Acta Derm Venereol 2003; 83: 194–201

Taylor & Francis
healthsciences

CLINICAL REPORT

Type I Sensitization in Adolescents: Prevalence and Association with Atopic Dermatitis

The Odense Adolescence Cohort Study on Atopic Diseases and Dermatitis (TOACS)

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The prevalence of Type I sensitization and its relationship to atopic dermatitis were assessed in a cohort of 1501 8th grade schoolchildren (aged 12–16) in Odense, Denmark. The protocol included a questionnaire, a clinical examination, IgE measurements and skin prick tests. A history of atopic dermatitis was found in 21.3%, allergic asthma in 6.9% and allergic rhinitis in 15.7% of the adolescents. One or more positive specific IgE measurements (CAP FEIA) were found in 29.6% of the schoolchildren (inhalant allergens 28.4%, food allergens 8.5%, pityrosporum ovale 1.5%) and a considerable proportion were sensitized without clinical relevance. The association between atopic dermatitis and Type I sensitization was related to concomitant inhalant allergy. A clear association with atopic dermatitis was indicated only for the allergen pityrosporum ovale. ***Key words: CAP FEIA; cohort study; inhalant allergy; schoolchildren; skin prick test.***

(Accepted 16 January 2003.)

Acta Derm Venereol 2003; 83: 194–201.

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Atopic diseases are common (1–4) and an increasing prevalence is found in the general population (5–8). Recent studies in children and adolescents show a lifetime prevalence of atopic dermatitis (AD) of between 12% and 37%, of allergic rhinitis between 2% and 21% and of asthma between 3% and 13% (1–4, 9–13). Children with AD usually have a family history of atopic diseases, and as many as 60–70% will develop allergic rhinitis or asthma, often delayed by some years (14–19).

Type I sensitization (IgE-mediated hypersensitivity) can be determined by skin prick testing or by measuring specific IgE antibody in a blood sample. The prevalence of Type I sensitization evaluated by these methods has been estimated in different populations and the figures in children and adolescents vary between 18% and 50% (2, 20–29).

Several studies have shown a clear association between a history of inhalant allergy and Type I sensitization to common inhalant allergens (2, 20, 26, 30, 31). However, the association between AD and Type I sensitization is less clear when there is no history of inhalant allergy (20, 31, 32). Furthermore, Type I sensitization has been reported to occur in 7–37% of asymptomatic individuals (2, 20, 21, 26, 27, 31).

The aims of this study were to estimate prevalence measures for Type I sensitization in an unselected population of adolescents and to study these in relation to a history of AD.

MATERIAL AND METHODS

Population and study design

The Odense adolescence cohort study is an epidemiological follow-up study. Phase one (1995–1996) was conducted as a cross-sectional study among 1501 8th grade schoolchildren (mean age 14.1 years) in 40 of 43 schools in the municipality of Odense, Denmark. It included questionnaire, interview and clinical examination, blood sample for IgE measurement and patch test. The population and study design have been described in detail previously (33).

The second phase of the study was carried out in the school year August 1996 to May 1997 as a case-control study. Along with a control group, the following four groups of schoolchildren from phase one were invited to further examinations at the Department of Dermatology: 1) possible AD during the previous year, 2) hand eczema during the previous year, 3) present or past inhalant allergy (allergic asthma and/or allergic rhinitis), and 4) one or more positive patch test reactions. Eligible controls were randomly numbered sex-matched individuals from the same school groups not included in one of the four case groups. A common control group, equal to the largest case group, included every second of the eligible sex-matched controls. Control group selection was therefore considered as frequency-matched by sex, and not an individually matched group. For each control not participating in phase two, another eligible sex-matched control from the same school group was invited, since a lower participation among the controls was expected. In the second phase of the study, the schoolchildren were offered an interview, a clinical examination for eczema and skin prick tests. The interview and clinical examination were performed by the same person (CGM) assisted by a registered nurse.

 ISSN 0001-5555

Definitions and description of terms

Atopic dermatitis. The lifetime prevalence (birth to present age) of AD was defined in accordance with published questionnaire criteria (12). The one-year period prevalence and the point prevalence of AD were based on the Hanifin & Rajka criteria (34), excluding two minor criteria – keratoconus and anterior subcapsular cataract.

