

Original article

Asthma in adults: comparison of adult-onset asthma with childhood-onset asthma relapsing in adulthood

The prevalence of asthma in children and young adults is rising. Although the general features of asthma are similar in children and adults, there are several differences. Studies of the differences between childhood- and adult-onset asthma may provide new insight into the phenotypic heterogeneity of asthma. The aim of this cross-sectional study was to compare the characteristics of asthmatic adults who reported having ($n=84$) or not having ($n=235$) asthma in childhood. The participating patients were recruited by chest specialists throughout France and were examined from March to November 1995. The specialists completed a standardized questionnaire, and carried out a clinical examination and spirometric tests. Male sex; greater severity, particularly lower spirometry values related to small airways; greater severity and earlier onset of allergy; and maternal history of atopic dermatitis and perennial rhinitis were found to be associated with reported childhood asthma. This study exhibits highly internally consistent results and indicates that subjects who did have childhood asthma and relapse in adulthood appeared to have a potentially more severe form of asthma.

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The prevalence of asthma in children and young adults (1–3) is rising. Over the past few decades, the natural progression of asthma from childhood to adulthood has been the subject of several longitudinal studies. Most have followed a group of asthmatics over time, mostly asthmatic children (4–9), but also asthmatic adults in one recent study (10). Other studies have followed a subgroup of the general population, studying the occurrence of and risk factors for the onset of asthma (11–14). Epidemiologic studies have shown that there is a reasonable chance of remission or a reduction in asthma symptoms during the teenage years (5, 11, 15). However, a recent review of the literature (16) showed that asthma symptoms persist in 30–80% of adult patients and that the relapse rate after a symptom-free interval is high (11). Conversely, although the incidence of asthma is lowest among subjects aged 15–50 years (17), adult-onset asthma does occur (18). The general features of asthma are similar in children and adults, but several differences exist. Ideally, investigation of the risk factors for the onset of asthma requires a temporal perspective that only large follow-up studies can provide. A cheaper, but less valid approach is to use retrospective information provided by cross-sectional studies carried out in adulthood. The question is this: does adult-onset asthma

differ from asthma that begins in childhood and relapses in adulthood? The aim of this study was to describe the characteristics of asthma in young adults, and to compare these characteristics between patients with adult-onset asthma and patients with childhood-onset asthma relapsing in adulthood.

Material and methods

This cross-sectional study was carried out as the first stage in a longitudinal study. The aim of this 3-year longitudinal study was to describe the natural history of asthma in young adults and to investigate prognostic factors. Chest specialists throughout France were asked by regional medical associations to participate in this study by including the first two patients that met the inclusion criteria, examined between March and November 1995. The inclusion criteria were as follows:

- 1) patients 20–42 years old
- 2) a documented asthma diagnosis during the preceding 12 months (i.e., recurrent episodes of wheeze or cough, with either an increase of 15% of FEV₁ after bronchodilator or a fall of 20% of FEV₁ after bronchoconstrictor)

- 3) a forced expiratory volume in 1 s (FEV_1) of at least 60% of the predicted value
- 4) willingness to participate in a 3-year study.

The exclusion criteria were as follows:

- 1) having a chronic pulmonary disease other than asthma (such as emphysema or COPD)
- 2) having been treated with inhaled steroids (more than 1500 μ g/day) for at least 1 month since asthma diagnosis
- 3) having nonstable asthma (e.g., asthma exacerbation during the last 3 months with emergency care or systemic steroids for 15 days or more).

The relapse of childhood asthma was not a criterion for exclusion. A total of 251 specialists participated: they recruited a total of 352 patients (some specialists had only one patient that met the inclusion criteria during the study period). For this specific analysis of cross-sectional data, we used the following definition of reported childhood asthma:

- 1) beginning before puberty (<12 years)
- 2) remission before the end of puberty (<18 years)
- 3) a period of at least 5 years with no asthma symptom and no asthma treatment, between childhood asthma and the onset of asthma in adulthood.

