

Natural history of bronchial asthma in childhood

A prospective study from birth up to 12–14 years of age

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In a cohort of 1654 consecutively born children followed from birth, the cumulated incidence of asthma up to 11 years was 5.3% and the prevalence 3% between 10 and 11 years of age. The asthma début was prior to 1.5 years in 1/3 and before 3 years in 1/2 of the children. Among 59 children examined at 11.5–14.5 years of age, 16 (27%) had no prevalent asthma. On the other hand, inadequate medication was found in 13, undiagnosed chest deformity in four, and wheezing in seven children. All 54 tested children including those with no prevalent asthma had a PC₂₀ histamine <8 mg/ml. Tread mill test gave a significant reaction in 15 children.

Animal danders and pollens were the most common allergens giving reactions at skin prick test. Compared to one earlier Swedish study an increase in mite sensitivity was found. Cord-blood IgE concentration and a positive immediate family history of atopic disease had no predictive value for the severity of asthma at this follow-up. A new total asthma score including number of days with functional impact of asthma during the last year and present medication was used for group comparisons. Children with a high score at 11.5–14.5 years had more exercise-induced asthma, more concomitant allergic diseases, earlier asthma start, more chest deformity, hyperreactivity both on tread mill and histamine challenge tests, elevated IgE, positive Phadiatop and more reactions at skin prick test, especially to animals and mites. Bronchial asthma was found more often in children born during August through October, possibly due to unsuitable indoor climate and more virus infections during their first 6 months of life. The severity of the asthma was, however, not influenced by the month of birth. No significant differences were found between boys and girls regarding the age at début, asthma severity at follow-up, or bronchial histamine threshold levels.

Key words: asthma; children; cord blood IgE; histamine challenge; asthma score

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Bronchial asthma constitutes one of the most common chronic and disabling diseases in childhood (32). Several reports, including some from Scandinavia, indicate that the prevalence of asthma in childhood is increasing (6, 7, 8, 21, 40). Attempts have been made to predict the development of childhood asthma in healthy subjects. We have previously reported on the follow-up from birth to 11 years of age of a cohort of 1701 children (15). The development of asthma and other atopic diseases in this cohort was related to family history of allergy/atopic disease, season of birth and neonatal serum IgE concentration in cord blood (CB-IgE). A family history of allergy doubled the risk for asthma but an elevated CB-IgE (≥ 0.9 kU/l) increased the relative risk for asthma by a factor of five. A subsequent

validation of the questionnaire used at 11 years of age in a random sample of 133 children blindly investigated (i.e. with no knowledge of CB-IgE nor family history) showed that questionnaire data were relevant for a diagnosis of respiratory allergy including bronchial asthma.

In the present study we wanted to find the natural history of asthma from birth up to 12–14 years of age in the same cohort of non-selected children. A new total asthma score was established to describe the total impact of the disease – severity and frequency of symptoms as well as medication. This score was compared both with potential predictors of subsequent state of health and various laboratory tests, i.e. potential markers of the severity of the disease. Thus, the influence of, e.g. a family history

of asthma and other atopic diseases, or of an elevated CB-IgE on the prevalent total asthma score, was evaluated. Similarly, findings at clinical check-up, including evaluation of lung function, bronchial reactivity, total and specific IgE and skin prick tests were compared with the total asthma score.

Material and methods

A total of 1654 children born at our hospital between December 1st, 1974 and December 31st, 1975 have been investigated at 1.5, 6–7 and 10–11 years of age by means of evaluated questionnaires (Q1, Q2, Q3) regarding the development of atopic diseases (12, 13, 15). All children reporting symptoms of asthma at any time received a fourth, detailed questionnaire (Q4) regarding their asthma disease and were asked if they also wanted to take part in a clinical evaluation of their current state of health (Fig. 1).

Asthma was defined according to Godfrey (17). A diagnosis of prevalent asthma was defined as symptoms present during the last 12 months before the clinical investigation.