Allergic asthma and allergic rhinitis (inhalant allergy). The lifetime prevalence of inhalant allergy (allergic asthma and/or allergic rhinitis) was evaluated from the interviews of the schoolchildren. Asthma was defined as three or more episodes of wheezing/whistling in the chest and/or dyspnoea and/or cough. Allergic asthma was defined as three or more episodes of symptoms either at exposure to known allergens (pollen, animal dander, house dust mite, mould, food) or in certain periods (seasonal variation, diurnal variation, inside/outside). Rhinitis was defined as one or more of the following symptoms: itching in the nose, watery rhinorrhoea, sneezing, nasal congestion (35). Allergic rhinitis was defined as one or more symptoms either at exposure to known allergens or in certain periods, or continuing for at least 2 weeks without infectious rhinitis or other infections. Allergic rhinitis was separated into intermittent and persistent rhinitis.

Type I sensitization. This was defined as at least one positive skin prick test (inhalant allergens, food allergens or pityrosporum ovale (*Malassezia furfur*)), or at least one positive specific IgE measurement, i.e. increased specific IgE level (>0.35 kU/l) in serum to at least one allergen (inhalant allergens, food allergens or pityrosporum ovale). The terms indicate only a positive test result, and not whether the finding is clinically relevant.

IgE measurements

All serum samples were stored at -20°C until analysis. The total and specific IgE measurements were performed using the Pharmacia CAP FEIA System® (Pharmacia & Upjohn, Uppsala, Sweden). Sera from the schoolchildren were tested for total IgE and for specific IgE antibodies against inhalant allergens, food allergens and pityrosporum ovale. A screening strategy was applied: series with inhalant allergens (Phadiatop®) and food allergens ($f\times1$, $f\times5$) were performed and only positive samples were subjected to further analyses with the individual allergens. All analyses were performed in duplicate and the results expressed as means. Maximal deviation on the two measurements was 10%. Serum levels higher than 0.35 kU/l (corresponding to class 1) for specific IgE and higher than 150 kU/l for total IgE were considered as increased.

Skin prick tests

The skin prick tests were carried out with 19 commercially available allergen extracts (Soluprick®) from ALK-ABELLÓ, Hørsholm, Denmark and with 3 fresh foods. Both a positive control (histamine dihydrochloride 10 mg/ml) and a negative control (Soluprick solution) were included. Prick test extracts from the same batches were used throughout the study.

The allergen extracts comprised inhalant allergens, food allergens and pityrosporum ovale, while the fresh foods consisted of wheat flour and soya flour diluted in NaCl (1:10) and fresh apple.

Short-acting antihistamines were discontinued during at least the 4 days prior to skin prick testing, and long-acting antihistamines, e.g. astemizole, during at least 4 weeks. Local corticosteroids were discontinued during at least one week prior to the skin prick tests, which were performed according to EAACI guidelines (36).

Ethics

The ethics committee for Vejle and Funen County approved the study (case number 95/22). Informed consent was obtained from the schoolchildren and from their parents in phase one. Only children who had given informed consent were invited to phase two.

Statistics

All data were entered twice in the database. When differences were found, a comparison with raw input forms was made and corrections done accordingly. All statistical analyses were performed with Stata 5.0 for Windows 95 (Stata Corporation, TX, USA) except in the case of graphical models. The prevalence proportion was defined by the number of positive answers divided by the total number of schoolchildren questioned. The 95% confidence intervals are given in parentheses (95% CI).

Comparisons were made by chi-square-based table analysis. Odds ratio (OR) is given as Mantel Haenzel odds ratio stratified by sex, with associated confidence intervals in parentheses (95% CI). Differences by sex are noted when the stratum-specific estimates indicate significant "effect modification". Statistical significance was defined as $p<0.05$ after application of the Bonferroni procedure.

