Eur Respir J, 1993, 6, 509–516
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European Respiratory Journal
ISSN 0903 - 1936

Skin reactivity and eosinophil count in relation to the outcome of childhood asthma

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Skin reactivity and eosinophil count in relation to the outcome of childhood asthma. R.J. Roorda, J. Gerritsen, W.M.C. van Aalderen, K. Knol. ©ERS Journals Ltd 1993.
ABSTRACT: **The aim of this study was to determine whether an association can be found between childhood skin reactivity and the outcome of asthma in young adulthood in a group of 406 asthmatic children, of whom 348 (86%) could be followed up in adulthood. A complete data set on skin tests and eosinophil count was available in 259 allergic subjects. They were stratified into three classes, according to initial skin test score in childhood.**

An increase in skin reactivity was noted from childhood to adulthood, while the differences in skin reactivity between the three classes remained significant. In childhood, a marked difference in total eosinophil count was found between the classes. Towards adulthood, a decrease in eosinophil count was noted, and the differences between the classes were no longer significant.

The children with lowest skin reactivity also had the lowest symptom score in childhood. In adulthood, the prevalence of respiratory symptoms in this class was lower than in the other two classes. The prevalence of bronchial responsiveness to histamine was lowest in subjects with the lowest skin test score in childhood. Ventilatory parameters revealed no differences between the three classes.

We conclude that although a low skin reactivity in childhood might be associated with a relatively favourable prognosis for asthma symptoms in adulthood, there is only limited evidence to support this hypothesis in our study.
Eur Respir J., 1993, 6, 509–516.

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Keywords: Allergy
asthma
bronchial responsiveness
eosinophils
skin reactivity
symptoms

Received: February 26 1992
Accepted for publication November 15 1992

This study was supported by the Netherlands Asthma Foundation (Grant 87.38).

Most children with asthma are allergic. Several studies have shown that, in these atopic subjects, skin reactivity to inhalant allergens is age-dependent, and increases from childhood to adulthood [1–6]. Few studies have documented the progress of skin reactivity in relation to the changing pattern of asthma towards adulthood. Although, in some studies positive skin tests were significantly associated with a more severe form of asthma, on completion of these studies the skin test did not affect the prognosis [6–8]. The increase in skin reactivity from childhood to adulthood appeared to be independent of the course of asthma.

An association between atopy and bronchial hyperresponsiveness was first suggested by CURRY [9], and has since been confirmed by others [10–13]. The degree of bronchial responsiveness is assumed to be one of the major determinants of asthma. Thus, allergy may exert an influence on asthma severity, either directly, by specific allergic reactions, or indirectly, by an increase of nonspecific bronchial responsiveness.

As opposed to skin reactivity, the number of eosinophil granulocytes is known to decrease with age in asthmatic subjects [4]. The predictive value of blood eosinophilia in relation to outcome of childhood asthma is relatively unknown. It is, therefore, of interest to assess changes both of skin reactivity and of eosinophil count in a group of asthmatic subjects from childhood to adulthood.

The aim of the study was thus to analyse the association between skin reactivity and the evolution of asthma from childhood to young adulthood. We identified as outcome variables in adulthood the presence of current respiratory symptoms and symptom severity, eosinophil count, skin reactivity, level of pulmonary function, and degree of bronchial responsiveness. In addition, the influence of skin reactivity on nonspecific bronchial responsiveness was examined.

Patients

The original study group consisted of 406 children, aged 8–12 yrs, referred by their general practitioners to the out-patient clinic of the department of Pediatric Pulmonology of the University Hospital of Groningen, from January 1972 to December 1976. The diagnosis of asthma was based on clinical symptoms and the exclusion of specific respiratory diseases. The children were included in the study if a satisfactory set of childhood data on symptoms, physical examination, pulmonary function tests, bronchial responsiveness and allergy

(skin reactivity and eosinophil count) was available. Sex ratio was 1 to 2, 133 girls (33%) and 273 boys (67%). The prevalence of associated eczema and hay fever in children with asthma in the study was 41 and 13%, respectively.