The protocol was approved by the Bureau de Recherche des Etudes Biomédicales of INSERM and by the National Committee for Data Processing and Freedom. Informed written consent was obtained from the 352 participating patients, who were then examined by their pulmonologist. The pulmonologists

- 1) administered a standardized questionnaire (demographic data, personal and familial asthma and allergy history, asthma severity and medication, and lifestyle and environmental factors), most of the questions being adapted from the ECHRS questionnaire (19), and the questions on asthma symptoms having been validated in a previous study (20)
- 2) performed a clinical examination
- 3) carried out atopy testing and spirometric tests with the instruments and methods currently used in their practice.

The spirometry measurements were performed when the patient was not suffering asthma exacerbation and had not used an inhaled bronchodilator during the preceding 4 h. The severity of current adult asthma was scored by several indices. Intermittent asthma was defined as asthma attacks less than once a week, and nocturnal asthma symptoms less than once a week, the patient being asymptomatic between exacerbations and exhibiting $FEV_1 > 80\%$ of the predicted value. Moderate persistent asthma was defined as daily asthma attacks, or daily nocturnal asthma symptoms, or a $FEV_1 < 80\%$

of the predicted value. All subjects not fulfilling the criteria for either of these categories were classified as mild persistent asthmatics.

A family history of allergy (father, mother, and siblings) was recorded if there was a previous history of asthma, allergic dermatitis, rhinitis, or conjunctivitis in these family members. Atopy was defined as at least one positive prick test.

The study was cross-sectional in design. It compared the characteristics of asthma in two groups of asthmatic patients: subjects that reported having had asthma in childhood and subjects that did not. We used chi-square tests to analyze categorical variables, and analysis of variance to compare the mean values between groups. Multivariate analysis was carried out by logistic and linear regressions, adjusting simultaneously for age, sex, country of birth, smoking, educational level, and asthma severity. A P value less than 0.05 was considered to be statistically significant.

Results

We classified the patients into two groups: 1) those reporting childhood asthma ($n=84$); 2) those not reporting childhood asthma ($n=235$).

The characteristics of the two groups of asthmatics are given in Table 1. We found that 35% of subjects reporting childhood asthma and 25% of subjects not reporting childhood asthma were 25 years old or younger at the onset of asthma in adulthood ($P=0.19$). The majority of the subjects reporting childhood asthma were male (62% vs 42%, $P=0.002$), and there tended to be slightly more subjects born in France in this group (95% vs 88%, $P=0.08$). Although the differences were not significant, more subjects reporting a history of childhood asthma had a higher educational level (62% vs 54%), and fewer of this group were current smokers (10% vs 18%). The time lag between the onset of symptoms and inclusion, and between diagnosis and inclusion in the study, was similar for both groups of patients. Asthma attacks were the most frequent first symptom in the group reporting childhood asthma, whereas wheeze and cough were the most frequent first symptoms in the other group.

A comparison between the two groups in terms of the clinical and functional characteristics used to determine asthma severity is given in Table 2. One-third of the adult patients reporting no childhood asthma had less than one asthma attack per month, as opposed to only 14% in the group with childhood asthma ($P=0.03$). The frequencies of nocturnal asthma and use of β_2 -agonists were similar in the two groups. However, impaired respiratory function was more frequent in patients that reported childhood asthma than in those that did not. The means (SD) of FEV_1 % of predicted and forced

Table 1. Characteristics of two groups of asthmatics

	Reported childhood asthma (<i>n</i> = 84)	No reported childhood asthma (<i>n</i> = 235)	<i>P</i>
Age (%)			
≤ 25	35	25	0.19
26–35	40	43	
> 35	25	32	
Males (%)	62	42	0.002
Country of birth (%)			
France	95	88	0.08
Smoking (%)			
Current	10	18	0.22
Ex-	19	17	
No	71	65	
Education level (%)			
No high school diploma	38	46	0.20
High school diploma and above	62	54	
Onset of symptoms – inclusion time lag (months)	9.6 (10.9)	10.6 (12.9)	0.57
Diagnosis – inclusion time lag (months)	4.9 (3.8)	4.7 (3.9)	0.64
First symptom at onset of asthma (%)			
Asthma attack	59.5	41.9	0.03
Wheeze	28.6	38.4	
Cough	7.1	15.4	
Other	4.8	4.3	

mid-expiratory flow 25–75% (FEF_{25–75}) of predicted were as follows: 80.3 (12.9) *vs* 86.7 (15.1), *P* = 0.0006 for FEV₁, and 53.2 (17.7) *vs* 72.4 (25.0), *P* = 0.0001 for FEF_{25–75}. No significant difference was observed for forced vital capacity (FVC).