Because of the close association between the investigated diseases, a multivariate analysis was performed which at the same time could account for the interdependence and possible association with external factors (control for all associations at the same time). The analysis was performed using specialized software, Digram, with the same principles as described in an example from the Framingham Heart Study (37). The results are expressed in the form of a graph on which non-random associations between variables are represented by a line. The direction of association (arrow) is chosen by the researcher based on contents; it does not come out as a result of the analysis. The final graph is settled by a procedure in which the user works towards the simplest overall representation of the associations controlled for (conditional on) all other variables. Because the variables are binary or ordinal, the strength and degree of statistical significance of an association can be measured by Kruskal and Goodman's gamma coefficient in the form of a con- ditional or partial gamma (38). By "partial" we mean that the coefficient is a weighted average across the variable(s) that is (are) used in the particular conditioning. Because of the many statistical tests in these analyses a significance level of 0.01 was used to compensate for false associations (Type I error). Gamma coefficients less than 0.15 indicate weak associations, those between 0.15 and 0.30 moderate associations, and more than 0.30 strong associations.

RESULTS

Response pattern in phase two

The proportion of participation among the schoolchildren in phase one has been given previously (33). In phase two, 702 schoolchildren (429 girls, 273 boys) were invited (4 case groups and 1 control group); 80.2% (girls 82.1%, boys 77.3%) participated in the interview and clinical examination and 79.5% (girls 80.9%, boys 77.3%) were skin prick tested. A flow table for the four case groups and the control group from phase one to

Table I. *Flow table for the four case groups and the control group from phase one to phase two*[a]

	No. identified in phase one	No. invited to phase two (% of phase one)[b]	No. participating in phase two (% of invited)
Hand eczema	105	101 (96.2)	84 (83.2)
Possible atopic dermatitis[c]	106	103 (97.2)	86 (83.5)
Inhalant allergy	237	219 (92.4)	191 (87.2)
Positive patch test	174	174 (100)	144 (82.8)
Total cases (one/more groups)	460	436 (94.8)	363 (83.3)
Primary controls	978	217 (22.2)	168 (77.4)
Extra controls[d]		49	32 (65.3)
Total controls	978	266 (27.2)	200 (75.2)
Total cases and controls	1438	702 (48.8)	563 (80.2)

[a]Possible atopic dermatitis and hand eczema are given as one-year period prevalence figures, and inhalant allergy as lifetime prevalence. For definitions, see Methods section, and for hand eczema and positive patch test, see (33). Originally, 435 cases and 218 controls were invited to phase two. However, because the phase one interview took place at the time of phase two for six schoolchildren, two were reclassified: one from control to case (inhalant allergy), and one from one case group (hand eczema) to two case groups (hand eczema and inhalant allergy).
[b]Only schoolchildren for whom informed consent had been given were invited to phase two.
[c]The results of IgE measurements and skin prick tests first became available during phase two. In phase one we therefore had a group of schoolchildren with dermatitis during the previous year who would fulfil the Hanifin & Rajka criteria if they had a positive skin prick test and/or an elevated total IgE level (>150 kU/L). This group of schoolchildren were invited to phase two along with children who already fulfilled the Hanifin & Rajka criteria for atopic dermatitis during the previous year. The groups were pooled and designated possible atopic dermatitis. After total IgE measurement and skin prick tests, 76 were classified as atopic dermatitis, 3 as another case group only and 7 as controls, giving a final control group size of 207 in phase two.
[d]For each control not participating in phase two, another sex-matched control from the same school group was invited.

phase two is given in Table I. Schoolchildren in one of the four case groups were more likely to participate, whereas controls were less motivated ($p<0.009$). In this article, only data from two of the case groups are presented (AD and inhalant allergy).

Disease prevalence and associations

The lifetime prevalence of AD was 21.3% (girls 25.7%, boys 17.0%; $p<0.001$ for sex difference), the one-year period prevalence 6.7% and the point prevalence 3.6%. The lifetime prevalence of allergic asthma was 6.9%, and allergic rhinitis was found in 15.7% (intermittent allergic rhinitis 12.5%, persistent allergic rhinitis 9.0%). A total of 17.7% were found either to have or to have had inhalant allergy (allergic asthma and/or rhinitis). The lifetime prevalence of atopic diseases (inhalant allergy and/or AD) was estimated to be 31.3%, with a significant sex difference (girls 34.6% vs. boys 27.7%; $p<0.007$).

