

Total and specific serum IgE levels in adults: relationship to sex, age and environmental factors

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Summary

We studied total and specific serum IgE levels cross-sectionally, potential predictors of obstructive lung disease, in a stratified random sample of 18–73-year-old adults ($n = 1512$). The attendance rate was 84%. The total IgE level and prevalences of specific IgE antibodies against house dust mite and cat were higher for men than for women. Specific IgE levels decreased by increasing age, while total IgE decreased in women only. Smokers had a higher IgE level than non-smokers, while non-smokers had more often specific IgE antibodies against timothy and birch than smokers. Subjects with occupational dust or gas exposure had a higher total IgE level than unexposed. The general population prevalences were for specific IgE antibodies against timothy 4.5%, house dust mite 3.2%, birch 2.6%, cat dander 1.6% mould 0.2% and against any of these 7.6%. In a multivariate analysis age, occupational dust or gas exposure as well as the interaction terms between sex and age and between smoking and pack-years were independent predictors for total IgE levels. Male sex, young age, never having smoked and the season of the year were independent predictors for having one or more of the five specific IgE antibodies. Subjects with total serum IgE in the highest quintile (≥ 66 kU/l) had an adjusted odds ratio of 37 (95% confidence interval: 11–120) for having one or more of the specific IgE antibodies examined, compared with those in the lowest quintile (< 5 kU/l). Demographic and environmental factors were thus predictors of total and specific IgE levels in this adult community. These factors should be taken into account when examining relationships between IgE levels, markers of allergy and inflammation, and airways disease.

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Introduction

High levels of total serum IgE in humans have been associated with wheeze [1,2], hay fever [1,3], dermatitis [4] and asthma [5,6,7]. Total serum IgE levels are suggested to be dominantly inherited [8], however, this has not been confirmed [9]. Some studies in adults have found IgE levels to be influenced by sex [4,5,10], age [4,10], race [4,7] and environmental exposures such as tobacco smoke [11,12], allergens [12] and occupational exposure [13]. However, most of these determinants remain controversial and it is unknown whether occupational dust or gas exposure, area of residence or educational level can

explain any variation in total serum IgE levels in a general adult population. In selective populations specific IgE levels have been related to age [14,15], current smoking and occupational exposure [16–18]. However, the relationships between specific IgE antibodies and sex, environmental factors, as well as total serum IgE levels have not been reported for a wide adult age range of a European community.

As part of a cross-sectional community study in Norwegian adults [19,20] examining risk factors for obstructive lung disease we wanted to estimate levels of total IgE and prevalences of some specific IgE antibodies in a general population. Furthermore, we wanted to examine the association between levels of total IgE and prevalences of specific IgE antibodies on the one hand and sex, age, smoking habits, season, area of residence,

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occupational dust or gas exposure and educational level on the other. Finally, we wanted to examine the inter-relationship between total and specific IgE levels.

Materials and methods

Study design

The survey was a two-phased cross-sectional study performed in the city of Bergen and 11 surrounding municipalities in the county of Hordaland on the south-west coast of Norway. As at 1 January 1985 the target population contained 298 110 inhabitants, of whom 205 478 were between 15 and 70 years of age. A random sample of 3740 persons in this age group was sent a postal questionnaire in 1985 and a total of 3370 persons (90%) responded.

The responders were categorized into four groups according to information from the postal questionnaire. Subjects who had ever been treated by a practitioner or were admitted to hospital due to asthma or emphysema were classified as having a physician's diagnosis of asthma or emphysema, and formed one group ($n=127$). Subjects without a physician's diagnosis of asthma or emphysema who had ever been exposed at work to asbestos dust, quartz dust or stone dust with quartz, constituted the second group ($n=244$). The third group consisted of subjects who were non-smokers without respiratory symptoms, disease or occupational dust or gas exposure ($n=737$). The fourth group was made up of the remaining responders ($n=2262$) not included in the three previous groups. Sub-samples were drawn from groups 1 to 3 collectively with a 0.91 fraction, while the sub-sample from group 4 was drawn with a 0.22 fraction using a random number generator [21]. The multifractional stratified random sampling design of this study served the purpose to examine large numbers of subjects with particular characteristics, for example asymptomatic non-smokers for reference values of lung function [22]. Thus, a total of 1512 subjects aged between 18 and 73 years were invited to a lung health examination between April 1987 and August 1988. Of the 1275 subjects who met (84%) only seven refused blood sampling. Subjects were invited randomly with those born on the first day in every month being examined first, thereafter those born on the second day and so forth.