In the group reporting childhood asthma, spirometry results were related to the reported severity of asthma in childhood. The means (SD) were as follows: 86.1 (13.8) in patients with mild childhood asthma *vs* 76.7 (11.1) in patients with moderate or severe childhood asthma for

Table 2. Asthma severity in two groups

	Reported childhood asthma (<i>n</i> = 84)	No reported childhood asthma (<i>n</i> = 235)	<i>P</i>
Asthma attacks (%)			
< 1 month	14.5	30.7	0.03
Monthly	15.6	11.7	
Weekly	41.0	30.3	
Daily	28.9	27.3	
Nocturnal asthma (%)			
< 1 month	40.7	49.5	0.21
Monthly	12.4	9.4	
Weekly	33.3	23.2	
Daily	13.6	17.9	
Being symptomatic between exacerbations (%)	71.6	66.2	0.37
Use of β ₂ agonists (%)			
No	6.0	15.4	0.14
Daily (regular use)	13.2	9.6	
As needed: 1/day and less	65.1	62.7	
As needed: several times daily	15.7	12.3	
Pulmonary function			
FEV ₁ (% of predicted)			
> 80	46.4	65.1	0.006
70–80	28.6	21.7	
60–70	25.0	13.2	
FVC (% of predicted)			
> 80	86.9	88.0	0.03
70–80	6.0	10.3	
60–70	7.1	1.7*	
FEF _{25–75} (% of predicted)			
> 80	8.6	33.6	0.001
70–80	5.7	14.5	
60–70	11.4	18.7	
≤ 60	74.3	33.2	

*One subject had FVC (% of predicted) ≤ 60%.

FEV₁ % of predicted, and 59.3 (20.3) in patients with mild childhood asthma vs 49.2 (14.9) in patients with moderate or severe childhood asthma for FEF₂₅₋₇₅ % of predicted. Fig. 1 shows pulmonary function values according to the existence and severity of childhood asthma. We compared severity classes of current adult asthma (constructed with clinical and spirometric indices) and found a nonsignificant trend toward higher severity in adults reporting childhood asthma than in those that did not (intermittent asthma: 5.2% vs 12.8%, mild persistent asthma: 28.6% vs 32%, and moderate persistent asthma: 66.2 vs 55.2%). Similar results were obtained after adjustment for age, sex, country of birth, smoking, and educational level.

Adults reporting childhood asthma more frequently reported that allergy was a factor in the onset of their asthma and the trigger of their asthma attacks (84.0% and 82.1%, respectively, for patients reporting childhood asthma; 68.4% and 68.0% for patients not reporting childhood asthma (Table 3). The frequency of a personal history of allergy did not differ significantly between the two groups, although perennial rhinitis tended to be more frequent in adults reporting childhood asthma (47.0% vs 39.3%, $P=0.22$). However, the age at the onset of allergy was significantly lower for the group reporting childhood asthma (Table 4), except in