The second survey was performed between June 1987 and December 1990 (table 1). Three hundred and forty eight persons (86%) participated in the follow-up study. In the out-patient clinic, 285 adults (70% of the original childhood patients) were reinvestigated. Sixty three adults (16%) replied to the questionnaire, but were unable or unwilling to perform the tests. A total of 58 subjects (14%) were lost to follow-up. In adulthood, 27% of 348 subjects had concurrent eczema, and 20% had seasonal complaints of hay fever.

Table 1. – Overview of paticipants in the first and second survey, and subjects lost to follow-up.

	n	%*
First survey 1972–1976		
Total number	406	100
Second survey 1987–1990		
Total number	348	86
Lost to follow-up	58	14
Questionnaire answered	63	16
Follow-up visit	285	70
Complete data set on skin tests and eosinophil count	259	64

*: of first survey population

Follow-up skin tests were available from 278 subjects. In childhood, 269 children (97%) had at least one positive skin test. Some allergens (weeds, spring pollen and tree pollen) were not tested in all children. In adulthood the proportion of subjects with at least one positive test was 99% (n=276). Data on eosinophil count were available from 259 subjects, who were all allergic and underwent skin tests for the three most important allergens included in the skin test score. Therefore, these 259 subjects were finally included in the present study of the influence of skin reactivity and eosinophil count on the outcome of childhood asthma.

Identical methods were used in both surveys. In adulthood, subjects were seen, as far as possible, in the same season of the year as in the first survey, to avoid potential seasonal influences.

Both in childhood and adulthood, inhaled bronchodilators were withheld for at least 12 h before the tests, anti-histamines and xanthine derivates for a minimum of 48 h. If necessary, maintenance treatment with cromoglycate or inhaled corticosteroids was continued.

Informed consent was obtained from all participants. The study was approved by the Medical Ethics Committee of the University Hospital of Groningen.

Methods

Questionnaire

An identical extended Dutch version of the standardized questionnaire of the British Medical Research Council-European Community of Coal and Steel (MRC-ECCS questionnaire) was used both in childhood and in adulthood [14]. Subjects were considered symptomatic if they had at least one of four major symptoms. The symptom score used to quantify these symptoms is a cumulative score, ranging from 0–4, being the sum of four categories of binary symptoms: cough, wheeze, exercise-induced asthma and asthma attacks. A score of 1 indicated the presence of a symptom and a score of 0 indicated its absence. Symptoms were scored according to the guidelines of the ECCS questionnaire: cough, if subjects coughed for at least 3 months in a year; wheezing, if wheezing or whistling chest sounds were heard more or less frequently; exercise-induced dyspnoea, if the subject reported frequent shortness of breath at physical exertion or sports; attacks of breathlessness with wheezing in the last three years were noted as asthma attacks.

Pulmonary function

Spirometry was performed with a water-sealed spirometer (Lode spirograph D75, Groningen, The Netherlands). Inspiratory vital capacity (IVC), and forced expiratory volume in one second (FEV_1) were measured until three technically satisfactory recordings were produced. The best of these three efforts of baseline pulmonary function measurement was used as pre-challenge value for the histamine provocation test, as well as for statistical analysis.

The reference values of TAMMELING [15] were used. FEV_1 data are expressed as FEV_1 % pred = (FEV_1/FEV_1 predicted) × 100%.

Histamine inhalation test

A histamine threshold was used to express the degree of bronchial responsiveness. A modified method of Tiffeneau, described by DE VRIES *et al.* [16] and KNOL [17], was used in order to meet standardization guidelines. A 30 s tidal breathing method with a Wiesbadener Doppel inhalation device, filled with 4 ml of test solution was used. With an airflow of approximately 5 $l \cdot min^{-1}$ the output of the nebulizer was 0.06 $ml \cdot min^{-1}$.