Smoking habit

Non-smokers were subjects who reported never having smoked daily. Ex-smokers were subjects who had smoked daily and given up. Smokers were those who smoked daily at the time of the study. Amount of lifetime smoking was assessed as pack-years. This was arrived at by using the

duration of smoking in years multiplied by the number of cigarettes smoked per day and divided by 20. In order to validate the answers on smoking habit carboxyhaemoglobin was measured from a venous blood sample with an OSM3 Hemoximeter, Radiometer, Denmark [23]. A self-administered questionnaire filled in within 1 h prior to the blood sample classified 35% of the women and 42% of the men as smokers. The carboxyhaemoglobin measurements indicated that 39% of the women and 43% of the men were smokers when using a cut-off level of $\geq 1.7\%$.

Airborne occupational dust or gas exposure

The examination included completion of a questionnaire on all jobs held lasting more than 6 months since leaving school. For each job the occupational title was recorded. They were coded according to the three digit numbers of the Nordic Classification of Occupations which follows the recommendations of the International Standard Classification of Occupations [24]. The occupational titles were allocated into those with and those without anticipated airborne exposure according to the assessment of each occupation by an expert team. The term 'airborne exposure' included dusts, fumes, mists and gases [25]. The last held occupational title was used in this analysis giving 383 subjects with and 885 subjects without exposure.

Area of residence

The urban population in Bergen was divided into two: subjects living in the city area which was more densely populated and more prone to traffic congestion ($n=199$) and those living in the suburban area ($n=660$) which partly included agricultural areas and was less densely populated and there was less traffic. The rural population ($n=409$) consisted of people living in 11 municipalities surrounding Bergen. The levels of nitrogen oxides were above the lower limit of $100 \mu\text{g}/\text{m}^3$ for 21% of the inhabitants in the city area, while the air in the suburban and the rural areas did not exceed this lower limit [26]. The levels of sulphur dioxide and black smoke did not surpass $100 \mu\text{g}/\text{m}^3$ in either area.

Season

The pollen season for birch is May, for timothy from June to July and for mould from late June to August [27]. Mould and house dust mite are indoor allergens which exist throughout the year due to the mild and wet climate [28]. In the winter months from October through to March 505 subjects with blood samples were examined, while 763 subjects were examined in the summer months from April through to September.

Educational level

A self-administered questionnaire allowed us to categorize the subjects into the following educational levels: primary school, secondary school and university. Primary school level ($n=240$) included former elementary school, present 9-year compulsory elementary school, people's college and bible school. Secondary school level ($n=788$) included former middle school or lower secondary school, upper secondary school and any vocational or technical school. The university level ($n=240$) included all education after and based on upper secondary school level.

Blood sampling

The blood samples were taken from Monday through to Friday between 08.00 hours and 16.00 hours. The samples were drawn from the cubital vein with the subject sitting in a chair. Four millilitres of blood were collected in a sterile vacutainer (Becton Dickinson) without any preservative or anticoagulant. The blood was clotted in the tube at room temperature. The serum (approximately 2 ml) was decanted, and if there was macroscopic sign of red blood cells in it, they were removed by centrifugation. Every afternoon the serum samples were brought to the laboratory and kept in a refrigerator at 4°C. The samples were analysed within 3 days.

Total serum IgE concentration was measured by a double antibody radioimmunoassay in duplicates, with reference sera in three levels, using paper discs as the solid phase (IgE RIA, Pharmacia, Sweden). The within-assay coefficient of variation in our study was 4% at 100 kU/l IgE and the between-assay coefficient of variation was 7% at the same level.

The specific IgE levels for house dust mite (*Dermatophagoides fariniae*), timothy, birch, cat and mould (*Cladosporium herbarum*) were analysed in single samples by a radioallergosorbent test (Phadebas RAST, Pharmacia, Sweden). The results were classified in Phadebas RAST classes [29]. Prevalences were estimated on the presence of Phadebas RAST class 2 or higher (≥ 0.35 Phadebas RAST units/ml).

Statistical analyses

The observed levels of total serum IgE and prevalences of specific IgE were standardized for the different sampling fractions of the sub-samples and were hence made representative of the general population of Bergen and 11 surrounding municipalities [30]. All the statistical analyses and values in sub-sets of the population used log IgE values. Differences in prevalence rates were tested by chi-square technique. Analysis for linear trend was per-

formed by a bi-variate regression analysis with weighted least square technique, using weights equal to the inverses of the variances.