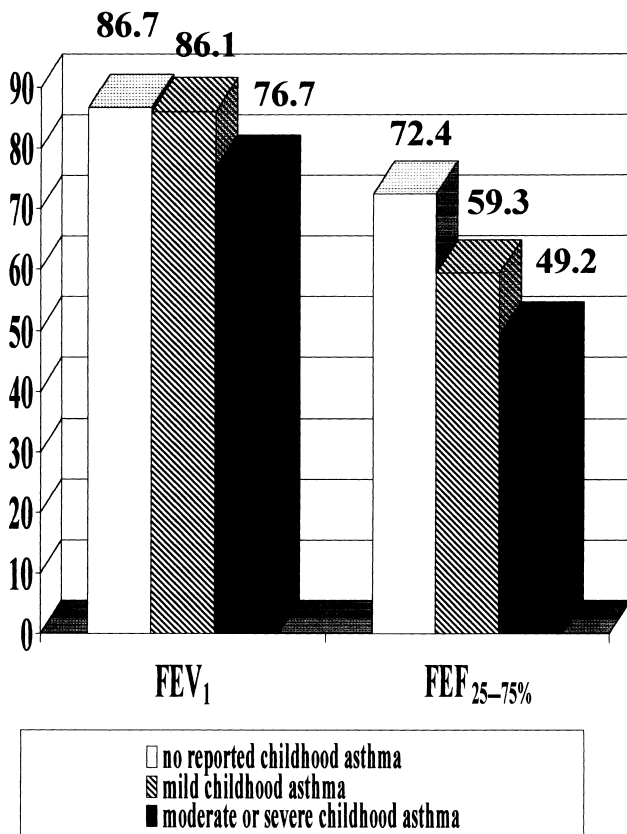


Figure 1. Pulmonary function in patients with adult-onset asthma and in those reporting childhood asthma, according to asthma severity in childhood.

Table 3. Allergy history in two groups

	Reported childhood asthma (n=84)	No reported childhood asthma (n=235)	P
Circumstances of asthma onset (%)			
Allergy	84.0	68.4	0.007
Infection	33.3	29.4	0.51
Personal events	12.3	11.4	0.82
Exercise	25.9	19.7	0.24
Trigger of asthma attacks (%)			
Allergy	82.1	68.0	0.01
Infection	40.5	40.0	0.94
Stress	27.4	18.2	0.08
Exercise	53.6	38.2	0.01
Personal allergy (%)			
Conjunctivitis	24.1	23.1	0.85
Perennial rhinitis	47.0	39.3	0.22
Seasonal rhinitis	24.1	22.6	0.79
Atopic dermatitis	16.9	16.7	0.97
Drug allergy	10.8	10.7	0.97
Positive prick tests % (n)			
<i>D. pteronyssinus</i>	83.6 (61)	63.9 (129)	0.002
<i>D. farinae</i>	81.7 (58)	59.3 (118)	0.001
Cat hair	27.3 (18)	25.0 (47)	0.72
Dog hair	19.7 (13)	9.7 (18)	0.03
Fungi	12.9 (8)	13.9 (26)	0.84
Grass pollens	58.6 (41)	33.5 (67)	0.001
Tree pollens	35.1 (20)	19.7 (37)	0.02

cases of allergy to drugs. Significant differences were noted between the two groups, with sensitization more frequent in adults reporting childhood asthma, to perennial (indoor) allergens such as *Dermatophagoides pteronyssinus*, *D. farinae*, and dog hair, and to seasonal allergens (grass and tree pollens). No differences were observed between the two groups in terms of sensitization to cat hair and fungi. The percentage of tests not done was similar for the two groups, except for tree pollen (32% in the group with reported childhood asthma; 20% in the other group). Adjusting for age, sex, educational level, country of birth, smoking, and severity of asthma did not affect the results of the analysis.

Paternal and sibling histories of asthma and allergy did not differ between the two groups (Table 5), whereas there was a significantly higher frequency of a maternal history of asthma and allergy in adults reporting childhood asthma (32.1% vs 19.8%, $P=0.03$). The

Table 4. Age at onset of personal allergy in two groups

	Reported childhood asthma (n=84)		No reported childhood asthma (n=235)		P
	n	Mean (SD)	n	Mean (SD)	P
Childhood asthma	84	6.2 (3.0)	—	—	—
Conjunctivitis	18	11.6 (6.5)	51	19.1 (9.3)	0.002
Perennial rhinitis	36	11.1 (6.3)	88	21.1 (9.2)	0.0001
Seasonal rhinitis	20	11.7 (8.4)	52	20.0 (10.4)	0.002
Atopic dermatitis	12	5.3 (5.6)	37	14.3 (10.7)	0.0006
Drug allergy	7	22.6 (12.1)	16	20.9 (7.2)	0.68

