prick test	Specific IgE
Living in Göteborg	1.1 (0.78–1.55)	0.9 (0.65–1.33)	2.0* (1.34–3.01)	1.5 (0.98–2.26)
Living in Västerbotten	1.4 (0.97–1.93)	0.9 (0.63–1.36)	1.2 (0.72–1.87)	0.8 (0.49–1.37)
Male sex	1.2 (0.91–1.60)	1.0 (0.80–1.46)	1.3 (0.92–1.80)	1.9* (1.29–2.70)
Age (10 years' difference)	0.8 (0.64–0.96)	0.8 (0.62–0.95)	1.1 (0.85–1.37)	1.0 (0.76–1.27)
Birth in Scandinavian country	4.0* (1.46–11.18)	2.9 (1.14–7.19)	0.4* (0.24–0.68)	0.5 (0.29–0.95)
Day care before age of 5 years	0.9 (0.66–1.35)	1.2 (0.84–1.75)	1.1 (0.72–1.64)	1.3 (0.82–1.95)
Atopic heredity	1.5* (1.11–1.95)	1.4* (1.02–1.86)	1.1 (0.80–1.60)	0.9 (0.61–1.29)

Logistic multivariate analysis includes atopic heredity, sex, age, area of residence (Uppsala, OR = 1), birth in Scandinavian country, and attendance at day-care center before age of 5 years. * $P < 0.01$.

Sensitization and exposure in childhood

No significant relationship to overall atopic sensitization or specific sensitization was found in terms of exposure to pets at home, parental smoking, a mother smoking during pregnancy, or month of birth.

Subjects who attended day-care centers before the age of 5 years had a higher prevalence of SPT and specific IgE to grass pollen and a tendency to

a higher prevalence of specific IgE to cat, mite, and birch pollen. Correspondingly, the overall prevalence of any positive specific IgE was higher in the day-care group. However, subjects with day care were younger (mean age 30 years compared to 34 years in the group without day care). The only statistically significant finding in a logistic multivariate analysis was that day-care attendance was related to one or more positive specific IgE (Table 3).

Table 6. Distribution by age group of positive skin prick test, specific IgE, and total IgE for five most common allergens. Values are given in percentage. Total IgE values are given as geometric mean in kU/l

Age (years)		20–25	26–30	31–35	36–40	40–46	All ages
<i>n</i>	SPT	322	331	289	304	326	1572
<i>n</i>	Specific (S) IgE	292	306	269	297	306	1470
Cat (%)	SPT*	17.7	17.5	14.5	13.8	12.6	15.3
	SIgE Ab**	17.5	16.3	12.6	12.5	10.1	13.8
Dog (%)	SPT**	16.5	16.3	14.2	12.8	9.5	13.9
Mite (%)	SPT	10.3	7.9	11.8	8.6	12.0	10.1
	SIgE Ab	11.0	7.5	10.0	7.4	10.5	9.3
Grass (%)	SPT***	22.7	18.1	17.0	14.1	8.9	16.2
	SIgE Ab***	24.7	20.6	15.2	17.9	8.5	17.3
Birch (%)	SPT**	22.4	16.0	15.2	14.1	13.5	16.3
	SIgE Ab**	20.2	14.4	14.9	13.5	11.1	14.8
One or more SPT (%)**		41.0	36.9	37.0	33.2	30.1	35.6
One or more specific IgE (%)**		36.0	35.0	31.6	29.6	26.5	31.7
Total IgE (kU/l)		25.4	22.6	23.4	24.4	26.8	

Linear trends in prevalence values for five age groups. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.

Sensitization and smoking habits

In a logistic multivariate analysis including atopic heredity, sex, age, area of residence, country of birth, day-care attendance before the age of 5 years, current smoking, and previous smoking, smokers had an increased risk of specific IgE to mite (OR = 1.8, CI: 1.2–2.7), but no other statistically significant differences were found.

Total IgE was higher in smokers (geometric mean 28.3 kU/l) than in nonsmokers (22.9 kU/l) and ex-smokers (23.7 kU/l), and the difference remained statistically significant when adjusted for age and sex ($P < 0.01$).

Sensitization and atopic heredity

Reported nasal allergy and/or skin allergy in either parent was associated with atopic sensitization. The prevalence of one or more positive SPT was 32.5% among subjects without known atopic heredity and 40.1% in persons with it ($P < 0.01$). A corresponding analysis of one or more positive specific IgE gave similar results. Moreover, a logistic multivariate analysis indicated that atopic heredity was a determinant for overall atopic sensitization and sensitization to individual allergens such as cat, grass, birch (Tables 3–5), and dog (OR = 1.5, CI: 1.35–2.04), but not to mite.

