

Longitudinal Observations of Serum IgE and Skin Prick Test Response

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The objective of the study was to assess skin prick test and IgE changes in a working population surveyed 5 yr apart and to determine whether age and smoking habits modify these changes. SPTs were performed on 223 subjects by the same method and common allergens (a mixture of grass pollens and a mixture of 95% house dust and 5% house dust mite). IgE measurements were done in duplicate by the same technique at each survey. A SPT-positive response at the first survey was highly predictive of a positive value at the second survey. The prevalence of positive SPT significantly increased in 5 yr (from 17.5 to 24.7%). A strong correlation was observed between IgE levels 5 yr apart ($r = 0.92$), and the IgE level appeared very stable. The initial IgE level was significantly greater among the converters than in consistently negative subjects (92.3 versus 30.1 IU/ml). Conversely, the initial IgE level was lower for the reverts than in consistently positive subjects (36.8 versus 97.0 IU/ml). In SPT negatives, non- and exsmokers had a greater decrease in IgE than current smokers ($p = 0.06$). IgE level appears to be a good predictor of SPT changes for both conversion and reversion. The IgE level appears very stable in midadulthood, which suggests that the adult environment may play a small effect in IgE level. **Oryszczyn M-P, Annesi I, Neukirch F, Doré M-F, Kauffmann F. Longitudinal observations of serum IgE and skin prick test response. Am J Respir Crit Care Med 1995;151:663-8.**

Allergic diseases are important causes of morbidity, and their incidence has increased in recent years (1, 2), ranking sixth in disease prevalence according to the World Health Organization. Skin tests corresponding to IgE-mediated hypersensitivity represent a major tool in clinical practice and in epidemiologic surveys. Cross-sectional studies have shown that age, sex, and smoking may modify skin prick test (SPT) response and IgE level. Among adults, skin prick test response and IgE have been reported to decrease after a given age (3), the level of which varies within studies. Nonsmokers and exsmokers exhibited in most studies more often an atopic response than current smokers, a phenomenon attributed to the healthy smoker effect (4-6), but some did not find any relation (7). Current smoking in several epidemiologic surveys was associated with higher IgE level (4, 8-10), especially in SPT-positive subjects (9), but some studies in occupational groups did not find any relation (11) or were restricted to heavy smokers (12). The relation of smoking to IgE may depend on age, with larger differences between smokers and nonsmokers and among old than young subjects (9). Most authors based positivity on wheal response (5, 7, 11), although erythema response has been included in some surveys (13). We observed a significantly higher IgE level in subjects with erythema without wheal than in

subjects without a response (12), so it remains to be established whether erythema in the absence of wheal could predict definitive atopy. Only one longitudinal epidemiologic study (14) among adults looked at the interrelationships of SPT, IgE, age, and smoking. The second cross-sectional survey conducted in the general population of Tucson, Arizona, 8 yr from the first confirmed the associations of the first survey and further suggests that a high initial IgE predicts SPT conversion (14, 15).

The aim of our study was to assess SPT and IgE changes in a working population surveyed 5 yr apart and whether age and smoking habits modify these changes.

METHODS

Subjects

The initial study population in 1985 (June 1985 to June 1986) consisted of 386 policemen in the Paris area. All had SPT, but for technical reasons, only 331 men had IgE determinations. In 1990 (April 1990 to April 1991), a new survey was conducted in the same population. Of the 386 men initially examined, 6 were dead, and vital status cannot be determined for 8 men. Of the 372 men known to be alive, 9 refused, 52 were lost because they moved, 12 were living too far from the examination center, 70 were lost for unknown reasons, and 229 came for the examination. Skin prick tests were performed for 223 men. Overall, 189 men had two IgE determinations.