At clinical follow-up, performed between ages 11.5 and 14.5 (mean 12.5) years, special care was taken to establish the degree of asthma up to present age and during the last year. The age at which the disease started as well as use of asthma medications, the frequency of acute visits and hospitalizations for asthma were noted. Functional impact of asthma was graded according to a modification of the score described by Bremberg & Kjellman (5). Asthma was graded according to the patient's or parents' own estimation of the number of days or nights during the last year where there had been impairment of physical function, restriction of daily activities or disturbed sleep due to asthma (0 days/nights = grade 0; 1–9 days/nights = grade I; 10–100 days/nights = grade II; over 100 days/nights = grade III). Present medication was scored giving inhaled β_2 -agonists, used when needed, 0.5 points (p), β_2 -agonists or theophyllines used regularly 1 p, disodium-cromoglycate (DSCG) used regularly 2 p, and inhaled steroids used regularly 3 p. One third of the total medication score was added to the asthma grade giving a new total asthma score. For comparison the children were divided into three groups ac-

cording to this new score (0–0.5 p = group I, 1.0–3.0 p = group II, over 3.0 p = group III). When available, medical records were scrutinized. Thus a global assessment of the current asthma situation was accomplished. Inadequate medication was noted. At physical examination weight, height, wheeze, chest deformity and other atopic manifestations were noted. Pubertal staging was performed according to Tanner (37).

Skin prick test (SPT) was done using Phazet® (Pharmacia Diagnostics, Uppsala, Sweden) to birch, timothy, mugwort, *Cladosporium herbarium*, *Alternaria*, dog, cat, horse, *D. pteronyssinus* and *D. farinae*. In addition, SPT was performed with pasteurized cow's milk (protein content 3.4 g%), histamine hydrochloride (10 mg/ml) and a negative control. All tests were performed in duplicate. The mean wheal diameter was calculated for each allergen. If the mean diameter was ≥ 3 mm the test was regarded positive, as no patient showed dermographism. Inhaled β_2 -agonists were not allowed 6 h, theophyllines and DSCG 12 h and antihistamines 48 h before testing. Serum IgE concentrations were determined by Phadebas IgE PRIST® and presence of IgE antibodies to common inhalants was assessed by Phadiatop® according to the manufacturer's instructions (Pharmacia Diagnostics, Uppsala, Sweden).

Exercise test on a tread mill (Rodby Elektronik, Södertälje, Sweden) was performed at room temperature between 21 and 24°C and a relative humidity of 30–50%. The test was done according to recommendations of Silverman & Andersson (33). It was stopped when a maximal pulse rate ≥ 170 beats/min was reached. The maximal drop in FEV₁ (forced expiratory volume in 1 s) and MEF₅₀ (maximal expiratory flow at mid half of the vital capacity) was recorded on a dry spirometer, Vicatest 5® (Mijnhardt B.V., Bunnik, Holland). A drop in FEV₁ $\geq 15\%$ and/or MEF₅₀ $\geq 30\%$ from baseline was considered as a sign of exercise-induced bronchial hyperreactivity. PEF (peak expiratory flow on a Mini Wright Peak Flow meter) was measured by the patient every hour up to 9 h and in the morning after tread mill testing. The best of three recordings was used for calculations. A drop $> 20\%$ from baseline level was taken as a sign of a late response to exercise.

Age	0	1.5	6–7	10–11	11.5–14.5
	-----	Q1	-----	Q3	-----
n		1701	1651	1654	89
Prevalent asthma (%)		1.7	2.4	3.0	
Cumulative asthma (%)		1.7	3.8	5.3	

Fig. 1. Flowchart showing age (years) of children when different questionnaires were filled in and numbers of children.

After another week, bronchial histamine provocation test was done using a jet nebuliser (Aiolos®, Medicinsk Teknik AB, Karlstad, Sweden). After inhalation of saline for 2 min the FEV₁ was recorded and used as baseline level. Histamine chloride was inhaled during tidal breathing over 2 min. The first concentration was 0.03 mg/ml, whereafter the concentration was increased at 5-min intervals by four-fold increments (0.03–0.125–0.5–2–8 mg/ml). The inhalation was stopped as soon as the FEV₁ reached 80% of the baseline FEV₁. The PC_{20Hi} (i.e. the histamine concentration causing a 20% fall in FEV₁) was calculated by data interpolation according to Cockcroft (11).