After baseline pulmonary function measurement, an aerosol of phosphate buffered saline was inhaled. Sequential aerosols of histamine biphosphate, in concentrations of 0.5, 1, 2, 4, 8, 16, 32 and 64 $mg \cdot ml^{-1}$, were then given. The 64 $mg \cdot ml^{-1}$ concentration was used in adulthood only. FEV_1 values were measured 30 and 90 s after the end of each inhalation step. As soon as a decrease of at least 10% of baseline FEV_1 was reached in all recordings after a certain step, or the highest histamine

concentration had been given, the provocation was stopped. The histamine concentration at which there was a decrease in FEV_1 of at least 10% from baseline value (PC_{10}-histamine) was taken as the threshold value. The exact PC_{10}-histamine was calculated from the log-dose response curve [18]. Determination of PC_{10} had been the standard method used to define bronchial responsiveness in the first survey and was, therefore, used again in the present survey to allow comparison.

Skin tests

A panel of seven (in adulthood eight) allergens and the solvent for the allergens (Coca's - buffer negative control) were tested on the volar surface of the forearm. The allergen solutions were prepared in identical fashion by the same manufacturer (Diephuis Laboratory, Groningen, The Netherlands) throughout the study. The antigens tested are listed in table 2. One tenth of a millilitre of each solution was injected intradermally with a 27 gauge syringe.

Eosinophil count

Eosinophil granulocytes in peripheral blood were counted in a Bürker counting chamber. They were stained with eosin solution; containing 10 ml of eosin 1%, 10 ml formol 40% and 80 ml of water. Reference values for the age-dependent criterion of eosinophilia were published by VEENING [19]. Eosinophilia is defined as a total eosinophil count above 500, 400, 350 and 275× $10^6 \cdot l^{-1}$ for patients from 0–5 yrs, 6–10 yrs, 11–15 yrs and >16 yrs of age, respectively.

Statistical analysis

Statistical analysis was performed on a personal computer with the Superior Performing Software System for Personal Computers (SPSS - PC+ 4.0) programme.

Prior to statistical analysis, PC_{10}-histamine measurements were logarithmically (Ln) transformed. To obtain a normal distribution, eosinophil counts were also Ln transformed.

Table 2. – Number of positive skin tests and mean score for each allergen in childhood and adulthood

Allergen	n	Childhood % Positive	Childhood Mean score (SD)		Adulthood % Positive	Adulthood Mean score (SD)	
House dust 0.5 mg·ml^{-1}	259	95	2.2	(0.7)	72*	2.7	(0.5)**
House dust mite 100 NE·ml^{-1}	259	not tested+			82	2.7	(0.7)
Animal dander 0.25 mg·ml^{-1}	259	85	2.0	(0.7)	83	2.3	(0.7)**
Grass pollen 1,000 NE·ml^{-1}	259	68	1.9	(0.8)	81*	2.2	(0.8)**
Moulds 0.20 mg·ml^{-1}	259	59	1.5	(0.7)	81*	1.4	(0.7)
Weeds 1,000 NE·ml^{-1}	147	54	1.5	(0.6)	78*	1.8	(0.8)**
Spring pollen 1,000 NE·ml^{-1}	145	58	1.7	(0.7)	80*	1.8	(0.9)
Tree pollen 1,000 NE·ml^{-1}	146	53	1.4	(0.6)	81*	1.6	(0.7)**

*: $p<0.05$, adulthood *versus* childhood, McNemar's Chi-squared test; **: $p<0.05$, adulthood *versus* childhood, paired Student's t-test; +: tested in adulthood only; NE: Noon equivalent/unit.

Wheal diameters for each allergen were measured to the nearest half millimetre. After 15 min, the wheal diameter was scored bi-directionally, using the following criteria: mean diameter <5 mm, score 0; 5–10 mm, score 1; 10–15 mm, score 2; >15 mm, score 3.