The association between present or past AD and present or past inhalant allergy adjusted for sex was significant (OR 4.59, 95% CI 3.35–6.29; $p<0.001$). Inhalant allergy was reported by 38.1% of those with AD, and 47.3% of those with inhalant allergy reported AD.

Type I sensitization evaluated by measurement of specific IgE: prevalence and associations (phase one)

Among the schoolchildren, 29.6% (95% CI 26.6–32.7%) had at least one positive specific IgE measurement (inhalant allergens, food allergens and/or pityrosporum ovale). Significantly more boys, 37.8% (95% CI 33.3–42.8%), than girls, 22.7% (95% CI 19.0–26.7%), had positive measurements. A positive CAP FEIA measurement for inhalant allergens was found in 28.4% (247/869), with a significant sex difference (girls 21.4% vs. boys 36.8%; $p<0.001$), and a positive CAP FEIA measurement for food allergens was found in 8.5% (73/863), with no significant sex difference (girls 7.3% vs. boys 9.8%). Sensitization to the different allergens is given in Table II. Reactions to two or more different allergens were seen in 60.7% of the sensitized schoolchildren (AD 70.8%, inhalant allergy 82.5% and controls (without AD and inhalant allergy) 39.1%).

The association between Type I sensitization (at least one positive specific IgE measurement to inhalant allergens, food allergens and/or pityrosporum ovale) and a history of AD and inhalant allergy is indicated in Table III. Present or past AD was found to be significantly associated with Type I sensitization, suggesting an increased prevalence of Type I sensitization among those with AD. However, when excluding schoolchildren with a concomitant history of inhalant allergy the association was no longer significant. The same results were obtained when analysing IgE measurements for inhalant allergens and food allergens separately. As expected, present or past inhalant allergy by interview was significantly associated with Type I sensitization.

Among schoolchildren with no history of atopic diseases (AD or inhalant allergy), at least one positive specific IgE measurement was found in 19.4% (girls 14.5%, boys 24.7%; $p<0.003$ for sex difference). Using a multivariate graphical analysis we found that inhalant

Table II. *The distribution of positive specific IgE measurements to inhalant allergens, food allergens and pityrosporum ovale (CAP FEIA®)*

	Positive specific IgE measurement (%)		
	Girls (n = 467–469)[a]	Boys (n = 395–397)[a]	Total population
Inhalant allergens			
Birch pollen	6.8	8.8	7.7
Grass (timothy) pollen	13.6	23.2**	18.0
Mugwort pollen	6.4	10.3*	8.2
Cat dander	6.2	6.0	6.1
Dog dander	6.4	7.6	6.9
Horse dander	2.6	2.5	2.5
House dust mite[b]	11.9	25.3**	18.0
Mould[c]	2.3	2.5	2.4
Food allergens			
Cow's milk	2.1	3.3	2.7
Hen's egg	1.1	0.3	0.7
Codfish	0.2	0.0	0.1
Wheat	3.4	4.1	3.7
Soya bean	3.4	3.5	3.5
Peanut	5.1	6.6	5.8
Hazelnut	3.2	3.5	3.4
Brazil nut	1.7	3.0	2.3
Almond	2.6	3.5	3.0
Coconut	2.4	3.0	2.7
Other			
Pityrosporum ovale	1.5	1.5	1.5[d]

[a]Lacking IgE measurements for a few persons due to sparse serum.
[b]Dermatophagoides pteronyssinus.
[c]Cladosporium herbarum.
[d]Eight of 13 had present or past atopic dermatitis.
**$p < 0.001$ for sex difference.
*$p < 0.04$ for sex difference.

Table III. *The associations between Type I sensitization (positive specific IgE measurement) and atopic dermatitis and inhalant allergy*[a]

		Type I sensitisation	
	OR[b]	95% CI	*p* value
Atopic dermatitis	2.32	1.65–3.25	$p < 0.001$
AD excl. inhalant allergy	1.25	0.77–2.02	0.372
Inhalant allergy	9.86	6.39–15.22	$p < 0.001$

[a]Atopic dermatitis (questionnaire) and inhalant allergy (interview) were evaluated as lifetime prevalence figures. For criteria, see Methods. Type I sensitization was evaluated by specific IgE measurements (CAP FEIA®) of inhalant allergens, food allergens and pityrosporum ovale.
[b]Odds ratio (OR) is given as Mantel Haenzel odds ratio stratified by sex.
Cl: confidence interval.

allergy was strongly associated with Type I sensitization (χ^2 162.6, d.f. 2, gamma 0.81; $p < 0.0001$), whereas AD was not (data not shown).

