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Sensitization to airborne and food allergens in Reykjavík (Iceland) and Uppsala (Sweden) – a comparative study

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Background: The aim of this study was to compare the prevalence of atopic sensitization and possible risk factors for allergies in two ethnically similar but geographically widely separated urban populations.

Methods: Data from two centers of the European Community Respiratory Health Survey, Reykjavík, Iceland, and Uppsala, Sweden, were utilized. This included a structured interview, skin prick tests, and blood samples for total and specific IgE for common aeroallergens. Additional measurements of specific IgE antibodies to common food antigens were performed. Furthermore, data on social environment, lifestyle, air pollution, and meteorologic variables were compared.

Results: Skin prick tests were done on 540 individuals in Reykjavík and 527 in Uppsala. The overall prevalence of at least one positive prick test was 20.5% in Reykjavík and 34.2% in Uppsala ($P<0.001$). Total and specific IgE were measured in serum from 521 subjects in Reykjavík and 472 in Uppsala. The geometric mean value for total IgE was significantly lower in Reykjavík (13.4 kU/l) than in Uppsala (24.7 kU/l) ($P<0.001$). Similarly, the overall prevalence of at least one specific IgE to airborne allergens was 23.6% in Reykjavík and 32.3% in Uppsala ($P<0.01$). Specific IgE to a food panel (fx5) was measured in 502 subjects in Reykjavík, and 434 in Uppsala. In Reykjavík, 20 individuals (4.0%) were positive to one or more of the allergens in the food panel compared to 27 (6.0%) in Uppsala. When the single allergens present in the food panel were measured, altogether 16 positive reactions were found in Reykjavík compared to 47 in Uppsala ($P<0.05$).

Conclusions: The prevalence of sensitization to both airborne and food allergens was lower in Reykjavík than in Uppsala. The difference may be due to environmental and/or dietary differences or to some yet undefined factor.

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Atopy is partly due to genetic susceptibility (1), but recent surveys from several developed countries have revealed an increasing prevalence of this condition, indicating an important role of environmental factors (2–5). Simultaneously, atopic diseases have been increasing in prevalence (6–10).

Several possible explanations of these findings have been advanced (11–13). The causative role of air pollution and cigarette smoking, once held to be at least partly responsible for the increasing prevalence of allergy, has not been borne out by the data from eastern and western Europe (14). Similarly, allergic diseases are increasing in the UK despite a steady decrease in air pollution since the 1950s (15). Other differences that seem pertinent to this comparison include differences in living standards between East and West, which will affect factors such as dietary habits and the indoor environment.

The purpose of this study, which is partly based on the protocol used in the European Community Respiratory Health Survey (ECRHS), was to compare the prevalence of atopic sensitization in two ethnically similar urban populations, living under different climatic, environmental, and dietary conditions.

Material and methods

Study population

The ECRHS was planned to estimate prevalence of asthma, asthma-like symptoms, and bronchial lability in Europe

Table 1. Air pollutants and pollen counts

	Reykjavík	Uppsala
Air pollutants		
Sulfur dioxide, 24-h average		
Annual arithmetic mean (ppb)	1.2	1.9
Annual 98th percentile (ppb)	6.7	8.3
Total suspended particulates (24-h average)		
Annual arithmetic mean ($\mu\text{g}/\text{m}^3$)	18.6	6.6
Annual 98th percentile ($\mu\text{g}/\text{m}^3$)	75.6	20.3
Nitrogen dioxide (maximum hourly daily mean)		
Annual 98th percentile (ppb)	33.1	39.7
Pollen counts		
Mean values (per m^3) for years 1988–92		
Birch (<i>Betula</i>)	199	6117
Grass (<i>Poacea</i>)	2688	1217

(16). This report is based on data from two of its centers: Reykjavík, Iceland, and Uppsala, Sweden.

Iceland is located in the north Atlantic ocean just beneath the Arctic Circle. The population is of Scandinavian origin with some Irish influence (17). Since its settlement in the 9th century, the island has been relatively isolated from other nations until this century, and the level of immigration is low.