The whole investigation was performed out of the pollen season.

Statistical methods

Significance was tested using Fisher's exact test, Mann-Whitney U-test, t-test and, finally, the chi-square test, the method being determined by the nature of the data for comparison. Single-tailed tests were used throughout, since expected differences were always predictable in the tests performed.

Ethics

The investigation was approved by the Human Research Ethics Committee, Faculty of Health Sciences, Linköping University.

Results

Our previous investigation of the cohort of initially 1701 newborn children followed prospectively to 11 years of age ($n = 1654$) revealed asthma symptoms at any time as reported by the parents in 89 (5.3%) of the children (15). Sixty percent of the asthmatics were boys. Fifty of the 1654 children (3%) had prevalent asthma between 10 and 11 years of age (15) compared to 1.7% at 1.5 years (12) and 2.4% at 6–7 years of age (13) (Fig. 1).

The families of all the 89 asthmatic children filled in the questionnaire (Q4) when the children had reached 12–14 years of age. Fifty-nine of the children (30 boys and 29 girls) were also available for clinical investigation. The 30 who could not be investigated (23 boys and 7 girls) were classified according to questionnaire data and available medical records (Table 1). In the non-examined group mild asthma was overrepresented ($p < 0.001$). Unfortunately, 12 children with a cumulative asthma grade I who were now reported to be free from asthma symptoms did not want to participate. Another nine grade I asthmatics had moved far away from the catchment area of our hospital and two could not be investigated due

Table 1. Asthma grades in 89 children up to 14 years of age

	0	I		II		III		
	P	C	P	C	P	C	P	Total
Investigated by Questionnaires + medical records	19	23	6	6	4	1	1	30
Questionnaires + clinical examin. + medical records	18	17	15	26	19	16	7	59
Total	37	40	21	32	23	17	8	89

Cumulative (C) and prevalent (P) asthma.

to mental retardation. Six children with asthma grade II lived far away and a boy with asthma grade III had severe mental retardation. Nineteen of 30 children who were not examined and 18 of 59 examined children, i.e. a total of 37 of the 89 children (42%) had no prevalent asthma symptoms at 12–14 years of age. Bronchial asthma developed more often in those born during the period August through October than during the rest of the year (Table 2).

The mean age when asthma started was 3.6 years (range 0.5–10 years) among 80 children where data were available. Twenty-five of them (31%) had their asthma début before 1.5 years, 42 (53%) before 3 years, 64 (80%) before 6 years, and 76 (95%) before 9 years of age. There was no significant difference in the mean age at début between boys and girls (3.4 and 3.8 years, respectively).

Thirty-eight of all 89 children (43%) had an elevated (i.e. ≥ 0.9 kU/l) CB-IgE concentration and 51 of them (57%) had an immediate family history of allergic/atopic disease including asthma. An elevated CB-IgE was associated with earlier asthma début as

Table 2. Development of bronchial asthma and mean total asthma score in relation to the month of birth

Month	No. of children born	Asthma (n)	Asthma %	Scored (n)	Mean score
1	144	8	5.5	5	0.6
2	140	8	5.7	4	1.8
3	155	13	8.4	11	1.9
4	178	7	3.9	4	2.7
5	149	6	4.0	5	2.3
6	143	4	2.8	2	1.2
7	149	5	3.4	4	2.3
8	104	10	9.6*	7	1.3
9	116	8	6.9*	5	2.9
10	112	12	10.7*	8	1.8
11	89	3	3.4	1	0
12	173	5	2.9	3	2.4
Total	1652	89		59	

* August–October compared to the rest of the year $p < 0.002$.