Total IgE levels

An elevated total IgE level (>150 kU/l) was found in 18.9% (164/868); in 28.7% of those with AD; in 48.2% of those with inhalant allergy; and in 10.5% of those without AD and inhalant allergy.

Type I sensitization in the cases and controls evaluated by skin prick test reactivity (phase two)

The distribution of positive skin prick tests to inhalant allergens, food allergens and pityrosporum ovale in cases and controls is given in Table IV. Among schoolchildren with AD (during the previous year in phase one), skin prick test reactivity was found in 63.5% (Table V). Compared to the control group, AD during the previous year was significantly associated with skin prick test reactivity, and when those with a concomitant history of inhalant allergy were excluded the association was still significant. By excluding pityrosporum ovale from the analysis and including only skin prick tests with inhalant and food allergens, a less pronounced and non-significant association was found (OR 2.27, 95% CI 0.97–5.33; $p < 0.06$). Neither inhalant allergens nor food allergens alone demonstrated a significant association with AD. As expected, a significant association was found between present or past inhalant allergy by interview and skin prick test reactivity (Table V). Among the controls, 21.0% (girls

Table IV. *The distribution of positive skin prick tests in schoolchildren with atopic dermatitis, inhalant allergy and in controls in phase two*

	Positive skin prick test (%)		
	AD ($n=74$)	IA ($n=190$)	Controls ($n=205$)
Inhalant allergens			
Birch pollen	36.5	36.3	4.9
Grass (timothy) pollen	37.8	53.2	9.8
Mugwort pollen	6.8	16.3	3.9
Horse dander	14.9	14.2	0.5
Dog dander	32.4	33.7	2.4
Cat dander	27.0	30.5	2.9
D. Pteronyssinus	21.6	37.9	9.8
D. Farinae	23.0	35.3	6.8
Alternaria alternaria	9.5	10.5	0
Cladosporium Herbarum	9.5	6.3	0
Food allergens			
Cow's milk	0	1.1	0.5
Hen's eggs	1.4	1.1	0
Codfish	5.4	2.6	0.5
Shrimp	8.1	11.6	2.0
Wheat flour	5.4	3.7	0
Soya bean	2.7	3.2	0
Peanut	16.2	8.4	0.5
Hazelnut	14.9	11.1	0
Fresh apple	14.9	10.0	0
Fresh wheat flour	9.5	9.5	0.5
Fresh Soya flour	1.4	1.1	0
Pityrosporum ovale	12.2	6.8	0.5

AD: atopic dermatitis; IA: inhalant allergy.

16.4%, boys 28.6%; $p<0.04$) had one or more positive skin prick tests.

During the year from phase one to phase two, some schoolchildren additionally fulfilled the criteria for AD and inhalant allergy. However, adjustment of the case and control groups according to these changes did not affect the result.

All histamine reactions were more than 3 mm in diameter. Only 0.2% (2/558) of the schoolchildren had a reaction to the negative control on 3 mm or more.

Relationship between atopic dermatitis and sensitization to pityrosporum ovale and house dust mite

In phase one, 13 out of 863 reacted to pityrosporum ovale using CAP FEIA measurements; 8 of the 13 had present or past AD. A significant association between AD and sensitization to pityrosporum ovale was found using the CAP FEIA results (OR 4.77, 95% CI 1.62 – 14.06; $p<0.002$) and also using the skin prick test results in phase two (OR 9.60, 95% CI 1.08 – 85.27; $p<0.013$).