To compute a cumulative skin test score, the scores for the 3 most prominent allergens (house dust, animal dander and grass pollen), ranging from a minimum of 0 to a maximum of 3 for each allergen tested, were added. These allergens were chosen because they were tested in all participants. This also holds for moulds, but mean score for this antigen was much lower. Therefore, it was considered to be less important. The "total" skin test score was then considered as a categorical variable: class 1: total score 1–3; class 2: total score 4–6; Class 3: total score 7–9.

Within each class of skin reactivity, childhood and adulthood data were analysed with a paired Student's t-test and McNemar's Chi-squared test.

The data of the three classes of skin reactivity were compared for statistically significant differences by means of either a Chi-squared test, when absolute numbers or proportions were compared, or analysis of variance (ANOVA) techniques for continuous variables.

For comparison of data of subjects with and without respiratory symptoms in adulthood, a Chi-squared test or an unpaired Student's t-test were used.

To assess correlations between skin reactivity and degree of bronchial responsiveness, Pearson's correlation coefficient was used. A p-value <0.05 was considered statistically significant.

Results

Skin tests

The results of the skin tests for each allergen tested are presented in table 2. The most prominent allergens in childhood were house dust, animal dander and grass pollen. With the exception of house dust and animal dander, the proportion of subjects with a positive skin test increased towards adulthood. For each allergen, skin reactivity data were studied using paired Student's t-test, comparing the skin test score for every subject in childhood and adulthood. With the exception of spring pollen and moulds, mean skin test score increased significantly from childhood to adulthood for each allergen.

Relation of skin test score to respiratory symptoms

We studied the association between total skin test score in childhood and age of onset of respiratory symptoms, symptom score in childhood, percentage of subjects with current symptoms in adulthood, and symptom score in adulthood.

To assess the prognostic value of skin reactivity in childhood, subjects were stratified, based on skin reactivity in childhood, into classes 1–3. Data were available from 259 subjects. The results are presented in figure 1.

No relationship was found between skin test score in childhood and age of onset of respiratory symptoms ($p=0.35$). In childhood a difference in symptom score was found between Class 1 and the remaining two classes 2 and 3 ($p<0.01$). The proportion of subjects with current respiratory symptoms in adulthood was lowest in Class 1 ($p=0.19$).

Relationship of skin test score to level of pulmonary function and bronchial responsiveness

Mean level of pulmonary function (IVC % pred, FEV_1 % pred) and geometric mean level of bronchial responsiveness were separately assessed for each class of childhood skin reactivity. Results are given in table 3. Data of pulmonary function revealed no significant differences between the three groups, either in childhood or in adulthood. In both surveys the prevalence of subjects, who were hyperresponsive to histamine, was significantly smaller in Class 1 (children with the lowest skin reactivity) compared with Class 2 and Class 3. Both in childhood and in adulthood, geometric mean PC_{10}-histamine was comparable in each class. This means that in each class, in subjects who were hyperresponsive, the mean degree of bronchial responsiveness was comparable.

Skin reactivity to inhalant allergens was only weakly correlated to the degree of bronchial reactivity to nonspecific stimuli, in this case histamine (childhood data: $r=0.11$; adulthood data: $r=0.13$; $p>0.05$ in both surveys).

Relationship of childhood skin test score to adulthood skin test score and total eosinophil count in both surveys

The relationship between total skin test score in childhood and the proportion of subjects with eosinophilia in childhood and mean eosinophil count in childhood, as well as the proportion of subjects with eosinophilia, mean eosinophil count, and mean skin test score in adulthood for each class is presented in table 4.