14 of 25 children (56%) with an asthma start before 1.5 years had an elevated CB-IgE compared with 18 of 51 children (35%) with a later onset of asthma ($p < 0.05$). The proportion of children with high CB-IgE was similar in children born during the periods March–May (8 of 19) and August–October (10 of 20).

The 59 examined children were divided into three groups according to their prevalent total asthma score (Table 3). Group I consisted of 18 children who had a median score of 0 (range 0–0.5 p), Group II ($n = 30$) had a median score of 2.3 (range 1–3 p), and the median score in Group III children ($n = 11$) was 4.0 (range 3.3–5.3 p). The mean score in Groups II and III ($n = 41$) was 2.6 p. No significant difference in the mean asthma score was seen between boys and girls. No significant difference in mean age at asthma début was found between children in Groups I and III but seven of 11 Group III children compared with four of 18 Group I children started to have asthma already before 1.5 years of age ($p < 0.05$). No significant difference was found regarding the presence of a family history of asthma or other atopic disease between the children with a low or high asthma score (Groups I and III) (Table 3).

Any other atopic disease had been present at any time in 51 (86%) of the children (Table 4). Forty-one of them (68%) had at least one other prevalent atopic disease at 12–14 years of age. Allergic rhinoconjunctivitis (ARC) was present in 33 children (56%) and atopic dermatitis in 21 children (36%). AD preceded asthma in 28 children (47%). Twelve of them had AD before 1.5 years. Prevalent ARC was significantly more common among children in Group III compared to Group I ($p < 0.05$). A significantly higher number of prevalent concomitant atopic diseases were found in children with higher, as compared with lower, total asthma score (Table 5).

At examination, seven of 59 (12%) presented wheezing without being aware of ongoing asthma, i.e. they had evidence of subclinical bronchial obstruction. Chest deformity was found in six children (10%). In four of these, the deformity had not pre-

Table 4. Concomitant allergic disease (cumulative or prevalent) in 59 extensively investigated children with a history of bronchial asthma at any time before 12–14 years of age

	Cumulative		Prevalent	
	<i>n</i>	%	<i>n</i>	%
AD+ARC	26	44	15	25
AD	6	10	6	10
ARC	14	24	19	32
Other allergic disease	5	8	1	2
Any allergic disease	51	86	41	69

AD: atopic dermatitis; ARC: allergic rhinoconjunctivitis.

viously been registered in the medical records. They already had asthma at an early age (3 at 0.5 yr, 2 at 1.5 yr and 1 at 3 yr). Two of them were, however, asthma free during the last year.

The use of medication for present asthma was not adequate in 13 (22%) of the 59 children, i.e. they did not use bronchodilators prior to exercise and/or did not use inhaled steroids. One fourth of the 59 children had been hospitalized due to acute asthma more than once (range 0–10 times) and one third of the group had been to the emergency ward more than once (range 0–20 times).

Prevalent exercise-induced asthma (EIA), as reported in the questionnaire, was present in 40 (68%) children (17 boys and 23 girls, NS). Thirty-six of these had some regular medication. A tread mill provocation test provoked a significant drop in FEV₁ (15–66%) in 12 children and in MEF₅₀ (31–85%) in 13 of the 40 children. Thus in total, 15 children had a significant fall in lung function after tread mill testing. Of these only one girl did not experience any asthma symptoms after exercise. A later drop in PEF $\geq 20\%$ was only found in four of the 15 children with an early fall in lung function. Three of them had the most profound initial drop in FEV₁ and MEF₅₀ of all children.