Discussion

We found that about one-third of adults aged 20–46 were sensitized in the three Swedish regions.

Birch, grass, cat, and dog were the most common allergens. Mite sensitization was also common in the southern area. Positive SPT to *Parietaria*, not previously described in Sweden, was found in 3.4% of people living in Göteborg. Male sex and young age were associated with atopic sensitization. Birth in a Scandinavian country was positively associated with sensitization to cat and negatively with sensitization to mite.

Norrman et al. found a prevalence of one or more positive SPT of 43.2% among 14-year-old schoolchildren from Umeå (22). This agrees with our finding of 41% in the 20–25-year age group. In a survey from Copenhagen, Denmark, from 1990–1, atopic sensitization occurred in 38.9% of men and 26.3% of women aged 15–34 (23). We found a slightly lower prevalence in men, but this could be due to the higher age among the persons in our study. However, in spite of the age difference, there was a higher prevalence of atopy (33.5%) among women in the Swedish population than in the Danish one. In the Danish study, particularly among women, sensitization to pets was less common. Only 7.6% were sensitized to cat, dog, or horse compared with 14.3% who were sensitized to cat in our study. It is not known whether there are more domestic pets in Sweden than in Denmark, so this difference is unexplained. Sensitization to mite was more common in Copenhagen than in Uppsala and Västerbotten. The difference between Copenhagen and Göteborg, the most southern of our areas, was small.

In contrast to the studies by Åberg (11) and Åberg et al. (12), this study does not reveal a higher