A backwards, stepwise multiple linear regression analysis was performed to assess predictors of log IgE levels. A backwards, stepwise logistic regression analysis was used to examine the relative importance of potential risk factors for specific IgE levels and for examining the interrelationship between quintiles of total IgE and specific IgE antibodies. Sex, age, smoking, occupational dust or gas exposure, sub-sample, area of residence, season and educational level as well as all first order interactions were included in the starting model for both analyses. In the multivariate analysis season was scored as a trend variable with six levels going from the winter months December/January [1] to the summer months June/July [6]. Subjects with no present occupational title (students, homemakers, disabled or retired subjects, etc.) were included in the non-exposure group when analysing multivariate relationships.

All multivariate analyses were performed with sub-samples (sub-samples 1–3 vs sub-sample 4) as an independent variable, however, removing this independent variable did not influence the final results significantly. The multivariate analyses were performed with the BMDP package [21] and a significance level of $P=0.05$ was used for all the analyses as well as for inclusion of interaction terms into the final model.

Results

Total serum IgE

The distribution of IgE values was positively skewed with 50, 90, 97.5 percentiles of 17 kU/l, 137 kU/l and 563 kU/l respectively. The 20, 40, 60 and 80 percentiles were 5 kU/l, 12 kU/l, 27 kU/l and 66 kU/l.

The population adjusted log IgE value (Table 1) was higher for men than for women ($P=0.03$). There was no sex difference in the age group 18–54 years, while men above 55 years had higher IgE levels than women ($P<0.01$). This difference appeared to be present in non-smokers as well as in smokers. The IgE values in women decreased by increasing age (test for trend: $P<0.01$), more pronounced in non-smoking than in smoking women (Fig. 1). Smokers had a higher ($P=0.01$) IgE level (log IgE 1.26 kU/l; SEM: 0.04) than non-smokers (log IgE 1.13 kU/l; SEM: 0.04). Male smokers above 55 years tended to have the highest IgE level (Fig. 1). A dose response relationship between smoking categories (test for trend: $P=0.01$) or between number of cigarettes smoked per day (test for trend: $P=0.04$) on the one hand and IgE levels on the other was observed in women only.

IgE levels in subjects examined during the summer

Table 1. Total serum IgE levels in relation to sex, age and smoking habit in a Norwegian general population aged 18–73 years

	Men (n=650)		Women (n=618)	
	Mean log IgE (SEM) (kU/l)	Geometric mean (kU/l)	Mean log IgE (SEM) (kU/l)	Geometric mean (kU/l)
Age (years)				
18–34	1.19 (0.05)	15.5	1.23 (0.06)	17.0
35–54	1.25 (0.06)	17.8	1.18 (0.05)	15.1
55–73	1.32 (0.06)	20.9	1.00 (0.06)	10.0
Smoking habit				
Non-smokers	1.25 (0.05)	17.8	1.13 (0.03)	13.5
Ex-smokers	1.11 (0.06)	12.9	1.18 (0.05)	15.1
Smokers	1.34 (0.06)	21.9	1.26 (0.04)	18.2
Total	1.25 (0.03)	17.8	1.14 (0.03)	13.8

months from April through to September tended to be higher than in those examined in the winter months from October through to March ($P=0.06$). This winter/summer difference appeared to be present independent of sex, age and smoking habit. Subjects with occupational exposure to dust or gas had a higher ($P<0.01$) IgE level (log IgE 1.29 kU/l; SEM: 0.04) than those not exposed (log IgE 1.15 kU/l; SEM: 0.04). Levels of total IgE did not differ significantly between subjects by area of residence or educational level.

Specific IgE

The prevalences of the specific IgE antibodies increased in the population with decreasing Phadebas RAST classes (Fig. 2). The rank of order for all specific IgE antibodies was the same in different Phadebas RAST classes. The overall population estimated prevalences (Phadebas RAST classes 2, 3 and 4) were for house dust mite 3.2% (SEM: 0.6%), timothy 4.5% (SEM: 0.7%), birch 2.6% (SEM: 0.5%), cat 1.6% (SEM: 0.4%) and mould 0.2% (SEM: 0.1%). The prevalence of subjects with one or more specific IgE antibodies against five common allergens was 7.6% (SEM: 0.9%). Altogether 4.4%, 3.1%, 1.9% and 0.3% of this population had two, three, four or five specific IgE antibodies, respectively.

Men had significantly higher prevalences for antibodies against house dust mite ($P<0.01$) and cat ($P<0.05$) than women (Table 2). The prevalence of subjects with specific IgE antibodies against house dust mite ($P<0.01$), timothy ($P<0.01$), birch ($P<0.01$) and cat ($P<0.05$) fell by increasing age. The prevalences in the youngest (18–34 years) compared with the oldest age group (55–73 years)

were 61, 15, 4 and 4 times higher for timothy, birch, house dust mite and cat, respectively (Table 2). Non-smokers had approximately a three times higher prevalence for timothy ($P<0.01$) and birch ($P<0.05$) than smokers, while the other allergens did not vary significantly between smoking categories.