AD was associated with sensitization to house dust mite using the CAP FEIA measurement in phase one (OR 1.64, 95% CI 1.11 – 2.44; $p<0.012$) and also using the skin prick test in phase two (OR 3.25, 95% CI 1.60 – 6.61; $p<0.001$). However, when schoolchildren with concomitant inhalant allergy were excluded from the analysis, none of the associations were significant (OR 0.95, 95% CI 0.49 – 1.85; $p=0.888$, and OR 0.95, 95% CI 0.26 – 3.49; $p=0.943$ respectively).

DISCUSSION

High prevalence figures for the atopic diseases AD, allergic asthma and allergic rhinitis were found, which is in agreement with other recent studies (1 – 4, 9, 10, 12, 39). Children with AD usually have a family history of atopic diseases and 60 – 70% will develop allergic rhinitis or asthma (14 – 19). As expected, we found an increased prevalence of inhalant allergy in schoolchildren with AD.

In the cross-sectional part of the study, it was found that CAP FEIA measurements were positive in 29.6% of the schoolchildren. They had one or more positive reactions to common inhalant allergens, food allergens and/or pityrosporum ovale. Significantly more boys than girls had positive reactions (37.8% vs. 22.7%). In a study from Norway evaluating the prevalence of Type I sensitization to selected inhalant allergens and food allergens in 7 – 12-year-old schoolchildren, it was found that 30.2% had reactions in skin prick tests (20). This

Table V. *Results of skin prick testing in schoolchildren with atopic dermatitis and inhalant allergy versus the control group in phase two*[a]

	One or more positive skin prick tests (%)[b]			Mantel Haenzel test for each case group vs. the control group (stratified for sex)		
	Girls	Boys	Total	OR	95% CI	p value
Atopic dermatitis	56.8% (25/44)	73.3% (22/30)	63.5% (47/74)	6.78	3.54 – 12.98	<0.001
AD excl. inhalant allergy	30.0% (6/20)	54.5% (6/11)	38.7% (12/31)	2.50	1.09 – 5.74	<0.03
Inhalant allergy	63.6% (68/107)	86.8% (72/83)***	73.7% (140/190)	11.15	6.31 – 19.70	<0.001
Controls	16.4% (21/128)	28.6% (22/77)*	21.0%[c] (43/205)			

[a]Atopic dermatitis is given as one-year period prevalence figure in phase one, inhalant allergy as lifetime prevalence in phase one. For criteria, see Methods. Skin prick testing included inhalant allergens, food allergens and pityrosporum ovale.
[b]Two controls and 3 cases that participated in phase two did not participate in skin prick testing.
[c]Excluding schoolchildren with past atopic dermatitis (> one year ago from phase one) 19.5% (34/174) had one or more positive skin prick tests.
***$p<0.001$ for sex difference; **$p<0.01$ for sex difference; *$p<0.04$ for sex difference.

did not differ from our study despite the different test method and age difference. We could not give an estimate for Type I sensitization in the population using the skin prick test, because it was performed only in selected groups in phase two.

At least one positive CAP FEIA measurement for inhalant allergens was found in 28.4%, with a significant sex difference (girls 21.4% vs. boys 36.8%). Using Phadebas RAST, Hattevig et al. (2) found 18.1% of 10- and 14-year-old Swedish schoolchildren with positive reactions to inhalant allergens. Kjellmann (21) used the same method in 12-year-old Swedish schoolchildren and reported positive reactions in 26.1%. These frequencies are lower than in the present study, possibly because fewer inhalant allergens were included; another method for IgE measurement was used and the studies were carried out almost 20 years ago. In a random sample of Swiss adults (40), a positive CAP FEIA measurement for inhalant allergens was found in 28.9% (female 25.0% vs. male 32.9%; $p<0.001$ for sex difference), in agreement with our results.

The prevalence of Type I sensitization to inhalant allergens determined by skin prick tests has been investigated in other population-based studies (22–24, 26, 27, 29). The figures obtained in children and adolescents were higher (31–50%) than the specific IgE results in this study, with one exception (20.6%) (25). In an unselected Danish population of 15–69-year-old subjects, 28.4% reacted to inhalant allergens by skin prick testing (41). Of those with positive skin prick tests, 59.4% had two or more reactions. These Danish figures are comparable to those presented in our study using the specific IgE measurement.