Skin Tests

Skin prick tests were performed by the same method at both surveys, applying drops of allergen to the forearm. Only the angle used to prick through the drops with the steel lancet (Dome Hollister, Paris, France) was different between the two surveys: 45° in 1985 and 90° in 1990. In 1985 and in 1990, the same three common allergen extracts (1:10) were

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used for testing: a mixture of grass pollens (Dome Hollister, Paris, France) and a mixture of 95% house dust and 5% house dust mite (*Dermaphagoides pteronyssinus*); (Stallergenes Laboratories, Fresnes, France), but not from the same lots because of the duration of their conservation. A negative control consisted of saline solution. After 20 min the largest wheal and erythema diameters were recorded and the difference from the control wheal or erythema was computed. The analyses of wheal size were performed using both the crude value and the logarithm because the distributions were skewed. These gave essentially the same results, and the figures presented are the geometric means. Positivity was defined as any wheal diameter greater than that of the control wheal. The reaction was considered negative in the other cases. Independently of positive subjects, men with erythema in the absence of wheal were also separately studied because in 1985 that group exhibited a significantly higher IgE level than men without erythema or wheal (12). Converters ($n = 26$) were those men who were negative in 1985 and positive in 1990. Reverters ($n = 10$) were those men who were positive in 1985 and negative in 1990.

Comparison of the prevalence of the SPT response to the mixture containing *D. pteronyssinus* to the pure allergen (Dome Hollister, Paris, France) was performed in 1990. The prevalence of positive SPT to pure allergen was 12.6 and 17.9% with the mixture. Taking the pure allergen response as the reference, the sensitivity and the specificity of the response to the mixture were 78.6 and 90.8%. The predictive values of a positive and a negative response to the mixture were 55.0 and 96.7%, respectively. In 1990, skin tests to other allergens were performed (cat, *Alternaria*, *Cladosporium*, and *Betullaceae*) but not considered in the present longitudinal analysis. However, 90% of the subjects positive for any of the allergens used in 1990 were positive for the allergens used in 1985. For methodologic reasons, all longitudinal analyses were performed considering the same allergen extracts in both surveys.

IgE

Venous blood samples and plasma were obtained and kept frozen at -80°C until they were used for total IgE determinations. These measurements were done in duplicate using the Phadebas® PRIST (Pharmacia Diagnostics, AB, Bois d'Arcy, France) technique. If the duplicate measurements were not within 10% of one another in counts per millimeter, the assays were repeated, which occurred for two men (maximum difference was 23.7%). The intraclass correlation coefficient between the two measurements was 0.987 (and was unchanged when considering the initial assays for the two men with discordant values). The reported values represent the mean and are expressed in international units per milliliter. Samples too small to be detected (one man in 1985 and seven in 1990) by the PRIST method (less than 1 IU/ml) were ascribed a value of 1 IU/ml for logarithmic transformation. All statistical analyses were carried out using log IgE values. Because IgE is log normally distributed, IgE changes between 1985 and 1990 were expressed as percentage change per year:

$$\text{IgE\% change/yr} = \frac{10^{(1990 \log \text{IgE} - 1985 \log \text{IgE})/(\text{no. mo elapsed between two surveys}/12)}$$

Questionnaire

At both examinations, a modified British Medical Research Council/European Coal and Steel Community questionnaire was used. The daily consumption of tobacco was evaluated considering one cigarette, one cigarillo, and one cigar equal to 1, 2, and 5 g, respectively. Decade age classes were used (28 to 37, 38 to 47, and 48 to 58). The age class ≥ 55 was also considered to allow comparison to the single longitudinal study published so far (14, 15). Pollen season was defined by the period April through September, and a four-class variable crossing examination during the pollen season or not at both surveys was constructed.

Follow-up

Men resurveyed and lost to follow-up had a similar initial mean age (range 28 to 58 yr) (Table 1). However, there was a significantly preferential loss of both the youngest (<38 yr, 49% resurveyed) and the oldest (≥ 48 yr, 44% resurveyed) compared with those of median age (67% resurveyed). Regarding smoking habits, nonsmokers were significantly more often resurveyed (67%) than smokers (51%), with exsmokers in the intermedi-

ate position (57%). There was no difference for health characteristics, such as FEV₁, allergic manifestations (eczema, hay fever, or asthma), positive skin prick tests, or IgE level, between those resurveyed and those lost to follow-up (Table 1).