During the summer months the prevalence of one or more specific IgE antibodies was higher (9.7%) than in the winter months (5.8%) ($P=0.02$). The antibodies against birch and timothy were approximately 80% higher in summer than in winter, while the other allergens were from 20–40% higher. The prevalence rates for house dust mite and timothy were between 1.5 and 2.0 times higher in subjects living in the suburban and rural areas, respectively, than in the city area, however, the difference was not significant. The prevalence rates of birch and mould antibodies did not vary by area of residence, while cat IgE was four times higher in subjects living in the suburban area than subjects in the city area ($P<0.05$) as well as those in the rural area, respectively ($P=0.06$). Occupational dust or gas exposure and educational level were not associated with the prevalence of specific IgE antibodies.

Inter-relationship between total and specific IgE

When comparing the prevalences of one or more of the examined specific IgE antibodies in the population according to quintiles of total serum IgE, we found approximately four and 13 times higher prevalences of any of the specific IgE antibodies in the fourth and fifth quintile, respectively, compared with any of the three lower quintiles. The increase in prevalence of specific IgE antibodies with increasing total IgE appeared more

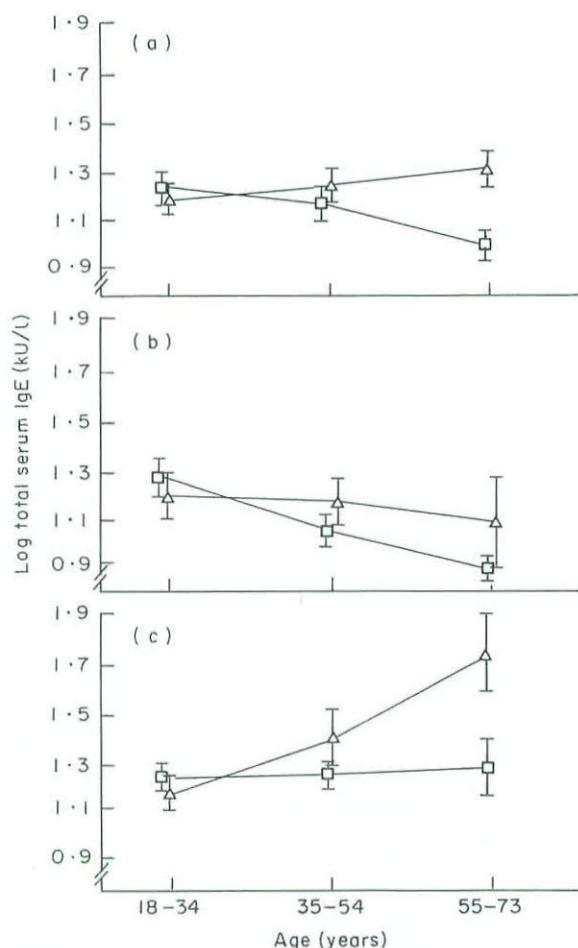


Fig. 1. Mean log total serum IgE (standard error) in three age groups by sex and smoking habit in 18-73 year-old adults in Bergen and 11 surrounding municipalities, Norway ($n=1268$); (a) Δ — Δ . Men. $\square$ — $\square$. Women; (b) Women: Δ — Δ . Smokers. $\square$ — $\square$. Non-smokers. (c) Men: Δ — Δ . Smokers. $\square$ — $\square$. Non-smokers.

evident in non-smokers than in smokers, in younger than in older subjects and in men compared with women (Fig. 3).

Multivariate relationships

Age, occupational dust or gas exposure, as well as the interaction terms between sex and age and between smoking and pack-years were significant independent variables included in the final regression model for log IgE levels (Table 3).