Reykjavík is the capital city of Iceland, a port located in the southwestern part of the country. In 1990, the population of Reykjavík and its suburbs was 160 000 or 60% of the total population of Iceland.

Uppsala is an old university city 60 km northwest of Stockholm in the interior part of Sweden. The population in 1990 was 167 000.

Meteorologic parameters

The meteorologic data for Iceland were obtained from the Icelandic Meteorologic Institute, and the Swedish data from the Swedish Meteorologic Institute. Despite its northern location, the Icelandic climate is rather mild because of the Gulf Stream, and the weather is rainy and windy. In Uppsala, the summer is longer and warmer, but the winter is colder and drier than in Iceland.

The seasonal variation in temperature is much larger in Uppsala than Reykjavík, and the yearly mean of daily observation ($^{\circ}\text{C}$) of minimum temperature is -4.6 in Reykjavík and -6.7 in Uppsala, while the yearly 98th percentile of daily observation ($^{\circ}\text{C}$) is $+10.5$ and $+21.2$ in Reykjavík and Uppsala, respectively. Relative humidity is of the same range in both centers (about 80%), but days with measurable rain number 221 in Reykjavík and 180 in Uppsala.

Air pollution

Air pollution is low in both areas (Table 1) in comparison to the WHO and EC air-quality guidelines for Europe (18). For Uppsala, data were obtained from the official environmental control office, and measurements were made during a period from October 1990 to March 1991. For Reykjavík, data were collected from March to December 1991. The procedures of collection and measurements were comparable.

Pollen counts

Grass pollen is the main cause of pollen allergy in Iceland, and birch pollen is scanty (Table 1). In Uppsala, the birch-

pollen count is high, while the grass-pollen count is similar to that in Reykjavík (Table 1). The yearly variation in pollen counts is high in Reykjavík (19, 20).

Socioeconomic factors

The socioeconomic data are comparable for both nations (21, 22). In Iceland, the death rate per 1000 live births is the lowest in the world, and the mean life expectancy in both countries is one of the highest in the world. The mean annual income per capita is comparable to that in nations with the highest living standard. The consumption of fish is high in Iceland (80 kg/person per year) compared to Sweden (31 kg/person per year), but the consumption of fat, meat, grain, fruit, and vegetables is comparable in both countries (21).

Study design and participation

In this study, we report data based on random samples of 800 men and women aged 20–44 years at both centers, who were invited to take part in the second stage of the ECRHS study (16, 23). In Reykjavík, 57 of them had moved away or died; the figure was 93 in Uppsala. Thus, 743 subjects participated in the study in Reykjavík and 707 in Uppsala (Table 2). The response rates were 570 (77%) in Reykjavík and 625 (88%) in Uppsala. In Reykjavík, 540 subjects underwent skin prick tests (SPT) and 527 in Uppsala. Blood samples for total IgE and specific IgE were taken from 521 individuals in Reykjavík and 472 in Uppsala, and blood samples for food allergens from 502 in Reykjavík and 434 in Uppsala (Table 2).

Among the 800 individuals at each center randomly selected for the second stage of the ECRHS, no age or sex differences were found between those who did and those who did not participate in the SPT.

Table 2. Study population and response rates

	Reykjavík <i>n</i>	Uppsala <i>n</i>
Random population sample	800	800
Had moved away or died	57	93
Applicable to study	743	707
Participated in study	570	625
Underwent SPT	540	527
Total IgE/specific IgE	521	472
Specific IgE to food panel	502	434

Questionnaire

The main questionnaire used in the second stage was the ECRHS modified version of the International Union Against Tuberculosis and Lung Disease questionnaire on symptoms and medical history (24, 25). In addition, there were some questions on home environment, medication, and the use of medical service. The questionnaires were administered by specially trained nurses.