Statistics

The associations of qualitative variables were evaluated with the chi-square test. Because the same subjects were examined twice and therefore the data are not independent, 5-yr changes in skin test responses should be examined looking only at discordant subjects using the McNemar chi-square test (16). For quantitative variables, analysis of variance and multiple regression were used (17).

RESULTS

Skin Prick Test

The prevalence of positive skin prick tests (wheal greater than control) was 17.5% in 1985 and 24.7% in 1990. In 1985 and in 1990, 36.8 and 11.7%, respectively, had erythema reaction in the absence of wheal. At both studies, the prevalence of a wheal or erythema response was greater for the house dust mixture than for grass pollens.

Positive responses were highly concordant (odds ratio, OR = 17.6; $p < 10^{-3}$) between the two surveys: 29 subjects were concordant positive, 158 concordant negative, and 36 discordant (26 converters and 10 reverters). The predictive value of a positive test at 5 yr was 52.7%. An increase in positive skin prick test response in 5 yr was observed, as shown by the significantly greater proportion of converters than of reverters among discordant subjects (McNemar paired chi-square test, see METHODS; $p < 0.01$). Similar results were observed for both allergens (Table 2). Highly dependent on prevalence rates, it is of clinical interest to note that among the 184 subjects negative in 1985, 26, that is, 14.1%, became converters, and among the 39 subjects positive in 1985, 10 (25.6%) became reverters.

The intensity of the reaction (wheal or erythema) was greater for grass pollens than for the house dust mixture. For grass pollens, the geometric mean diameters of the wheal reactions were 5.2 mm (range 1 to 28) in 1985 and 6.5 mm (range 3 to 18) in 1990 and those of the erythema reactions were 2.2 mm (range 1 to 58) and 9.1 (range 1 to 66), respectively. For the house dust mixture, the mean diameters of the wheal reaction were 3.2 mm (range

TABLE 1

COMPARISON OF THE INITIAL CHARACTERISTICS OF THE MEN LOST TO FOLLOW-UP AND INCLUDED IN SUBSEQUENT ANALYSES

	Included ($n = 223$)	Lost to Follow-up ($n = 157$)	p Value
Age, mean $\pm$ SD, yr	42.5 $\pm$ 6.4	43.0 $\pm$ 9.0	0.55
Smoking habits, %			
Nonsmokers	38.4	26.4	
Exsmokers	27.4	26.4	0.02
Smokers	34.2	47.2	
FEV ₁ , mean $\pm$ SD, L	4.02 $\pm$ 0.60	3.92 $\pm$ 0.65	0.15
FEV ₁ , score, mean $\pm$ SD*	0.06 $\pm$ 0.96	-0.09 $\pm$ 1.06	0.17
Asthma, %	6.3	8.9	0.34
Hay fever, %	22.6	22.3	0.94
Eczema, %	6.3	7.6	0.60
Positive skin prick tests, %	17.5	19.8	0.70
IgE GM (95% CI), IU/ml †	39.7 (2.0, 754.5)	43.9 (1.8, 1,056.1)	0.46

Definition of abbreviations: GM = geometric mean; CI = confidence interval; SD = standard deviation.

* Adjusted for age and height using the linear regression on the whole sample and standardized (mean $\pm$ SD = 0 $\pm$ 1).

† Data available for 189 men included and 137 lost to follow-up.

TABLE 2
5-YEAR SKIN PRICK TEST RESPONSES CHANGES ACCORDING
TO ALLERGEN, AGE, AND SMOKING HABITS

	n	1985 Survey Positive Response (%)	1990 Survey Positive Response (%)	Odds Ratio
All	223	17.5	24.7†	17.6§
By allergen				
House dust mite	223	11.7	17.9†	22.7§
Grass pollen	223	9.0	13.5‡	20.3§
By age, yr*				
28–37	37	16.2	35.1‡	14.4§
38–47	140	17.9	20.7	24.3§
48–58	46	17.4	28.3	13.3§
By smoking habit				
NS-NS	78	19.2	24.4	18.9§
ES-ES	49	18.4	26.5	19.8§
S-S	54	16.7	22.2	13.0§
S-ES	18	11.1	16.7	7.0
Miscellaneous	8	25.0	37.5	—

Definition of abbreviations: NS = nonsmokers; ES = exsmokers; S = smokers.