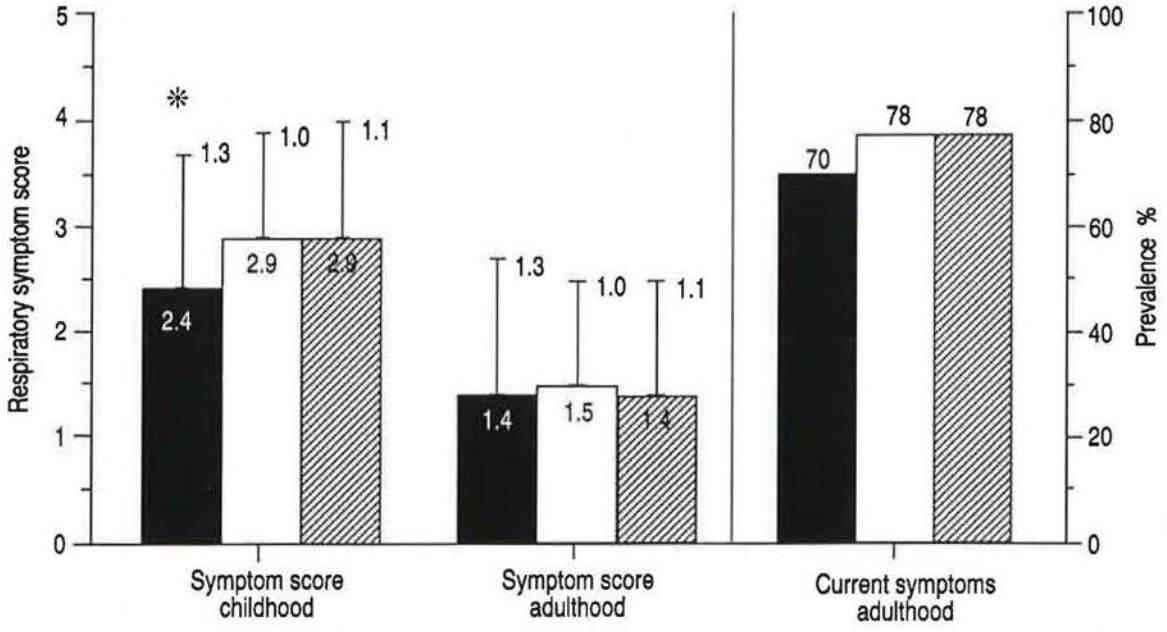

Fig. 1. – Relationship of childhood skin test score (class 1–3) to respiratory symptom score in childhood and adulthood and prevalence of respiratory symptoms in adulthood (Class 1 n=61, Class 2 n=113, Class 3 n=85). *: $p=0.01$. ■: Class 1; □: Class 2; ▨: Class 3.

Table 3. – Relationship between skin test score in childhood and ventilatory function and bronchial responsiveness in childhood and adulthood

	Total skin test score childhood						
	Class 1 score 1–3 n=61		Class 2 score 4–6 n=113		Class 3 score 7–9 n=85		p
Childhood							
IVC % pred*	95	(13)	99	(14)	99	(12)	0.16**
FEV_1 % pred*	91	(15)	91	(16)	92	(17)	0.72**
PC_{10} histamine of ≤16 $mg \cdot ml^{-1}$ n (%)	26	(42)	81	(72)	51	(60)	<0.01+
PC_{10} histamine#	5.2	(3.3)	5.0	(2.7)	6.8	(2.0)	0.18**
Adulthood							
IVC % pred*	104	(11)	105	(14)	103	(11)	0.61**
FEV_1 % pred*	99	(16)	96	(19)	95	(16)	0.32**
PC_{10} histamine of ≤16 $mg \cdot ml^{-1}$ n (%)	15	(25)	56	(50)	38	(45)	<0.01++
PC_{10} histamine#	3.3	(5.6)	3.1	(3.3)	2.8	(2.9)	0.90**

*: mean (SD); **: analysis of variance (ANOVA); +: Chi-squared test: Class 1 *vs* Class 2, p<0.01; Class 1 *vs* Class 3, p=0.05; Class 2 *vs* Class 3, p=0.11; #: geometric mean (% SD); ++: Chi-squared test: Class 1 *vs* Class 2, p<0.01; Class 1 *vs* Class 3, p=0.02; Class 2 *vs* Class 3, p=0.59. IVC: inspiratory vital capacity; FEV_1: forced expiratory volume in one second; PC_{10}: provocation concentration producting a 10% fall in FEV_1 from baseline.