Skin prick tests (SPT)

SPT was carried out according to the ECRHS protocol described previously (16, 26, 27) with the following panel of allergens: cat, house-dust mite (*Dermatophagoides pteronyssinus*), timothy grass, birch, *Cladosporium herbarum*, *Alternaria*, olive, common ragweed, and *Parietaria judaica*. In addition, dog was tested at both centers.

Specific and total IgE

Venous blood samples were drawn and frozen at –20°C for measurement of total serum IgE antibodies (total IgE) and specific serum IgE antibodies (specific IgE) to cat, *D. pteronyssinus*, grass, birch, and *Cladosporium*, as part of the ECRHS protocol (16). In addition, specific IgE to a panel of food allergens was measured at these two centers. The panel included the following allergens: egg white, milk, fish/cod, wheat, peanut, and soybean (Pharmacia CAP System, MultiCap fx5, Pharmacia and Upjohn Diagnostics, Uppsala, Sweden). Serum with a positive reaction to the food panel (fx5) was further analyzed for the single allergens in the panel. The results are presented in kU/l, and values of 0.35 kU/l and above were regarded as positive (28). All samples from Reykjavík and Uppsala were analyzed at the same laboratory in Uppsala. A report on food sensitization in Sweden, by the same methods, has previously been published (29).

Statistics

Mean values and one standard deviation ($\pm$ SD) were used for continuous variables and the two-sided *t*-test for comparison. Log values for total IgE were used for comparison between Uppsala and Reykjavík. The chi-square test was used for comparison of groups. Multiple logistic regression analysis was performed separately for the two centers.

Results

Questionnaire data

Data on age, sex, smoking habits, and present environment are listed in Table 3. The mean age of those who responded was 33 years in Reykjavík and 32.6 years in Uppsala. Smoking was significantly more common in Reykjavík ($P<0.001$). Smoking habits were the same among those who participated only in the stage 2 interview and those who participated in both the interview and the allergy testing at either center. Subjects living in Uppsala were both currently and during childhood more exposed to cats and dogs than those in Reykjavík ($P<0.01$) (Tables 3 and 4). The households differed in occurrence of water damage during the last 12 months, which was more common in Uppsala ($P<0.05$), and fitted carpets in living rooms, which were significantly more common in Reykjavík ($P<0.001$). The number of siblings and number of older siblings were significantly higher in Reykjavík ($P<0.001$) (Table 4).

Atopic sensitization to airborne allergens

SPT

The overall prevalence of atopic sensitization measured by SPT was 20.5% in Reykjavík and 34.2% in Uppsala ($P<0.001$) (Table 5). Sensitization to grass and cat was almost twice as common in Uppsala as in Reykjavík

Table 3. Demographics, smoking habits, and household factors

	Reykjavik <i>n</i> =570	Uppsala <i>n</i> =625
Demographics		
Age (years $\pm$ 1 SD)	33.0 $\pm$ 6.9	32.6 $\pm$ 7.4
Women (%)	51.7	51.3
Smoking habits		
Ever smokers (%)	62.3	48.5***
Current smokers (%)	39.8	25.1***
Households		
Detached or semi-detached dwelling (%)	64.2	59.6
Water damage last 12 months (%)	5.8	8.9*
Fitted carpet – living room (%)	38.3	5.6***
Fitted carpet – bedroom (%)	17.0	14.7
Electric cooker (%)	99.0	99.6
Cat at home now (%)	12.5	22.5***
Dog at home now (%)	5.6	12.1**

* $P<0.05$; ** $P<0.01$; *** $P<0.001$.

Table 4. Childhood risk factors and heredity (%)

	Reykjavik	Uppsala
Mother allergic	27.5	32.3
Father allergic	21.0	24.6
Maternal smoking	40.9	36.9
Paternal smoking	58.5	58.5
Number of siblings	2.9 ($\pm$ 1.9)	2.0 ($\pm$ 1.6)***
Number of older siblings	1.5 ($\pm$ 1.6)	1.0 ($\pm$ 1.4)***
Severe childhood respiratory infection	12.0	11.9
Day-care center	27.8	24.8
Cat at home in childhood	40.9	49.4**
Dog at home in childhood	25.9	47.2***

* $P<0.05$; ** $P<0.01$; *** $P<0.001$.