* Age at the time of the first survey.

† $p < 0.01$ (McNemar paired χ^2).

‡ $p < 0.05$ (McNemar paired χ^2).

§ $p < 0.001$.

1 to 8) in 1985 and 5.0 mm (range 1 to 9) in 1990 and those of the erythema were 2.1 mm (range 1 to 33) and 9.1 mm (range 1 to 45), respectively. Among concordant subjects for each allergen, there was no particular pattern regarding wheal size. Overall, a decrease of 1 mm for the house dust mixture and an increase of 1.2 mm for pollens was observed in 5 yr, a difference that was not statistically significant.

As expected, the size of the wheal in 1985 was significantly smaller among those who became reverters than among those who remained positive (1.6 versus 4.2 mm for the house dust mixture and 2.0 versus 8.8 mm for grass pollens). Conversely, the size of the wheal in 1990 was slightly smaller among those who were converters than among those who were positive in 1985, but not significantly (4.2 versus 5.2 mm for house dust mite and 5.7 versus 7.6 for grass pollens). Among the subjects who were negative in 1985, the proportion of converters was greater among those who had an isolated erythema reaction ($n = 82$) in 1985 than among those without it ($n = 102$) (18.2 versus 10.8%; OR = 1.82),

but not significantly. The small number of men with erythema 3 mm or greater (five men) precluded a detailed analysis of those with large erythema.

Cross-sectionally, age was not significantly related to SPT response (Table 2). The greatest prevalence of positive reactions was observed among the youngest in 1990, and no particular pattern was observed in 1985. The increase in positive skin test response between the two surveys was observed in all age classes and was significant in the youngest age group. Among the 10 subjects aged 55 yr or more, at both surveys 1 subject was positive.

Consistent smokers had a lower prevalence of positive response than consistent nonsmokers or exsmokers at both surveys (Table 2). The lowest prevalences were observed among the subjects who stopped smoking between the two surveys. Longitudinally, the increase in positive response was observed in all smoking habit classes. The analysis of SPT changes according to smoking habits was further analyzed looking at young and old subjects. The analysis was done separately for those aged ≤ 45 yr at the first survey (Figure 1). Whereas the young exsmokers were the less reactive, the old exsmokers were the most reactive at both surveys (interaction with age class, $p < 0.05$). Miscellaneous subjects included four exsmokers who took up the habit again (one of them was positive at both surveys) and four new smokers (one of them was positive at the first survey and two at the second survey).

Excluding the nine men who took antihistaminic drugs at any survey did not change any of these conclusions.

IgE

IgE geometric means and medians were 39.7 and 35.0 IU/ml, respectively, in 1985 and 34.2 and 32.5 IU/ml in 1990. Maximum IgE values reached 4,003 and 3,968 IU/ml for the first and second surveys. IgE values at the two surveys were highly correlated (Figure 2) ($r = 0.92$, $p < 0.001$). This high correlation was corroborated by the good prediction of a high IgE level (IgE > 100 IU/ml) at the second survey by a high IgE level at the first survey, with a predictive value at 5 yr of 76.4%. The IgE change that occurred between the two surveys corresponds overall to a slight decrease of 3%/yr (with a large confidence interval from a decrease of 35%/yr to an increase of 21%/yr). The correlation coefficient of