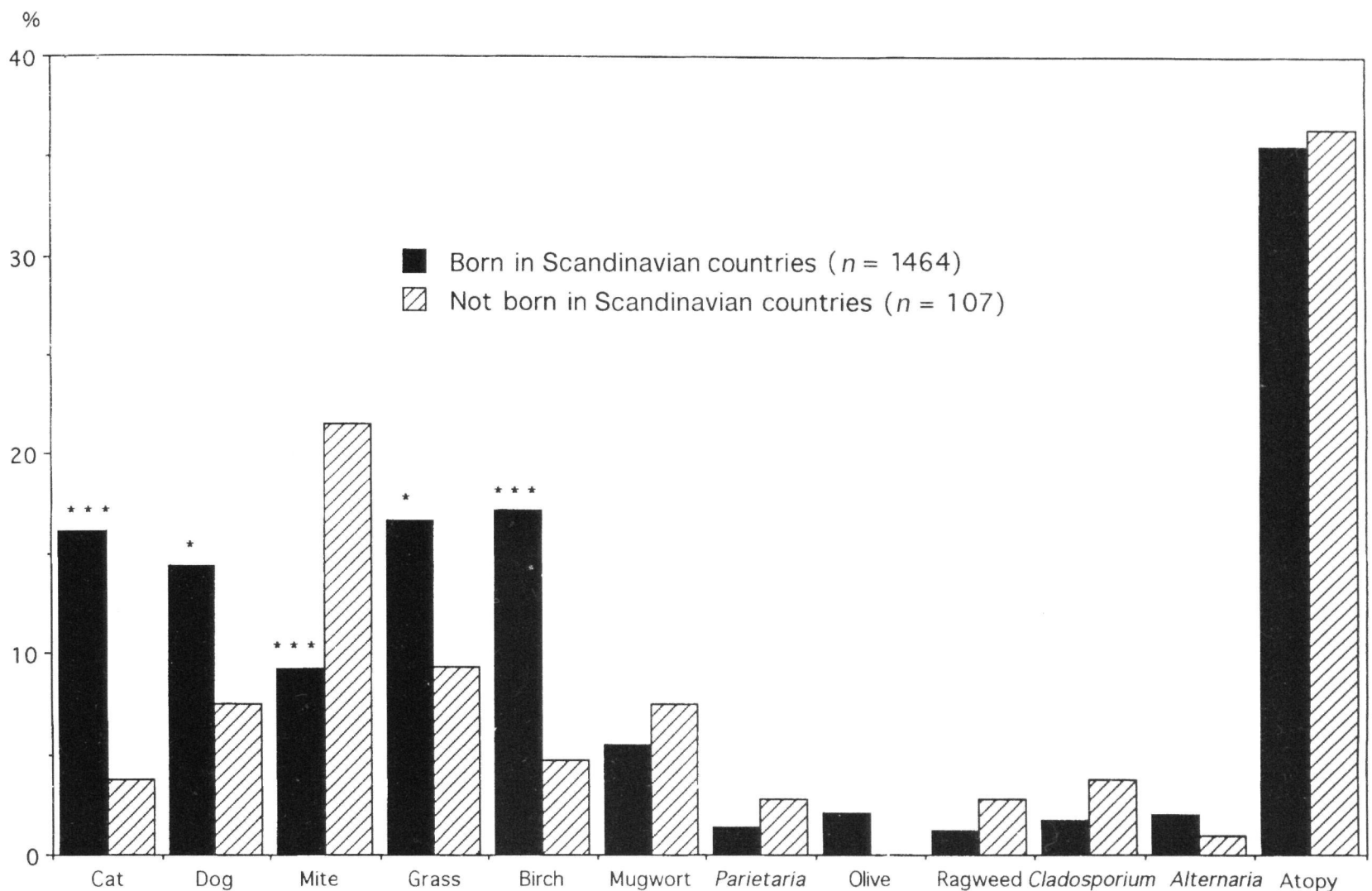


Fig. 3. Prevalence of positive skin prick tests in relation to place of birth. * $P < 0.05$; *** $P < 0.001$.

prevalence of atopic sensitization in the north of Sweden than in the south. Nor did the screening questionnaire of the Swedish ECRHS reveal any difference between areas for allergic rhinitis or asthma (15). This disagreement could depend on differences in the age of the investigated populations, the time of investigation, or the methods: Åberg investigated schoolchildren and adults who were younger than the persons included in our study, the studies were performed more than 10 years before ours, and the presence of atopy was not verified by skin tests.

Another Swedish study (24) revealed a higher frequency of atopic diseases in children from urban areas than rural ones. This supports the hypothesis that air pollution increases the risk of atopic diseases (25). The pollution that possibly increases the risk of atopic sensitization probably has its effect during childhood. Air pollution, at the time of childhood among the subjects in this study, included more SO_2 and soot particles than today, particularly in Göteborg (27), but complete historical data are not available. It is likely that the more urbanized Göteborg with its high concentration of industry and motor vehicles has always been the most polluted of the areas, but there are considerable local variations, particularly in Västerbotten.

In agreement with the ECRHS screening questionnaire study (15), we did not find a higher frequency of atopy in Göteborg. However, the screening questionnaire study revealed that bronchitis-related symptoms were more common in Göteborg. These findings are in agreement with a recent study by von Mutius et al. (28) which revealed less atopy, but more bronchitis in children from the more heavily polluted Leipzig and Halle in eastern Germany than in children from Munich in western Germany.

The highest prevalence of mite sensitization in the more southerly Göteborg was expected because of the warmer winters (29). There are occasional findings of mite sensitization and high levels of mites in house dust in northern Sweden (30). Our finding of a low prevalence of mite sensitization in Västerbotten was in agreement with Norrman et al.'s study from the same region (22). It thus appears that mite sensitization has relatively little importance in the north. Furthermore, in spite of a lower frequency of mite sensitization, the prevalence of overall atopic sensitization is not lower in the north than in the other regions.

Pellitory of the wall (*Parietaria judaica*) is a well-known cause of pollinosis in southern Europe (31),

and it may also have some importance in the UK (32). However, it is not known to grow in Sweden. Therefore, the finding of sensitization to *Parietaria* in 3.4% of the population in Göteborg was unexpected. The higher number of migrants in Göteborg could not explain the result, as the prevalence was the same when subjects not born in Sweden were excluded. In 1977, Weeke et al. (33) found high levels of pollen from the Urticaceae family during the first registration year of pollens in Denmark. Because of the botanic similarity, it was not possible to determine whether *Parietaria* pollens were present or whether there were pollens from nettles alone, which are the most common pollens from the Urticaceae family in the north of Europe. Although nettles and *Parietaria* belong to the same botanic family, there is no antigenic cross-reactivity (32). *Parietaria* pollen grains are small and may be transported over long distances. Our finding could therefore possibly be explained by airborne transport of *Parietaria* pollen to southwest Sweden.

The lower frequency of a positive SPT to dog in Uppsala has no obvious explanation and might be a random finding. The prevalence of dogs at home among the investigated subjects was slightly lower than in Västerbotten, but slightly higher than in Göteborg.

The higher frequency of positive SPT to *Cladosporium* in Västerbotten was not clearly confirmed by the comparison of specific IgE, and the importance of this finding is unclear.

Omenaas et al. found a higher frequency of specific IgE and a tendency to higher total IgE levels in subjects tested in summer than in winter (34). We did not find any independent difference between subjects tested in summer and those tested in winter, so influence of season should not be an important bias in our results.

Several other population studies have shown male sex to be a risk factor for atopic sensitization and higher total IgE (23, 34–37).