($P<0.001$), and sensitization to birch pollen five times as common ($P<0.001$). Sensitization to dog was significantly higher in Uppsala ($P<0.05$), but sensitization to mite and molds was similar in both areas (Table 5). Multisensitization on SPT was found in 8.5% in Reykjavík and 19.7% in Uppsala.

Total IgE

The geometric mean value for total IgE was 13.4 kU/l in Reykjavík but 24.7 kU/l in Uppsala. This difference was statistically significant ($P<0.001$). Very low IgE values (0–20 kU/l) were more common in Reykjavík than in Uppsala (64% vs 44%), and high values (200 kU/l) were more common in Uppsala (6.6% vs 4.2%).

Table 5. Skin prick tests (SPT) (%) and specific IgE in Reykjavík and Uppsala

Allergen	Skin prick tests		Specific IgE	
	Reykjavik (<i>n</i> =537)	Uppsala (<i>n</i> =527)	Reykjavik (<i>n</i> =522)	Uppsala (<i>n</i> =472)
Timothy grass	8.5	16.7***	11.9	17.9*
Cat	7.6	13.9***	7.5	14.3***
Mite	6.1	7.4	9.2	7.9
Birch	3.0	16.3***	5.9	15.3***
<i>Cladosporium</i>	1.1	1.0	6.5	2.3**
<i>Alternaria</i>	0.9	1.9	–	–
Olive	0.6	1.1	–	–
<i>Parietaria</i>	0.4	0.2	–	–
Ragweed	0.0	2.3	–	–
Dog	6.3	10.3*	–	–
One positive SPT	20.5	34.2***	–	–
One specific IgE			23.6	32.3**

* $P<0.05$; ** $P<0.01$; *** $P<0.001$.

Specific IgE

The difference in atopic sensitization between Reykjavík and Uppsala was less marked when assessed by specific IgE than SPT. The overall prevalence of specific IgE to airborne allergens was 23.6% in Reykjavík and 32.3% in Uppsala ($P<0.01$) (Table 5). The difference was significant for grass, cat, and birch, while sensitization to mite was slightly more common in Reykjavík although not significantly so. The results of specific IgE measurements to *Cladosporium* disagreed with SPT results, especially in Reykjavík. Measured by specific IgE, multisensitization was found in 9.4% of subjects in Reykjavík and 15.1% in Uppsala.

Atopic sensitization to food allergens

In Reykjavík, 20 subjects (4.0%) and in Uppsala 27 subjects (6.0%) were positive to the food allergen panel (Table 6). This difference was not statistically significant. The 47 subjects with a positive food allergen panel had a higher prevalence of specific IgE to airborne allergens (71% vs 24%) and higher total IgE (233 ± 402 vs 41 ± 99 , $P<0.001$). When the single allergens were measured, only nine individuals (1.8%) were positive in Reykjavík compared to 20 (4.6%) in Uppsala ($P<0.05$). Sensitization to peanut, wheat, and soybean were significantly more common in Uppsala (Table 6).

Age, sex, smoking, and atopy

Altogether, 27.4% of subjects in Reykjavík were sensitized to airborne allergens (specific IgE and/or skin prick test) compared to 40.7% in Uppsala ($P<0.001$). The largest differences in prevalence of allergic sensitization between Reykjavík and Uppsala were found in the older age groups

Table 6. Sensitization to food allergens (%)

	Reykjavík n=502	Uppsala n=414
Egg	0.4	0.2
Peanut	0.8	3.7**
Fish	0.2	0.2
Milk	1.2	0.7
Wheat	0.4	3.2***
Soybean	0.2	2.8***
Any food allergen	1.8	4.6*
Positive food panel	4.0	6.0
* $P<0.05$; ** $P<0.01$; *** $P<0.001$.		