Male sex was an independent predictor for the presence of antibodies against house dust mite (Table 4). Being aged between 35 and 54 years was an independent predictor for lower prevalence of birch, while being over 55 years of age was an independent predictor for lower

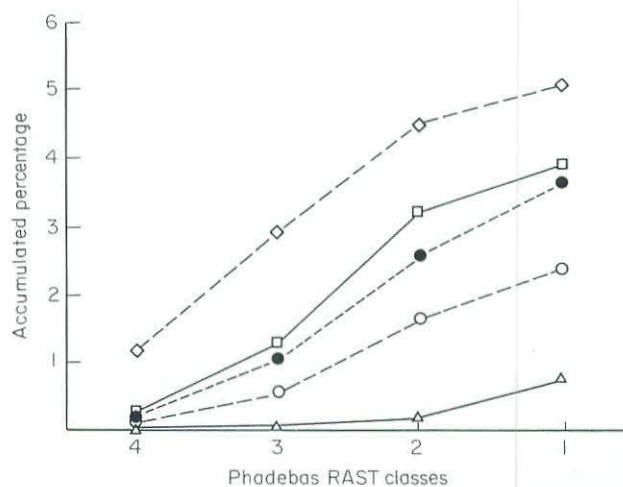


Fig. 2. The accumulated percentage with specific IgE antibodies in Phadebas RAST classes against ($\diamond$) timothy, ($\square$) house dust mite, ($\bullet$) birch, ($\circ$) cat and (Δ) mould in the adult general population of Bergen and 11 surrounding municipalities, Norway ($n=1268$).

prevalences of birch as well as timothy, house dust mite and cat antibodies. Current smoking was an independent predictor for lower prevalences of birch and timothy antibodies only. In a logistic regression analysis adjusting for sex, age, smoking habit, sub-sample and a significant interaction between sex and smoking habit there was a trend towards higher specific IgE levels in summer compared with winter months (adjusted odds ratio (OR) 1.1 per month; 95% confidence interval (CI) 1.0-1.3). This trend was observed for pollens and cat antibodies, but not for house dust mites. The adjusted odds ratio for men compared with women for having one or more of the specific IgE antibodies was significant in smokers (adjusted OR 3.1; 95% CI: 1.1-8.8), but not in non- and ex-smokers. Current smoking was an independent predictor for not having birch or timothy antibodies, as well as for not having one or more of the five specific IgE antibodies examined (adjusted OR 0.3; 95% CI: 0.1-0.9). Occupational dust or gas exposure, area of residence or educational level were not independent predictors for the presence of one or more of the specific IgE antibodies examined.

In the final logistic regression analysis subjects with total serum IgE in the fourth (≥ 27 kU/l) and fifth quintiles (≥ 66 kU/l) had an adjusted OR of 7 (95% CI 2-23) and 37 (95% CI 11-120), respectively, for having at least one of the specific IgE antibodies examined when compared with subjects in the lowest quintile (< 5 kU/l).

Discussion

We observed that total as well as specific IgE levels were cross-sectionally related to sex and age as well as such

Table 2. Estimated prevalence rates and standard errors of mean (SEM) in % of five specific IgE antibodies by sex, age and smoking habit in an adult Norwegian general population

	Sex		Age (years)			Smoking habit		
	Men (n=618)	Women (n=650)	18-34 (n=474)	35-54 (n=443)	55-73 (n=351)	Non-smokers (n=693)	Ex-smokers (n=225)	Smokers (n=350)
Timothy	5.3 (1.1)	3.7 (0.9)	9.3 (1.1)	3.0 (0.9)	0.2† (0.2)	7.1 (1.3)	3.1 (1.4)	2.6† (0.9)
Birch	2.8 (0.7)	2.4 (0.7)	4.6 (1.1)	2.3 (0.8)	0.3† (0.2)	4.5 (0.9)	0.5 (0.2)	1.8* (0.8)
House dust mite	5.3 (1.1)	1.2† (0.5)	4.7 (1.1)	3.4 (1.1)	1.2† (0.7)	3.5 (0.8)	1.6 (1.0)	3.9 (1.2)
Cat	2.5 (0.7)	0.8* (0.4)	2.1 (0.7)	2.0 (0.9)	0.5* (0.5)	1.3 (0.4)	1.8 (1.0)	1.9 (0.8)
Mould	0.3 (0.2)	0.1 (0.1)	0.3 (0.2)	0.1 (0.1)	0.2 (0.2)	0.4 (0.2)	0.0 (0.0)	0.1 (0.1)

P values, chi-square test and test for linear trend: *0.01 $\geq P < 0.05$, †*P* < 0.01.

environmental exposures as tobacco smoking. Furthermore, total serum IgE level was heightened in subjects exposed to occupational dust or gas exposure compared with unexposed subjects. We found no significant relationship between total or specific IgE levels and area of residence, season, or educational level after adjustment for other possible predictors, except for specific IgE antibodies which were higher in summer than winter months.

The 84% attendance rate to the clinical examination in this study gave comparable attenders and non-attenders with respect to sex and environmental exposures [20]. The mean age of the attenders was higher than of non-attenders. However, a 100% attendance rate would only have changed the mean age of the attenders from 42 years to 41 years, presumably having minimal influence on our results. Furthermore, the response rate to the postal questionnaire was high [19] and only seven subjects refused blood sampling, thus reducing a possible bias.