Eighteen children were negative in SPT. In 41 (70%) the test was positive for up to 10 (mean 5; boys 5.5 and girls 4.9, NS) different allergens. The allergens giving positive reactions are shown in

Table 3. 59 asthmatic children divided according to total asthma score. Predictive parameters. (Statistical comparisons only between groups III and I)

	I	II	III	p
<i>n</i>	18	30	11	
Prevalent score range (median)	0–0.5 (0)	1.0–3.0 (2.3)	3.3–5.3 (4.0)	
Mean age (yr) at asthma start (range)	3.0 (0.5–10)	4.2 (0.5–10)	2.8 (0.5–9)	NS
Asthma before 1.5 yr (<i>n</i>)	4	9	7	<0.05
CB-IgE ≥ 0.9 kU/l	8	12	7	NS
Heredity for any allerg. dis.	9	18	5	NS
Heredity for asthma	11	19	6	NS

Table 5. Number of prevalent concomitant allergic diseases in 59 children with bronchial asthma and different total asthma scores. *p*-values are given only for significant differences

Group/Score	No. of concomitant diseases			
	0	1	≥ 2	
I/0–0.5	7	8	3	<0.05
II/1.0–3.0	10	14	6	
III/3.3–5.3	2	3	6	<0.05

Table 6. 59 asthmatic children divided according to total asthma score. Prevalent parameters

	I	II	III	p
n	18	30	11	
Prevalent EIA	6	24	10	<0.01
Acute visits/hospital.	21/4	77/16	68/22	<0.01
ARC	8	17	9	<0.05
AD	6	9	6	NS
Any other allerg. disease	11	20	9	NS
Chest deformity	0	2	4	<0.05
Tread mill test				
FEV ₁ fall $\geq$ 15%	1	3	5	<0.01
MEF ₅₀ fall $\geq$ 30%	1	3	5	<0.01
Late PEF fall $>$ 20%	0	0	4	<0.01
PC _{20HI} $<$ 1.0 mg/ml	3	11	8	<0.01
Phadiatop positive	4	18	7	<0.05
IgE $>$ 100 kU/l and $\geq$ 5 SPT positive	4/4	13/14	6/7	<0.05

(Statistical comparisons only between Groups III and I).

Table 7. A positive Phadiatop was found in 29 of 56 (52%) tested children, all of whom were positive in SPT (2–10 allergens). Ten children had a negative Phadiatop but were positive in SPT (1–4 allergens). There was no significant difference in the proportion of SPT-positive children in the groups with severe and with no or very mild prevalent asthma (32 of 41 compared to 9 of 18). When combining an elevated IgE concentration with $\geq$ 5 positive SPT, a significant difference was found between the groups (Table 6).

Table 7. Frequency of positive skin prick tests in 59 asthmatic children

Allergens	n	%
Cat	31	53
Dog	29	49
Birch	28	47
Timothy	28	47
Horse	27	46
Cladosporium	18	31
<i>D. pteronyssinus</i>	16	27
Mugwort	15	25
<i>D. farinae</i>	12	20
Alternaria	8	14
Cow's milk	4	7
Any animal	34	58
Dog and cat	28	47
Dog, cat and horse	25	42
Only animals	5	8

An elevated IgE concentration, i.e. $>$ 100 kU/l (range 110–1240 kU/l) was found in 23 of 57 (40%) tested children. SPT was significantly more often positive in children with an elevated compared to a normal IgE concentration at 11.5–14.5 years of age. Thus the 23 children with an elevated IgE more often showed positive SPT to animals ($n=20$), pollens ($n=21$), moulds ($n=12$) and mites ($n=15$) than the 34 children with a normal IgE level of whom 12 were positive to animals, 13 to pollens, five to moulds and four to mites ($p<0.001$).

In the 54 tested children histamine provocation revealed four children with marked hyperreactivity