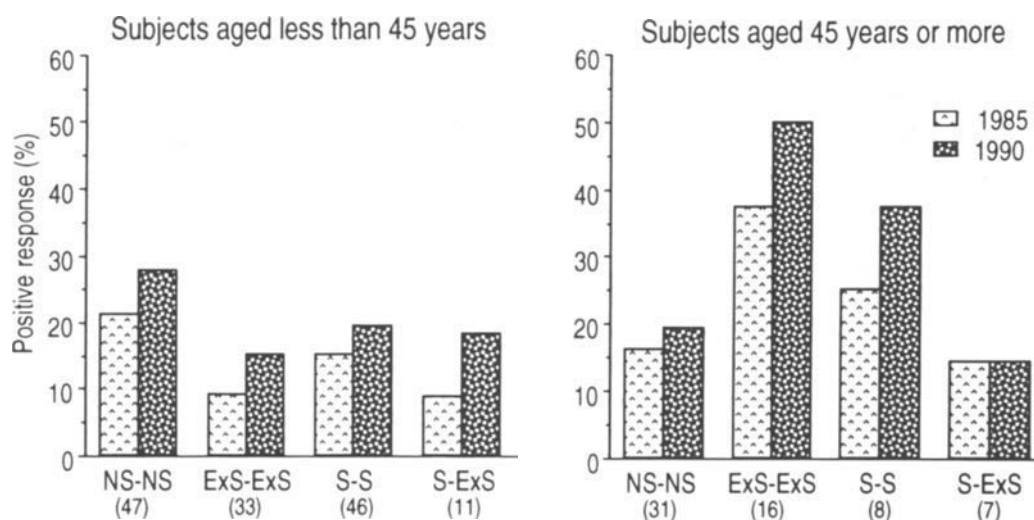


Figure 1. Prevalence of positive skin prick test responses according to age and smoking habits. NS = nonsmokers; ExS = exsmokers; S = smokers.

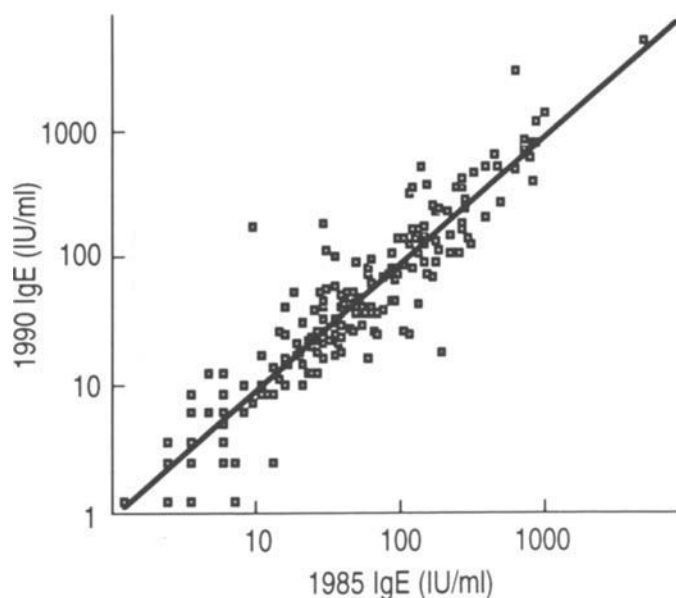


Figure 2. Relationships between 1985 and 1990 IgE levels. $r = 0.92$.
 $\log \text{IgE}_{1990} = (-0.056 \pm 0.053) + (0.99 \pm 0.031) \times \log \text{IgE}_{1985}$.

IgE levels were stable according to prick test response, age, or smoking habits, with values ranging from 0.88 to 0.98 (Table 3).

As expected, cross-sectionally, IgE levels were clearly increased among those with positive skin test responses compared with the other men (75.6 versus 34.4 IU/ml, $p = 0.005$ and 92.0 versus 25.3 IU/ml, $p < 0.001$ in 1985 and 1990, respectively). It should be noted that the 1990 IgE levels among men positive for the pure allergen *D. pteronyssinus* but negative for house dust mite, men positive for house dust mite but negative for the pure allergen *D. pteronyssinus*, and those positive for both were similar (151.4, 114.8, and 85.1 IU/ml, respectively, compared with 26.3 for those negative for both).