Table 4. – Relationship between skin test score in childhood and eosinophilia in childhood and adulthood

	Total skin test score childhood						
	Class 1 score 1–3 n=61		Class 2 score 4–6 n=113		Class 3 score 7–9 n=85		p
Childhood							
Subjects with eosinophilia n (%)	18	(30)	63	(56)	46	(54)	<0.01+
Eosinophil count $n \times 10^6 \cdot l^{-1}$*	319	(275)	496	(338)	529	(357)	<0.01**
Adulthood							
Subjects with eosinophilia n (%)	17	(28)	43	(38)	31	(36)	0.38++
Eosinophil count $n \times 10^6 \cdot l^{-1}$*	241	(262)	277	(189)	283	(271)	0.14**
Skin test score*	6.3	(2.4)	7.7	(3.0)	8.1	(1.6)	<0.01**

*: mean (SD), **: analysis of variance (ANOVA); +: Chi-squared test: Class 1 *vs* Class 2, p<0.01; Class 1 *vs* Class 3, p<0.01; Class 2 *vs* Class 3, p=0.93; ++: Chi-squared test: Class 1 *vs* Class 2, p=0.24; Class 1 *vs* Class 3, p=0.36; Class 2 *vs* Class 3, p=0.93.

In Class 1 (lowest skin test score in childhood) both the proportion of children with eosinophilia, and total eosinophil count in childhood, was significantly lower in comparison to Classes 2 and 3.

The mean number of eosinophils decreased from childhood to adulthood in all three classes. In adulthood the differences in total eosinophil count between the classes were smaller and no longer significant.

The significant difference in skin reactivity between the three classes persisted in adulthood.

Relationship of allergic indices and respiratory symptoms in adulthood

When subjects were stratified according to the presence of current respiratory symptoms in adulthood, mean eosinophil count in childhood was slightly, but not significantly higher in subjects with persistent symptoms in adulthood (p=0.12) (fig. 2). A comparable nonsignificant difference was found in adulthood (p=0.27). No relevant differences in skin test score were seen in childhood.