The methods for total IgE and specific IgE measurement in this study are the most commonly used methods for diagnostic and research purposes in northern Europe [31]. The within- and between-assay coefficients of variation for total serum IgE in our study were comparable with previous community surveys [10].

Classification of smoking habit in this survey was based on information from a standardized questionnaire. Furthermore, we have assessed smoking habit by a carboxyhaemoglobin cut-off level of 1.7%, possibly overestimating the fraction of urban smokers since non-smokers who are exposed to carbon monoxide from other sources than tobacco smoke may be included. However, using this carboxyhaemoglobin based smoking classification in the analyses of our data our conclusions remained unaltered.

The geometric mean of total IgE in our population was 16 kU/l, which is in accordance with 17 kU/l found with

the same method in subjects attending a health check-up programme in Sweden [16]. It is, however, lower than in young adults in south Wales [5], adults in Tucson, Arizona [32], in Italy [33] and in the Netherlands [34]. This may partly be due to differences in airborne allergen exposure, in methods as well as in mean age of the populations.

In healthy blood donors in Sweden [35] the prevalences of birch and timothy antibodies were at the same level as in the present survey. In a farming population in Denmark [18] the prevalences of specific IgE for timothy, birch and cat were more than 50% lower than in our population, while house dust mite and mould were at comparable levels. The mean age for this farming population in Denmark was approximately 10 years higher than for our population, which may partly explain our higher prevalence figures.

We observed higher total IgE levels in elderly men compared with women after taking age, smoking habit and sub-sample into account, thus supporting earlier studies [36]. The reason for this sex-difference has not been satisfactorily explained. A hypothesis is that a higher proportion of elderly men than elderly women has been heavily or widely occupationally exposed while this is more equally distributed in younger age categories, thus representing a cohort effect. This sex difference persisted independent of adjustment for dust or gas exposure in our study. However, the exposure characterization in our study may be too imprecise, especially concerning occupational allergies. Furthermore, men in the present survey had a higher adjusted odds ratio for having house dust mite antibodies than women. We have no explanation for this observed difference. However, one may speculate if women have a cleaner indoor environment than men. Furthermore, this observation may be another explanation for the sex-difference in total IgE levels. A sex-difference for specific IgE levels has previously been

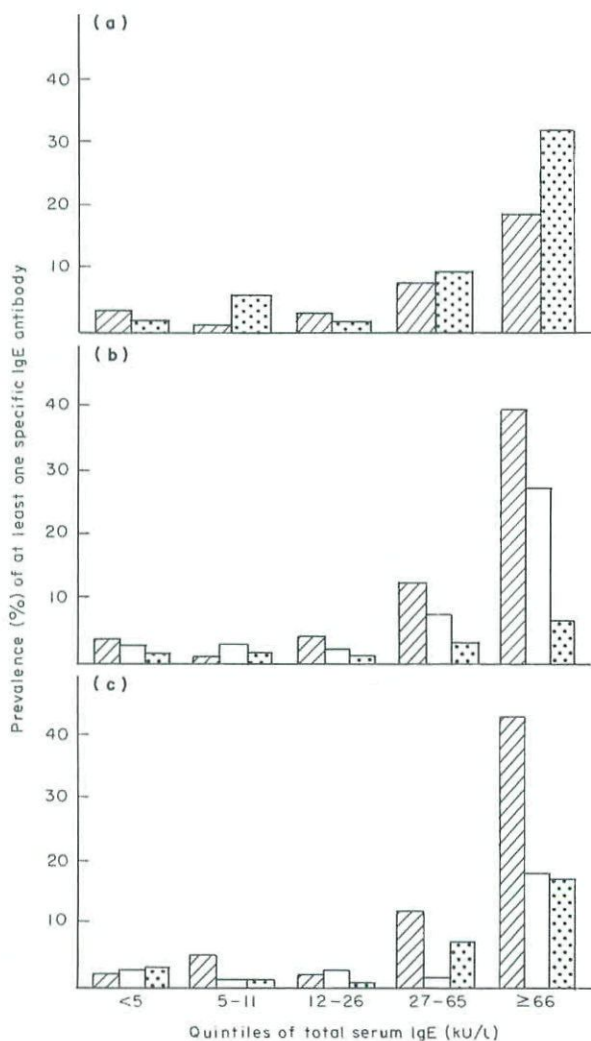


Fig. 3. Prevalence rates of one or more specific IgE antibodies by sex, age and smoking habit according to quintiles of total serum IgE in 18–73 year-old adults in Bergen and 11 surrounding municipalities, Norway ($n = 1268$); (a) ■. Women. □. Men; (b) □. 18–34 years. □. 35–54 years. ■. 55–73 years; (c) ■. Non-smokers. □. Ex-smokers. ■. Smokers.

reported in skin-prick tests of adolescents and adults as well as in RAST tests [37,38]. However, we observed no significant sex difference for antibodies against birch and timothy, which is in agreement with self-reported lifetime prevalences of hay fever in Norwegian adults [39] and school children [40].