The initial IgE level was greater among the converters than among those who remained negative (92.3 versus 30.1 IU/ml; $p = 0.003$), and this was true when considering differences in initial

IgE level separately for house dust mixture or grass pollens. A difference of the same order of magnitude was observed between the reverts and those who remained positive (36.8 versus 97.0 IU/ml; $p = 0.07$). Here, the difference in initial IgE level was stronger considering grass pollens (31.6 versus 111.5 IU/ml; $p = 0.13$) than house dust mixture (65.0 versus 96.6 IU/ml; not significant). IgE values for converters and reverts were intermediate between those of the consistent negative and consistent positive, but it may be noted that the levels in the reverts were very close to the values for the consistently negative and the levels for the converters were very close to the values for the consistently positive.

IgE changes were not significantly different according to skin prick test responses, although the highest percentage decrease was observed in subjects who were consistently negative for both allergens (Table 3).

According to age, there was no cross-sectional difference in IgE levels and no difference in IgE change (Table 3). No particular pattern was observed in those aged 55 yr or more who exhibited a decrease of 2.5%/yr. Similar results were observed in consistently negative subjects.

IgE levels were not significantly related to initial smoking habits considering either a three-class variable or contrasting heavy smokers with other men. Whereas among smokers there was no change in IgE level between the two surveys, the nonsmokers decreased by 3.1%/yr and the exsmokers by 7.1%/yr (comparison of the three smoking groups by analysis of variance, $p = 0.08$). In consistently negative subjects, changes in IgE level according to smoking habit remain similar (0.3, -3.6, and -8.9%/yr, respectively; $p = 0.06$).

Taking an arbitrary limit of 15%/yr for a "high" IgE change, 13 and 36 men exhibited a decrease and an increase greater than this threshold, respectively. Neither skin prick test response nor smoking habits change (those who stopped smoking between the two surveys) explained a high increase or decrease in IgE. However, 3 of the 7 new smokers had a high increase compared with only 16 of 110 consistent nonsmokers or exsmokers.

Exclusion of the 12 asthmatic men did not change the results.

Differences in pollen exposure could have influenced SPT responses or IgE levels. Cross-sectionally, pollen season (18.5% of

TABLE 3
 IGE LEVELS AND 5-YR IGE CHANGES ACCORDING TO SKIN PRICK TESTS, AGE, AND SMOKING HABITS

	n	1985 IgE (IU/ml) GM [95% CI]	1990 IgE (IU/ml) GM [95% CI]	1985-1990 IgE Correlation Coefficient	1985-1990 IgE change (%/yr) GM [95% CI]
All	189	39.7 [2.1, 754.9]	34.2 [1.42, 822.1]	0.92	-3.1 [-34.3, 20.8]
By prick test response					
Consistent negatives (-/-)	136	30.1 [1.7, 544.7]	24.9 [1.1, 552.6]	0.91	-4.0 [-36.1, 20.5]
Reverts (+/-)	9	36.8 [7.8, 1,211.4]*	33.1 [1.3, 828.2]*	0.88	-2.7 [-25.0, 16.5]
Converters (-/+)	18	92.3 [2.2, 624.0]†	90.7 [5.5, 1,502.4]†	0.98	-0.1 [-43.6, 26.6]
Consistent positives (+/+)	26	97.0 [7.6, 1,116.0]	92.9 [7.0, 1,238.7]	0.91	-1.1 [-26.1, 20.1]
By age class, yr					
28-37	30	51.6 [1.5, 1,818.0]	43.4 [1.3, 1,500.6]	0.97	-3.8 [-26.7, 14.9]
38-47	120	35.8 [2.1, 616.2]	31.1 [1.2, 726.2]	0.90	-2.9 [-38.3, 23.6]
48-58	39	44.8 [2.9, 685.6]	38.0 [1.9, 769.9]	0.94	-3.3 [-26.2, 15.5]
By smoking habit					
NS-NS	70	41.5 [2.4, 729.5]	35.6 [2.0, 626.4]	0.92	-3.1 [-33.5, 20.4]
ES-ES	40	36.1 [1.9, 679.2]	26.2 [1.0, 701.2]	0.91	-7.1 [-41.4, 18.9]
S-S	43	37.3 [2.0, 710.2]	36.8 [1.6, 868.5]	0.91	-0.2 [-35.2, 25.8]
S-ES	16	34.9 [1.5, 833.5]	30.8 [1.0, 924.7]	0.95	-2.7 [-30.0, 16.3]
Miscellaneous	7	53.2 [4.2, 670.5]	39.7 [1.7, 946.5]	0.96	-6.6 [-36.0, 16.4]