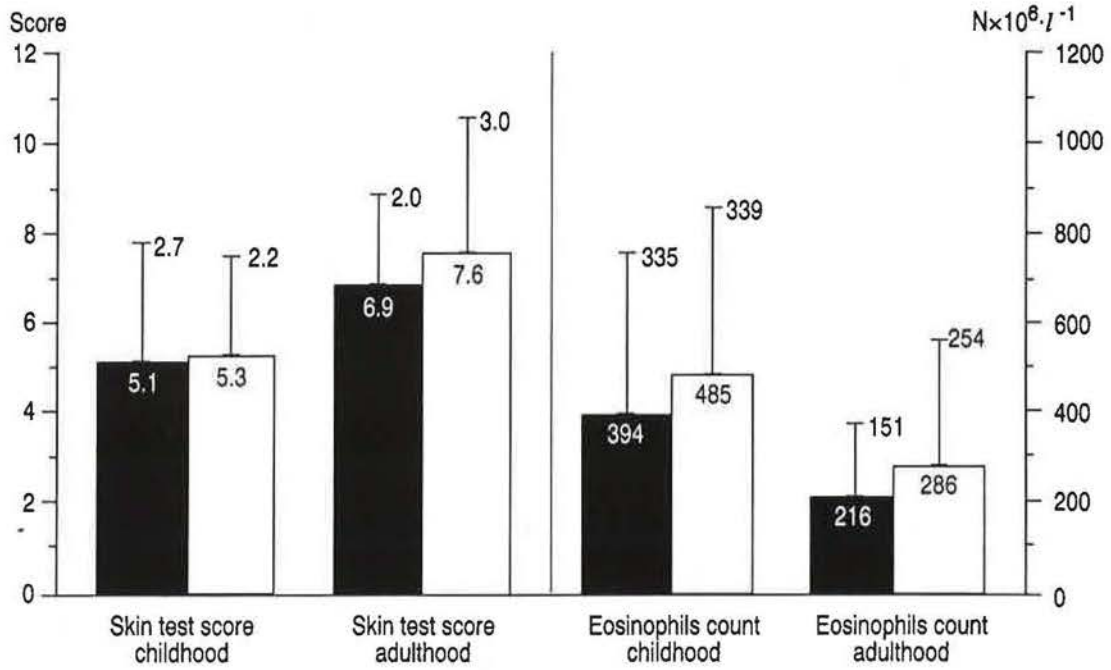

Fig. 2. – Skin test score and eosinophil count in both surveys for subjects with (n=201) and without (n=58) current respiratory symptoms in adulthood. ■: no symptoms; □: current symptoms.

In adulthood, mean skin test score was comparable in subjects with and without current symptoms, although it was slightly higher in subjects that remained symptomatic (p=0.30).

Discussion

Changes in the allergic status in allergic children, were studied, as reflected by skin test score and eosinophil count, in association with the evolution of asthma from childhood to adulthood. It was found that skin reactivity to inhalant allergens increased from childhood to adulthood. This increase was roughly similar in subjects with and without current symptoms in adulthood. Although the prevalence of current respiratory symptoms in adulthood was lowest in subjects with a low total skin test score in childhood, the symptom severity in adulthood was not significantly related to childhood skin test score. In contrast, a relationship was found between childhood skin reactivity and prevalence of bronchial responsiveness in both surveys.

The increase in skin reactivity in relation to age has been found in several other studies, both in epidemiological surveys and in clinical populations of asthmatic subjects. In an epidemiological study, BURROWS and co-workers [20] suggested that an atopic predisposition, as assessed by skin tests, relatively early in life may be a risk factor for the later development of chronic obstructive lung diseases. They found a marked relationship between skin reactivity and ventilatory function, as well as respiratory symptoms, in subjects younger than 55 yrs of age [21].

From these epidemiological surveys it is obvious that the acquisition of skin reactivity is highest among the young, with peak reactivity occurring between 25–34 yrs of age, and a decline after the age of 55 yrs [1]. In most studies in clinical populations of asthmatic subjects, an increase in number of positive skin tests and in wheal diameter towards young adulthood was noted. However, changes in skin reactivity were independent of the severity and the progression of asthmatic symptoms [2, 4, 6, 7, 22]. Nevertheless, after stratifying subjects on the basis of the severity of the disease in adulthood, skin reactivity is generally highest in subjects with more serious symptoms. The most recent report about a prospective follow-up study in Australia demonstrated a strong association between the severity of asthma and markers of atopic disease, including skin tests [8].

Since our study population was based on referrals from general practitioners to the Department of Pediatric Pulmonology, our results might differ from those obtained in epidemiological surveys. The great majority of children were allergic at study entry. A few children without positive skin tests were excluded. No marked differences in baseline characteristics were demonstrated between subjects that completed the study and those excluded or lost to follow-up. Therefore, subjects, who completed the study are likely to be representative for the initial cohort of allergic children that entered the study.

The results in our study also show an overall increase in skin reactivity with age. This increase in skin reactivity appears to arise from an increase in reactivity to both seasonal allergens and others, most important house dust and animal dander. It is likely that the increased reactivity is due to the cumulative exposure to

the allergens. However, a lower prevalence of a positive skin test in adulthood compared with childhood was found for house dust. This might be caused by the fact that for this allergen only, the same standardized batch was not available in both surveys. It is possible that in childhood, the batch had not been completely purified. Moreover, it is well-known that house dust, tested intradermally, may produce nonspecific reactions. This might partially explain the higher prevalence of a positive skin test for house dust in childhood compared to adulthood. In adulthood a positive skin test for house dust mite was more frequently found than a positive reaction for house dust. Unfortunately, the house dust mite antigen had not been available in childhood.