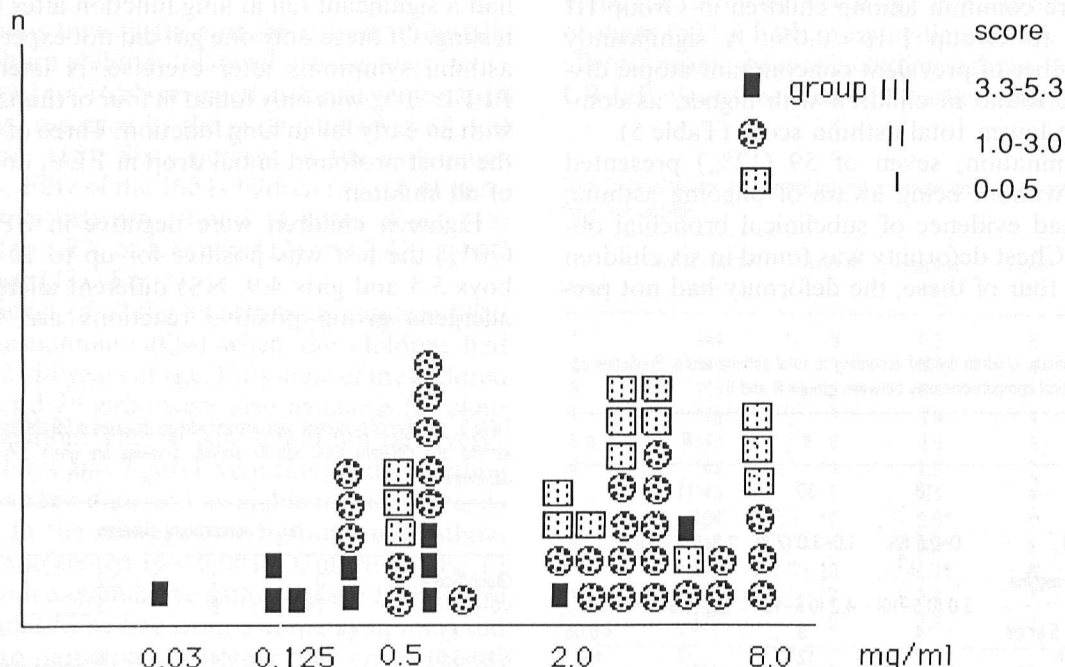


Fig. 2. Bronchial histamine provocative concentration (PC_{20HI}) in groups of asthmatic children divided according to total asthma score. (Group I: 0–0.5 p, II: 1.0–3.0 p, III: 3.3–5.3 p.)

($0.03 < PC_{20} \leq 0.15$ mg/ml), 18 with moderate reactivity ($0.15 < PC_{20} \leq 1.0$ mg/ml), and 32 with mild reactivity ($1.0 < PC_{20} \leq 8.0$ mg/ml) (Fig. 2). No significant difference was found in the mean histamine threshold between boys and girls. A late drop in PEF $> 20\%$ after exercise (3–9 h) was found only in four children having PC_{20} -levels below 1.0 mg/ml, all of whom were considered inadequately medicated (Fig. 2).

The six children with a chest deformity had a significantly higher total asthma score than those with a normal chest configuration ($p < 0.001$). No correlation was found between growth retardation or pubertal stage and total asthma score (results not shown).

Significant differences were found regarding the frequencies of several parameters between Groups III and I: Exercise-induced asthma ($p < 0.01$), on call visits and hospitalizations ($p < 0.01$), asthma start before 1.5 yr ($p < 0.05$), chest deformity ($p < 0.05$), bronchial reactivity on tread mill test (FEV_1 $p < 0.01$, MEF_{50} $p < 0.05$, PEF $p < 0.01$) and histamine inhalation ($PC_{20Hi} < 1.0$ mg/ml, $p < 0.05$). Group III children also more often had a positive Phadiatop ($p < 0.05$), an elevated IgE and more than five positive tests at SPT ($p < 0.05$), especially with animals and mites ($p < 0.05$) (Fig. 3a). The mean wheal sizes at SPT were generally larger in Group III children, but a significant difference was only

found with pollens ($p < 0.01$) (Fig. 3a,b). A negative correlation was found between PC_{20Hi} levels and the wheal sizes in SPT to animals ($r = 0.51$; $p < 0.001$), pollens ($r = 0.34$; $p < 0.01$), moulds ($r = 0.36$; $p < 0.01$) and mites ($r = 0.36$; $p < 0.001$). There was also a negative correlation between PC_{20Hi} levels and a FEV_1 or MEF_{50} fall at exercise test ($r = 0.30$; $p < 0.05$, and $r = 0.37$; $p < 0.01$, respectively) as well as an elevated IgE ($r = 0.40$; $p < 0.01$). Asthmatic children with concomitant ARC and/or AD had similar PC_{20Hi} levels to those without ARC/AD.