($P<0.05$ for age groups 30–34 and 40–44 years). In Reykjavík, no difference was found in sensitization to airborne allergens in relation to sex.

In Uppsala, overall sensitization to airborne allergens was 38.5% for men and 26.6% for women ($P<0.01$); to grass, it was 22.9% and 13.1%, respectively ($P<0.01$). In Uppsala, sensitivity to grass and birch was also significantly more common among those who had never smoked ($P<0.05$). In Reykjavík, the same results were found only for grass ($P<0.001$). When all allergens were added together, there was no difference between smokers and those who had never smoked.

In both cohorts, the prevalence of cat sensitivity was slightly, but not significantly, higher among those not exposed to cats in childhood. The relationship between atopy at each center and some possible risk factors for atopy is shown in Table 7. Only in Uppsala was a significantly higher sensitivity found among those without cats at home ($P<0.05$) or without dogs at home in childhood ($P<0.001$).

Multivariate logistic regression

Calculations were performed for each center separately, with atopy as the dependent variable (positive SPT and/or specific IgE). Independent variables were sex, age, smoking, mother smoking, older sibling, allergic heredity, stay at a day-care center, severe respiratory infection before age 5 years, and pets (dog or cat) at home during childhood (Table 8). In both centers, a negative association between having pets at home during childhood and atopy was found: Reykjavík, OR (95% CI) 0.60 (0.36–0.99) ($P<0.05$); Uppsala,

Table 7. Prevalence of atopic sensitization in subjects with or without certain variables (%)

Variables	Reykjavík		Uppsala	
	Yes	No	Yes	No
Ever smoker	25	32	39	42
Current smoker	23	30	44	40
Water damage	24	28	47	40
Fitted carpet in living room	27	28	32	41
Cat now	32	27	32	43*
Dog now	41	27	34	41
Older sibling (at least one)	26	30	27	45
Cat in childhood	26	40	37	45
Dog in childhood	22	27	32	49***
* $P<0.05$; *** $P<0.001$.				

0.52 (0.34–0.81) ($P<0.01$). In Reykjavík, a negative association between childhood infections and atopy was found; OR 0.25 (0.08–0.74) ($P<0.05$).

Discussion

The first part of the ECRHS suggested that there was considerable variation in the prevalence of allergic diseases within Europe (30). In this first part, Iceland had prevalence values that were among the lowest in Europe, while Sweden had midrange values. As these populations are genetically closely related, we felt that these differences deserved a closer look.

In this study, the prevalence rates of atopic sensitization were compared between Reykjavík and Uppsala. We found a significant difference between these two populations in allergic sensitization, estimated with skin tests and measurements of specific IgE to airborne allergens as well as some food allergens. Not only were different types of atopic sensitization more common in Uppsala than Reykjavík, but multisensitization was also more common in Uppsala. The difference in prevalence of sensitization is in accordance with the self-reported difference in respiratory symptoms and use of asthma medication between the two study groups (23). The causes are, however, obscure.

Ethnically, the study populations are similar; therefore, ethnic causes are rather unlikely. The climatologic differences explain the difference in prevalence of birch and wheat sensitization, as birch trees and wheat fields are common in Sweden, but not in Iceland. However, climatologic differences are not likely to explain the overall differences in specific and total IgE sensitization. The role of air pollution

as an adjuvant factor to atopic sensitization is controversial, and air pollution in the two study areas was comparable and low.

Evidence has been put forward that the dose of allergens in house dust to which children are exposed is important in determining whether they become sensitized (31, 32). In our study, there is no information about house-dust-mite allergen load in the environment of the participants, but the prevalence of childhood exposure to cats and dogs was higher in Uppsala. Surprisingly, atopic sensitization was more common among those not exposed to these animals in childhood, and exposure to cat or dog in childhood was an independent negative risk factor for atopy in both Reykjavík and Uppsala. This finding should, however, favor lower prevalence rates in Uppsala and does not explain the reverse situation which was observed.