Definition of abbreviations: GM = geometric mean; CI = confidence interval; NS = nonsmokers; ES = exsmokers; S = smokers.

* $p = 0.07$ versus positives by t test.

† $p < 0.002$ versus negatives by t test.

the men in 1985 and 42.3% in 1990) was associated with significantly greater positive responses in 1985 and significantly higher IgE levels in 1990, a difference that appeared clearer in nonatopic subjects. The longitudinal analyses of SPT and IgE changes were performed after adjustment of the four-class variable for pollen season and restricting the analysis to those men examined twice outside the pollen season. Neither analysis changed any of the previous conclusions.

DISCUSSION

In this epidemiologic study conducted in a middle-aged working population, IgE was very stable whereas SPT positivity significantly increased in the 5 yr of follow-up. Whereas current smokers did not change IgE values, non- and exsmokers exhibited some decrease, in particular those who were SPT negative at both surveys. Positivity of SPT at one survey was predictive of positivity 5 yr later. A high (>100 IU/ml) IgE level at one survey was highly predictive of a high IgE at the second survey because IgE exhibited very strong tracking. Becoming a converter or reverter was predicted by the initial IgE level.

Standardization in skin prick test procedure (allergens and lancets, for example) has improved in recent years, but the definition of a positive response is still not standardized enough. For comparability reasons, we used the same allergens for the longitudinal analysis of SPT responses. Although our longitudinal study is based on the response to mixtures of house dust and grass pollens, inclusion of more allergens would not have changed markedly the results: 90% of the subjects positive for a larger set of allergens were detected by the allergens used twice. The use of pure allergens is preferable to other extracts (18), but at the time of the first survey, such allergens were not used in epidemiologic surveys. Use of pure allergens would unlikely change the major conclusions because the sensitivity and specificity of the allergens used compared with the response to pure allergens were greater than 75% and the associations with IgE were similar considering house dust mixture or the pure allergen *D. pteronyssinus*. The observations remained after taking pollen season into account. It cannot be excluded that differences in some experimental conditions between the two surveys might explain some findings, but we standardized the methods the best we could. Standardization of SPT must be improved, in particular the availability of stable lots of allergens over long-term periods. As a whole, the prevalence of atopy observed (18 and 25% in 1985 and 1990) is consistent with other epidemiologic surveys conducted in general (3) or occupational populations (7). Whereas in clinical settings clear-cut delineation of positive is necessary to establish a diagnosis, more subtle responses may appear of interest in epidemiology, in which the primary aim is the understanding of early events. In this context, we previously suggested considering erythema response in the absence of wheal (12). We observed that initial erythema response related to an increase in conversion, with an odds ratio of 1.8, but the difference was not significant. It is possible that the relevant erythema would be large. Detailed analysis of the potential predictive value of erythema according to its size was not possible because few large erythema were observed. Gergen and colleagues also advocated the use of erythema response (19). Further studies are necessary to assess the usefulness of recording erythema response. In the present analysis, attention was especially given to the longitudinal nature of the data by looking at discordant pairs for the skin prick test and to percentage decrease per year in IgE.

In the present study, all IgE measurements were done in duplicate by the same technician. Because the intraclass correlation

coefficient was as high as 0.99, it is time to question the usefulness of duplicate measurements, at least in middle-aged adults, which could markedly decrease costs in large-scale epidemiologic surveys. Overall, IgE values among adults were lower in the general population studied in Arizona (15) and in Bergen (20) (around 30 and 20 IU/ml for those 35 to 54 yr of age) than in our working population (40 IU/ml).