There was no significant difference in the mean total asthma score between boys and girls (1.7 and 1.9 p, respectively). It was similar for children born during various periods of the year.

Children with $CB-IgE \geq 0.9$ kU/l did not significantly have IgE levels > 100 kU/l or a positive SPT at 11.5–14.5 years of age more often than those with lower neonatal IgE concentrations. Children with $CB-IgE \geq 0.9$ kU/l were slightly more reactive to histamine inhalation than those with a $CB-IgE < 0.9$ kU/l ($p < 0.05$). All four children with marked reactivity (< 0.15 mg/ml) had an elevated $CB-IgE$. Children with early onset of asthma (< 1.5 years of age), were not found to have more SPT reactions (mean 3.7 allergens) than those with later onset (between 1 and 3 or 3 and 5 years of age, 3.4 and 3.5 allergens, respectively).

Discussion

The prevalence of asthma in this cohort of children at 11 years of age (3%) is similar to recent reports from Sweden (6, 40) but slightly higher than previously reported (21). The prevalence of asthma in childhood has also increased in several other countries during recent decades (7, 8) and varies between 1.6 and 10%. The increase is only to some extent due to a change in the awareness of the disease, an increased availability of medical facilities or a change in classification (7, 31). Early exposure to mites, animals, pollens, indoor cigarette smoke in combination with an increase in air pollution and poorer indoor climate may explain this increase (1, 36). Children with atopic dermatitis and with mothers who smoke seem to run a special risk to develop asthma (26).

Childhood asthma usually begins during the first years of life (4, 34). One third of children have their onset before 2 years of age and 80% develop symptoms before the age of 5 years (32). Similar figures were found in this material (32% before 1.5 years and 81% before 6 years of age). The relation between the age of onset, presence of chest deformity and the ultimate outcome of asthma has been investigated by several authors (22, 23). We found children with more severe prevalent asthma (total asthma

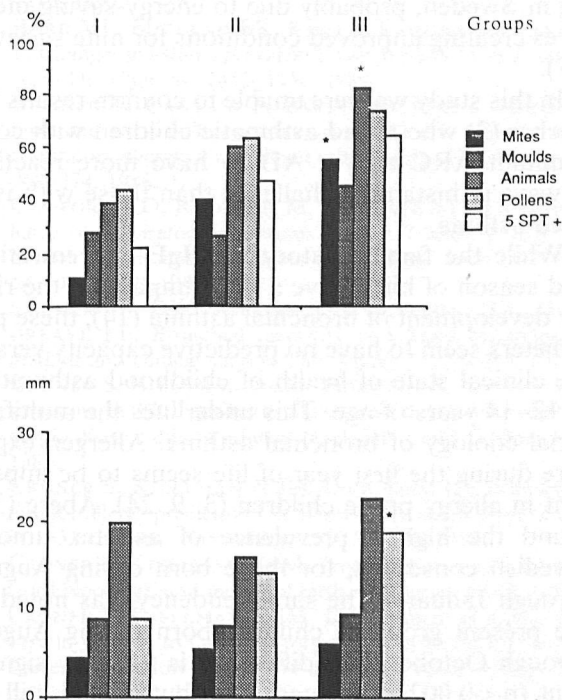


Fig. 3. Asthma score in 59 asthmatics at 11.5–14.5 years of age versus a. skin test positivity, b. wheal sizes at skin prick test. Statistical comparisons are only made between the extreme score groups (Group III and Group I). * $p < 0.05$.

score ≥ 3.3 p) and a chest deformity to have asthma before 1.5 years of age more often than children with less severe asthma. On the other hand, an early asthma début does not always imply a negative prognosis; four of 18 children with no prevalent asthma and nine of 30 with mild asthma had their asthma début before 1.5 years of age (Table 3).