We observed a fall in total IgE levels by increasing age in non-smoking women. However, no significant age trend was shown in non-smoking men, before or after adjustment for other possible predictors in the final regression model. A fall in IgE levels by increasing age in women as well as in men has been found in previous studies [10,33,34,36]. A lack of decline with age has been shown in studies including only men [2,41] or in a non-

atopic population [42]. Steady IgE levels by increasing age in men in the present study can be due to a cohort effect, where older men were more heavily exposed to tobacco smoke and occupational exposure than younger men. Furthermore, the adjustment for smoking and occupational dust or gas exposure in the statistical analysis may be incomplete.

The levels of specific IgE antibodies fell substantially with increasing age in our study as reported for Bermuda grass, a common aeroallergen in Tucson, Arizona, USA [14]. Further support is provided of hay fever in the present study population by the decrease with increasing age of self-reported life-time prevalence [39]. The decline in specific IgE levels by increasing age was found in both men and women, however, the total IgE levels showed a decline only in the women of our study population. This may indicate that factors other than specific IgE levels are important for the total IgE levels. Occupational exposure and/or current smoking may be such factors.

We observed that middle-aged and older smokers had higher IgE levels than non-smokers in the same age groups, which is in agreement with findings in Arizona, USA [12]. Higher levels of serum IgE among smokers than non-smokers have been reported in most studies [11,16,33,34]. An explanation for higher IgE levels in smokers than non-smokers may be change in regulatory mechanisms of the IgE synthesis [43] or increase of IgE related to frequent infestation of their airways with micro-organisms that induce specific IgE [44]. There has been no evidence of specific IgE antibodies against tobacco in smokers [45].

Intermediate levels of IgE in ex-smokers suggest a cause-effect relationship between tobacco smoking and IgE levels. This was only applicable to the women in our study. However, ex-smoking men tended to have IgE levels similar to non-smoking men, while ex-smoking women appeared to have IgE levels similar to smoking women. On average, the women stopped smoking 2 years prior to this study, however, the men had given up smoking more than 5 years ago. This may explain these differences, since it can take more than 8 years to show a decline in IgE levels after stopping to smoke [46]. Furthermore, our carboxyhaemoglobin measurements indicated that women tend to under-report current smoking. A cause-effect relationship between current tobacco smoking and IgE levels is further supported by the observation that amount of lifetime smoking assessed by pack-years was an independent predictor for total serum IgE levels in smokers but not in ex-smokers.

The increased prevalence of specific IgE antibodies against pollen in non-smokers compared with smokers in a general adult population has not been reported previously. Lifetime prevalence of self-reported hay fever in the present study population has previously been found to

Table 3. Linear regression coefficients (SEM) and *P*-values for independent variables included in the final model when examining predictors of log IgE levels (kU/l) in a stratified sample of adults living in Bergen and 11 surrounding municipalities, Norway (*n* = 1268)

	Regression coefficients	SEM	<i>P</i> -value
Intercept	1.4549		
Independent variables included in the model (<i>P</i> < 0.05)			
Age (years)	-0.0051	0.0016	< 0.01
Occupational dust or gas exposure	0.0872	0.0380	0.04
Sex* age	0.0061	0.0026	0.03
Pack-years* smoking habit			0.01
Pack-years* ex-smokers	0.0034	0.0028	0.23
Pack-years* smokers	0.0081	0.0023	< 0.01

Sex: men = 1, women = 0.