In 5 yr, 36 men changed in atopic status, with significantly more converters (26 men) than reverts (10 men). This increase in atopy supports other studies that have described an increase in allergic disease (1, 2). Regarding more specifically atopy, our results confirm the Barbee and coworkers (3) findings observed in a general population. The increase in positivity in 5 yr supports a role of environment, and Japanese authors recently suggested that diesel exhaust exposure may increase clinical allergy (21), an exposure that may concern our population of policemen. However, we previously showed that exposure to vehicular traffic was unrelated to IgE level in that population (22). A detailed analysis of conversion or reversion by age was difficult because of the small number of subjects in the extreme age groups but confirmed the greatest proportion of converters in the youngest subjects (14).

Becoming a converter or reverter was predicted by the initial IgE level. Barbee and coworkers (15) observed a twofold increase in initial IgE geometric means for subjects who were either converters and consistently negative or consistently positive and reverts. In our study, the association was even greater, around threefold. Some preferential loss to follow-up occurred for the youngest and oldest subjects. However, loss to follow-up was independent of SPT and IgE level and therefore unlikely to change the results notably.

Most cross-sectional studies have reported that adult smokers are less atopic, a result generally ascribed to the healthy smoker effect (4), and the results of the present study are consistent with these observations. In the Tucson longitudinal study, exsmokers younger than 34 and older than 55 were the most atopic at both surveys, whereas exsmokers aged 35 to 54 were intermediate between consistent nonsmokers and smokers. In our population, exsmokers older than 45 yr were definitely the most atopic, whereas those less than 45 yr were less atopic than current smokers. Different reasons for quitting smoking in the youngest than in the oldest cohort may explain these findings. Besides the healthy smoker effect, social pressure influences quitting smoking and depends upon antismoking campaigns, which have started at various times in different countries. Studying the effects of changing smoking habits would help to delineate the opposite effects of the healthy smoker effect and the potential role of smoking in atopy (4). However, there were too few subjects in our survey to allow such an analysis, and, unfortunately, data were not reported from the Tucson study.

The very strong correlation (0.92) between two measurements 5 yr apart means that 85% of the variance in the second measure of IgE is explained by the first measure and shows that IgE level tracks during midadulthood. Even in consistently SPT negative subjects, the percentage of variance explained was as high as 83%. In middle-aged adults, IgE level appears very stable, a phenomenon also noticed in the general population of Tucson (15). It suggests that the adult environment, although the described associations with smoking or occupational exposures (9, 20) may play a small effect on IgE level, may be mostly determined by earlier characteristics, such as genetics (23) and childhood environment (especially in infancy) (1, 24).

No relation of IgE with age was observed, but the population studied was rather homogeneous in age. A steep decline in IgE has been noted at the end of adolescence and after 55 yr of age

(10), especially in nonsmokers (9), age classes not represented in our study. Despite nonsignificant associations of SPT or IgE levels with age, results were consistent with the literature.

A significant increase in IgE level was observed in 1985 for heavy smokers compared with other men (12), which was consistent with the literature, in which most studies have found some (although rather weak) associations between IgE level and smoking (4, 20). We did not find among the subgroup of the men surveyed twice an association of IgE with smoking habits. However, in the larger group of men (350) examined in 1990 in the same occupational group (some of them were not examined in 1985), we found that smokers had a significantly higher IgE level than nonsmokers (unpublished results). Longitudinally, there was some indication that consistent exsmokers may decrease more in IgE than nonsmokers and current smokers. This fits well with the cross-sectional observations of lower IgE level in exsmokers for at least 5 yr than in recent exsmokers or current smokers in the Tucson (9) as well as in the present study.

In conclusion, a single measurement of IgE is very informative in the middle-age range because of its strong tracking. Current smoking may slow the decrease in IgE with age. IgE level appears to be a good predictor of SPT changes. Repeated skin prick tests in middle age provide better information than a single test. Further studies are needed to understand the various factors in SPT changes.

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