Bronchial asthma in childhood and adolescence still seems to be underdiagnosed and undertreated (10, 18, 28, 35). This was confirmed in our study where medication for prevalent asthma was not adequate in 22% of the children despite earlier check-up in the allergy out-patient clinic. More efforts must be made in instructing children with asthma and their parents in the correct use of asthma medication (35).

Lung auscultation may help in demonstrating subclinical asthma; 12% presented rhonchi at forced expiration without being aware of ongoing bronchial obstruction. The negative significance of wheezing at physical examination and persistence of asthma has been clearly shown by Martin et al. (22) when following asthma development up to 21 years of age.

Only in a minority of the children did the tread mill test provoke asthma despite more frequent reports in the questionnaire. This was probably to some extent due to the warm indoor climate where the test was performed. Some of the children were physically fit and probably would have needed a heavier working load or contributing factors in order to elicit EIA.

Concomitant allergic diseases in addition to asthma increase the likelihood of persisting asthma (4). In addition to asthma, 68% of the investigated children had other prevalent allergic disease, indicating a more doubtful outcome of their asthma.

We found 47% of the children having AD before their asthma start, which is similar to a previous report where 41% of 110 children had AD before AB (41).

Different asthma scores have been used when examining children with asthma (5, 25). Most scores only consider number of attacks or days with asthma. Symptoms are, however, modified by medication. The total asthma score evaluated in this study seems more adequate than previous scores since it takes into account both the severity of asthma and total medication. When using this new scoring system one group of children with no or mild prevalent asthma (Group I) differed significantly from those with severe prevalent asthma (Group III). The latter were found to have earlier début, significantly more EIA, chest deformity, ARC, reactivity to histamine challenge, elevated IgE and more reactions at SPT, especially towards animals and mites, and larger wheal sizes to pollens.

On the other hand, CB-IgE levels and family his-

tory of allergy/asthma were similar in the groups with milder and more severe current asthma at 11.5–14.5 years of age. This is in contrast to previous findings showing the value of these parameters for predicting the development of asthma (15).

Children with elevated IgE concentrations more often had a positive SPT than children with lower IgE concentrations. Neither the serum IgE concentration nor the Phadiatop test were ideal for identifying all children with a positive SPT.

Lower PC_{20Hi} levels and a more profound drop after tread mill testing were found in children sensitized to common allergens than in non-sensitized children. This is in accordance with a recent report by Gustavsson et al. (18) showing that asthmatic children sensitized to both dog and cat dander had lower FEV₁ and MEF₅₀ and were more reactive in their airways than non-atopic asthmatics.

Allergy to animal dander is one of the most common causes of asthma in school children in our area (18, 19, 20), while mites are the most important sensitizers in more humid climates (29, 30). Fifty-eight per cent of investigated children were sensitized to dog, cat or horse, confirming the importance of these allergens. Allergy to mites was found in 25% of children, which is the same prevalence as found by Gustavsson et al. (18). This indicates that these allergens are of great importance also in our region. Mite sensitization was more common than in a previous Swedish study (16). Mite infestation is increasing in Sweden, probably due to energy-saving measures creating improved conditions for mite survival (27).

In this study we were unable to confirm results by Backer (2) who found asthmatic children with concomitant ARC and/or AD to have more reactive airways at histamine challenge than those with isolated asthma.

While the family history, CB-IgE concentration and season of birth have a great impact on the risk for development of bronchial asthma (14), these parameters seem to have no predictive capacity versus the clinical state of health of childhood asthmatics at 12–14 years of age. This underlines the multifactorial etiology of bronchial asthma. Allergen exposure during the first year of life seems to be important in allergy prone children (3, 9, 24). Åberg (39) found the highest prevalence of asthma, among Swedish conscripts, for those born during August through January. The same tendency was noted in the present group of children born during August through October. The difference is formally significant ($p < 0.002$, chi-square test) but should still be considered to be more of a suggestion than a proof of actual periodicity. Increased exposure to unsuitable indoor climate, indoor allergens and viral infections during the first 6 months of life may explain this

increase in the asthma prevalence in children born during the autumn (38).

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