At least one positive CAP FEIA for food allergens was found in 8.5% of the population. However, the clinical relevance of a positive specific IgE measurement to a food allergen is uncertain, because the clinical relevance of a positive test result has not been assessed by history and double-blind, placebo-controlled food challenges.

The variation in Type I sensitization in different studies may be explained by a number of factors, including different study designs, differences in populations and exposure, different age groups, different test methods, allergens included and differences in the criteria for grading skin test reactions, and the cutoff limit for IgE classes. The reported frequency of Type I sensitization both in this study and in other studies may represent a minimum, because testing was only performed with the most common allergens, and additional testing tailored to the history of the individual subject was not performed. In our study, only 58% participated in the blood sample (IgE measurements) in phase one (33). This could have biased the result, if the proportion of participation differed between those with and those without atopic diseases. However, only boys with AD were more prone to participate in the blood sample, while no selection bias was found for those with asthma and allergic rhinitis. Any eventual selection bias is therefore expected to be of minor importance. In the cross-sectional part of the study it was found that both a history of inhalant allergy and AD were significantly associated with Type I sensitization (at least one positive specific IgE measurement). However, present or past AD no longer had any bearing on Type I sensitization when cases with a concomitant history of inhalant allergy were excluded. These results were based on a simple model using the Mantel Haenzel analysis stratified for sex. A more detailed multivariate graphical analysis was also performed. The multivariate graphical model verified the association between inhalant allergy and Type I sensitization and, as in the simple model, no association was found between AD and Type I sensitization when controlling for all associations at the same time.

In the case-control study in phase two, a significant association was found between recent AD and one or more positive skin prick tests, even when excluding those with a history of inhalant allergy. However, this association was related to Type I sensitization to pityrosporum ovale (42), because the association disappeared when pityrosporum ovale was excluded from the analysis. A few other studies have evaluated the association between AD and Type I sensitization with varying results (20, 32).

Inhalant allergy was significantly associated with Type I sensitization both in phase one and in phase two, which is in agreement with several earlier studies reporting that 53–95% of those with asthma and 71–83% of those with allergic rhinitis had a positive skin prick test or RAST to inhalant allergens (2, 20, 26, 30, 31).

In phase one, 19.4% of schoolchildren with no history of atopic diseases (AD or inhalant allergy) had at least one positive specific IgE measurement. In phase two, 19.5% of the controls with no history of atopic diseases had at least one positive skin prick test. Results from other studies show positive tests in 7–33% of persons without atopic diseases in accordance with results from our study (2, 20, 21, 26, 27, 31). A positive test without clinical relevance can be a precursor to symptoms (2, 43, 44) or can persist indefinitely without clinical relevance. Follow-up studies are needed to clarify the role and significance of immediate skin test reactivity or specific IgE antibodies in asymptomatic individuals for the appearance of allergic symptoms and the development of manifest disease in different populations.

In the case control study in phase two, a common control group was considered appropriate because of the interrelationship between the investigated diseases. It was not an individually matched control group, but a frequency matched control group by sex. In phase two,

a lower proportion of participation among the controls was expected and verified. Therefore, for each control not participating, another control was enrolled and a suitable control group size was obtained. Altogether, the proportion of participation in phase two was high (80%), and the case-control design rendered the differences between cases and controls less important.

In conclusion, high prevalence figures were found for AD and inhalant allergy and the diseases were closely associated. The prevalence of Type I sensitization was high and the association with AD was related to concomitant inhalant allergy, i.e. the group of AD patients with no inhalant allergy was not associated with Type I sensitization to inhalant or food allergens. A clear association to AD was indicated only for the allergen pityrosporum ovale.

ACKNOWLEDGEMENTS

We thank the schoolchildren, their parents, the schools involved and the Odense education authority for their cooperation, and nurse Annemarie Yde-Andersen for skilful technical help. The study was supported by the Faculty of Health Sciences, University of Southern Denmark – Odense University, the Danish Asthma and Allergy Association, Gerda and Aage Haensch's Foundation and Ingemann O. Buck's Foundation. Pharmacia & Upjohn financed the CAP FEIA® measurements. ALK-ABELLÓ donated the test materials to the skin prick tests.

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