The effect of smoking on atopic sensitization is controversial. Active smokers have previously been found to have higher total IgE, but not a higher rate of allergic skin test reactivity (33). Higher cord-blood IgE has been found in the children of mothers who smoke (34), and some investigators have found a correlation between exposure in infancy to maternal smoking and specific IgE (35). In our study, both current and previous smoking was more common in Reykjavík, but this factor does not explain the lower prevalence of atopy seen there. The reported parental smoking habits did not differ significantly between the centers.

Small sibship size has been reported to be a risk factor for atopic sensitization (36, 37). The number of brothers and sisters in Reykjavík is 50% higher than in Uppsala, a finding that might explain some of the lower prevalence found in Reykjavík. However, in the multivariate analysis, this finding did not stand out as an independent risk factor.

The only clue provided by the multivariate analysis to the differences in prevalence rates between centers was that respiratory infections in early life seemed to be a protective factor in Reykjavík, but not in Uppsala. However, the number of reports of such infections did not differ between the centers, and their number was not associated with the number of siblings.

There are some possible risk factors for atopy that differ between these countries but were not assessed by this study. Firstly, socioeconomic factors have been discussed as a cause of increasing atopic sensitization. In the study areas, both social and economic standards were relatively high and comparable. There was some difference in household habits, and more detached or semidetached dwellings and fitted carpets are found in Reykjavík. All houses in the Reykjavík

Table 8. Multiple logistic regression analysis of risk factors for positive SPT and/or specific IgE in Reykjavík and Uppsala (OR [95% CI])

	Reykjavík	Uppsala
Women	0.95 (0.58–1.56)	0.85 (0.57–1.28)
Age	0.80 (0.54–1.18)	0.82 (0.62–1.12)
Ever smoker	0.81 (0.50–1.33)	1.05 (0.69–1.61)
Maternal smoking	1.12 (0.68–1.86)	0.87 (0.56–1.33)
Older sibling (at least one)	0.78 (0.46–1.32)	0.74 (0.49–1.12)
Allergic heredity	1.40 (0.85–2.32)	0.91 (0.60–1.37)
Day-care center	1.35 (0.76–2.41)	0.81 (0.49–1.33)
Severe infection in childhood	0.25 (0.08–0.74)*	0.86 (0.46–1.61)
Cat or dog in childhood	0.60 (0.36–0.99)*	0.52 (0.34–0.81)*
* $P<0.05$.		

area use geothermal heating, which in Iceland is inexpensive and allows ventilation via open windows. Secondly, vaccination early in childhood might play a role, and an inverse association between tuberculin responses and atopy has been reported [38]. In both study areas, the vaccination practice was the same with one exception; in Uppsala, the population of this age is BCG vaccinated, but this is only rarely done in Reykjavík.

Thirdly, consumption of oily fish might possibly protect against asthma in childhood [39]. Black & Sharpe have discussed the possible protective effect of the consumption of oily fish against atopic diseases [40]. There is no individual information available about fish consumption in our study groups, but fish consumption in Iceland was almost triple that of Sweden at the time of the study, and daily consumption of cod liver oil is still very common in Iceland.

When we compared corresponding age groups in both centers, the difference in prevalence of atopy was greater in the older age groups. Interestingly, there was no significant difference in reported parental allergies between Reykjavík and Uppsala. Hence, it is possible that the population of Iceland, receiving the full impact of modern lifestyle later than their counterparts in Sweden, have yet to experience the vast increase in allergic diseases seen in other western countries. This and the influence of difference in fish

consumption between Iceland and Sweden on the prevalence of allergic diseases in these countries are now only speculation, but these issues may be clarified by the ongoing follow-up of the ECRHS.

Our cross-sectional study provides objective evidence of a lower prevalence of sensitization to both airborne and food allergens in Reykjavík than in Uppsala. These differences could partly be explained by lower allergic exposure, higher number of siblings, and more fish consumption in Reykjavík than in Uppsala. In addition, there may be some yet undefined factor, protective in Iceland or causative in Sweden.

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