Table 4. Adjusted* odds ratios (95% confidence intervals) for having specific IgE antibodies by sex, age and smoking habit in Norwegian adults

	Sex		Age			Smoking habit		
	Women (<i>n</i> = 618)	Men (<i>n</i> = 650)	18-34 (<i>n</i> = 474)	35-54 (<i>n</i> = 443)	55-73 (<i>n</i> = 351)	Non-smokers (<i>n</i> = 693)	Ex-smokers (<i>n</i> = 225)	Smokers (<i>n</i> = 350)
Birch	1	1.0 (0.5-2.1)	1	0.7 (0.3-1.3)	0.1 (0.0-0.5)	1	0.2 (0.3-4.0)	0.4 (0.2-0.9)
Timothy	1	1.6 (0.8-3.1)	1	0.4 (0.2-0.7)	0.1 (0.0-0.2)	1	1.5 (0.4-4.6)	0.3 (0.1-0.7)
House dust mite	1	2.9 (2.2-7.1)	1	0.7 (0.3-1.3)	0.2 (0.1-0.6)	1	0.5 (0.2-1.6)	0.9 (0.4-1.9)
Cat	1	2.0 (0.6-6.9)	1	0.6 (0.3-1.6)	0.1 (0.0-0.7)	1	6.5 (1.2-34)	0.6 (0.1-2.7)
Mould	1	3.6 (0.3-36)	1	0.4 (0.1-4.4)	0.7 (0.1-7.4)	1	†	0.4 (0.0-98)

*Adjusted for sex, age, smoking, sub-sample and season of the year, respectively, †No subjects observed in this category.

be inversely related to cigarette smoking [39]. Furthermore, skin-test reactivity to Bermuda grass has been observed to be lower in smokers than in non-smokers in a general population [14]. A hypothesis often given is that subjects with allergic symptoms and disease take up smoking less frequently or quit more often than subjects with no allergic symptoms and disease. However, this has never been proven in a prospective study. Other explanations for the lower levels of specific IgE antibodies in smokers compared with non-smokers may be a defect antigenic presentation to immunocompetent cells in the airways, as in other immunologically mediated lung disorders or difference in exposure between smokers and non-smokers. Impairment in macrophage effector functions, and reduction in T helper cells has been observed in relation to T suppressor cells in heavy smokers giving support to this hypothesis [47].

We found increasing adjusted odds ratios for having

one or more specific IgE antibodies with increasing level of total IgE. This is in agreement with a positive relationship between total IgE level, positive skin-prick tests and specific IgE levels [48,49]. Furthermore, the predictive value of having one or more specific IgE antibodies given total IgE level in the highest quintile is nearly double in men compared with women, in younger than in older subjects and in non-smokers compared with smokers. This has important practical implications for screening. Our results indicate that screening for the five specific IgE antibodies of adults in the present study should only be carried out in subjects having a total IgE level above the 60 percentile of the same population.

We found that non-smokers, ex-smokers and smokers all tended to have higher levels of total serum IgE in summer than in winter, however, it was only marginally significant in smokers (*P* = 0.05). In the Tucson study an increase in geometric mean total serum IgE levels was

observed only during spring for non-smokers [12]. However, when examining the relationship between the presence of specific IgE levels and season in a multivariate analysis there was a significant trend towards higher levels from winter to summer months.

The total IgE levels did not vary by area of residence. However, prevalences of specific IgE antibodies tended to be somewhat higher in subjects living in the suburban area, than in the city and the rural area, respectively. Only cat antibodies were significantly ($P < 0.05$) more frequent in subjects living in the suburban area than in the city area. An explanation may be a higher allergen exposure, poorer indoor air quality due to lower rate of air renewal in more recent and more well insulated buildings [50], as well as a higher frequency of indoor pets in the suburban than in the city and rural areas. However, after adjusting for sex, age, smoking and sub-sample, living in a suburban area was no significant independent predictor (OR 1.9; 95% CI 0.4–8.7) for cat antibodies.

Subjects with occupational dust or gas exposure had a higher IgE level than those not exposed, independent of sex, age and smoking habit. Even though our occupational exposure characterization may be rough, this indicates that there is a true association between occupational dust or gas exposure and total IgE. Furthermore, the results were similar in a logistic regression analysis when excluding subjects ($n = 357$) with no present occupational title (disabled and retired subjects, etc.) in the non-exposure group. However, we observed no relationship between antibodies against common airborne allergens and occupational dust or gas exposure. Whether the observed association between total IgE and dust or gas exposure reflects a non-allergic inflammatory response or it reflects an allergic response due to exposure of specific occupational allergens can not be highlighted further from our study. However, it has previously been documented that some occupational allergens can induce specific IgE antibodies [16,17].

Sex, age and smoking habit were independent predictors of total as well as specific serum IgE levels in this cross-sectional survey of adults. The season when examination of the subjects was carried out was an independent predictor for having one or more of the specific IgE antibodies examined, as were occupational dust or gas exposure for total IgE levels. These observations should be taken into account when examining the relationship between total and specific IgE antibodies as markers of inflammation and allergy on the one hand and airways disease on the other.

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