Atopic sensitization was also found to decrease with age in these studies. One possible explanation is a decrease in IgE production with age. In two North American studies (35, 37), there was a decrease in total IgE with age. In the study by Omenaas et al. (34), total IgE decreased with age in nonsmoking women. In smoking women and in men, there was no decrease with age. We found a decreasing prevalence of atopic sensitization with age, but no corresponding decrease in total IgE. Our results could therefore be a consequence, at least to some degree, of an increasing prevalence of atopy in the younger cohorts. Mite was the only common allergen which did not have a higher frequency of sensitization in the younger cohorts.

This contradicts the hypothesis that mite sensitization is the cause of the increasing prevalence of atopic diseases in Sweden.

In a study by Kalyoncu & Stålenheim (38), immigrants to Sweden were found to have a different pattern of sensitization than Swedish-born residents. Sensitization to birch and pets was less common among immigrants during their first 2.5 years of residence. After 10.5 years or more in Sweden, the prevalence of sensitization to pets was still lower, whereas the frequency of birch sensitization was similar to the Swedish-born subjects. Our results are in agreement with these findings. The low frequency of cat sensitization among immigrants was maintained even with a residence time of 10 years or more. SPT to birch was also less common among immigrants, but not among those who had been resident in Sweden for 10 years or more. The higher prevalence of sensitization to cats among Scandinavian born subjects could be explained by their being more likely to have cats at home. There was no adjustment for economic status, so the possible difference in economic status between the two groups might have influenced the results. The negative association between birth in Scandinavian countries and sensitization to mite, ragweed, and *Cladosporium* is in agreement with a lower exposure to these allergens in the Scandinavian countries than in many of the immigrants' countries of birth. Our findings are thus in agreement with the concept that atopic sensitization often takes place early in life (39) and with the hypothesis that sensitization to pets is a major problem in the Scandinavian countries (40, 41).

Day care in early childhood has been found to increase the risk of airway infections (42, 43). It has been suggested that early airway infections increase the risk of atopic diseases (44). However, in a study from Finland, day care and more frequent infections were not associated with atopy (45). In our study, day-care attendance before the age of 5 years was significantly associated to a marginal degree with one or more positive specific IgE. This finding was not supported by the analysis of one or more positive SPT.

The relationship between smoking and atopic sensitization is complicated. Some studies have found that sensitization to pollens is more common among nonsmokers (23, 34), but other studies have found that smokers run a greater risk of becoming sensitized to new allergens such as occupational allergens (46). In this cross-sectional study, the results are difficult to interpret because atopic patients might be less likely to become smokers, and, although smoking increases IgE production, it might also have inhibiting effects on the allergic

immune response (47). We found less atopic sensitization among smokers in the univariate analysis, but not when adjusted for age. Therefore, our study does not reveal that environmental tobacco smoke exposure in childhood is associated with atopy in adults. Although not associated with atopic sensitization itself, it still might increase the risk of clinical disease among atopics. In the study by Nielsen et al. (23), smokers were less likely to be sensitized to pets and pollens, but mite sensitization was as common as among nonsmokers. Our finding of a higher frequency of sensitization to mite among smokers supports the hypothesis that there is a difference between sensitization to mite and to other common allergens in relation to smoking habits. Our findings of higher total IgE in smokers than in nonsmokers agree with previous findings (48).

There is a well-known genetic susceptibility to atopy, but atopic heredity was only a modest risk factor in this study. Questioning adults about whether their parents have or have had allergic rhinitis or skin allergy is probably an imprecise method of identifying parents with atopic sensitization. Many atopic patients have only mild or temporary symptoms and some have no symptoms. This method of ascertaining atopic heredity may thus cause a random misclassification and thereby an underestimation of the association between atopic heredity and atopy. As atopic heredity was similar in the three areas, differences in the prevalence of sensitization generally reflect differences in exposure to allergens.

Nonparticipants had a lower frequency of self-reported allergic rhinitis, were more often male, and were slightly younger. This produces a slight overestimation of the prevalence of sensitization. However, the participation rate was high and the bias is therefore of minimal importance (49).

In spite of carefully trained fieldworkers and the performance of the tests in a standardized manner, the SPT in different areas might be biased by variations in the technique and registration of fieldworkers (50). This might in part explain the small differences in the results for SPT and specific IgE. Generally, SPT and specific IgE produced consistent results.

We conclude that the prevalence of atopic sensitization among adults was similar in three Swedish areas in spite of differences in geography, air pollution, and urbanization. Sensitization was associated to atopic heredity, male sex, and low age. The latter finding is consistent with an increasing prevalence of atopic sensitization. Persons born in the Scandinavian countries had a higher frequency of sensitization to cat, whereas birth in other countries was associated with sensitization to mite.

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