In the present study, mean total skin test score in adults was not significantly higher in subjects with current respiratory symptoms than in adults without current symptoms. This is in contrast to the studies in clinical populations mentioned above, but in agreement with the results of the study of RADFORD *et al* [23]. In the latter study, subjects who were symptomatic at follow-up after 18 yrs, had been significantly more atopic at their initial evaluation in comparison with subjects without symptoms at follow-up. In our study, skin test score in childhood did not differ between those with and without symptoms in adulthood, but when we focused on the three classes of skin reactivity in childhood and studied the data of current respiratory symptoms in adulthood within these three classes, we found a trend towards a lower prevalence of current respiratory symptoms in the subjects with the lowest skin reactivity in childhood (Class 1). Therefore, a certain influence of allergy on the persistence of respiratory symptoms in adulthood was established.

As expected, subjects with lowest skin reactivity in childhood (Class 1) also had a significantly lower number of eosinophils in childhood. The childhood eosinophil count was not significantly related to the persistence of respiratory symptoms in adulthood. Eosinophil count in childhood was not significantly different between subjects in whom symptoms persisted through adulthood and those without respiratory symptoms in adulthood. In adulthood, a slightly higher mean eosinophil count was found in subjects with current symptoms. The higher eosinophil count in subjects with current respiratory symptoms was also found in a study by GERRITSEN *et al* [4].

A relationship between atopic status and nonspecific bronchial responsiveness has often been found. In our study, the prevalence of bronchial hyperresponsiveness to histamine was lowest in Class 1 (subjects with lowest skin reactivity in childhood) in both surveys. However, in subjects that were hyperresponsive, the degree of bronchial responsiveness was not different between the three classes. In other studies, a correlation was demonstrated between the atopic state and the presence or the degree of bronchial responsiveness. VAN ASPEREN *et al.* [5] concluded that subjects with manifest atopy in infancy, are the ones most likely to develop the more severe degrees of bronchial responsiveness during later childhood. PEAT *et al.* [11] also concluded that atopy acquired at an early age is an important predictive factor for respiratory symptoms occurring with bronchial hyperresponsiveness and continuing into late childhood. In a study in school-age boys, whose histories of lower respiratory illness had been documented from early infancy, an association was found between house dust mite allergy and an increased prevalence of bronchial hyperreactivity at 12 yrs of age [24]. In young adults, aged 15–30 yrs, COOKSON *et al.* [25] found a strong positive association between the atopic state, and a high level of nonspecific bronchial responsiveness. In a large birth cohort study in New Zealand, both in asthmatic and in non-asthmatic 11 yr olds, bronchial responsiveness appeared to be closely related to an allergic diathesis, as reflected by the total immunoglobulin E (IgE) level [26]. In the latter study, no skin tests were performed. The same was concluded by CLOUGH and co-workers [10, 12] in a study in 7 and 8 yr old children with current respiratory symptoms. The atopic children in this study were significantly more responsive to exercise and methacholine than the non-atopic children.

No prospective data are available on the relationship between childhood atopic state, and outcome of bronchial responsiveness in young adulthood, except for the study of RADFORD *et al* [23]. In that study, asthmatic subjects who remained symptomatic during the follow-up period had been more bronchial responsive at their initial evaluation and remained so over time, in comparison with subjects without respiratory symptoms at follow-up. This is in agreement with our findings in the current study.

Conclusion

Although a lower prevalence of respiratory symptoms in adulthood was noted in subjects with the lowest skin reactivity in childhood, the differences between the classes were small and not significant (p=0.19). Although, as has been demonstrated in the literature [8], a low skin allergy in childhood might be associated with a relatively favourable prognosis of respiratory symptoms in young adulthood, there was only limited evidence to support this hypothesis in our study. Other allergic parameters, such as total eosinophil count in childhood, are not strongly related to the outcome of respiratory symptoms and symptom severity in adulthood. Childhood level of skin reactivity is significantly associated with the prevalence of nonspecific bronchial responsiveness to histamine, both in childhood and in adulthood.

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