Table 5. Familial asthma and allergy history in two groups

	Reported childhood asthma (n=84)	No reported childhood asthma (n=235)	P
Paternal allergy history (%)	20.5	23.6	0.58
Asthma (%)	16.7	17.9	0.80
Atopic dermatitis (%)	1.3	4.2	0.22
Perennial rhinitis or conjunctivitis (%)	2.6	3.8	0.62
Seasonal rhinitis or conjunctivitis (%)	2.6	2.4	0.92
Maternal allergy history (%)	32.1	19.8	0.03
Asthma (%)	16.7	16.0	0.90
Atopic dermatitis (%)	7.7	1.4	0.006
Perennial rhinitis or conjunctivitis (%)	7.7	4.2	0.24
Seasonal rhinitis or conjunctivitis (%)	3.8	2.8	0.66
Sibling allergy history (%)	25.6	32.1	0.29
Asthma (%)	17.9	24.1	0.27
Atopic dermatitis (%)	3.8	5.7	0.54
Perennial rhinitis or conjunctivitis (%)	6.4	5.7	0.81
Seasonal rhinitis or conjunctivitis (%)	6.4	7.6	0.74

relationship between reported childhood asthma and maternal asthma and allergy seems to be limited to maternal atopic dermatitis: 7.7% of adult asthmatics reporting childhood asthma had mothers with atopic dermatitis, whereas only 1.4% of the patients in the other group had mothers who suffered from atopic dermatitis. Multivariate analysis, adjusting for age, sex, educational level, country of birth, smoking, and severity of asthma, gave similar results. However, there was a nonsignificant trend for more maternal history of perennial rhinitis or conjunctivitis in cases of reported childhood asthma (7.7% vs 4.2%, $P=0.10$).

Discussion

Thus, in our study population of young adults, we found that childhood-onset asthma relapsing in adulthood was associated with the following factors:

- 1) male sex
- 2) more frequent asthma attacks
- 3) lower spirometric values, especially those related to small airways and especially if childhood asthma was severe
- 4) allergy being a factor in the initial onset of asthma and a trigger for asthma attacks
- 5) personal history of allergy with younger age at onset
- 6) more frequent sensitization to domestic airborne allergens such as *D. pteronyssinus*, *D. farinae*, and dog hair, and to grass and tree pollens
- 7) maternal history of atopic dermatitis and perennial rhinitis.

As the symptoms associated with asthma are highly variable, a long period with no active symptoms or need for medication is required to define a patient as being in remission (16). We chose 5 years as the length of time required to define subjects whose disease had gone into

remission. Nevertheless, it is known that a considerable number of patients thought to be in complete remission remain latently asthmatic until the symptoms are triggered again. Of course, with this type of study design, we must consider the possibility of misclassification related to a recall bias, as some people might ignore or have forgotten that they had asthma in childhood. Our criteria for childhood asthma followed the convention of most epidemiologic studies, by relying on the subjects' perception of whether or not they have had the disease. Subjects with more severe asthma might be more likely to remember having had asthma in childhood. A point against the likelihood of a recall bias is that in our data childhood asthma history was more frequent in cases of pulmonary impairment, especially for FEF₂₅₋₇₅, which is not perceived by patients. Another possible bias is the selection bias in our study population, in that subjects with childhood asthma might be more willing than patients with adult-onset asthma to consult pulmonary specialists at an earlier stage of the disease. If that was the case, the group of patients reporting childhood asthma would have less severe asthma, an effect which is the opposite of what we observed. Thus, despite its design, this study is unlikely to be heavily biased, and the results obtained are internally consistent.

This study carried out with the collaboration of 251 pulmonologists was feasible only by the procedures currently used in their practice for lung-function tests and allergologic investigation. As the main objective was to follow the patients over time, and in the longitudinal analysis to compare the patients to themselves, this approach was considered acceptable. Nevertheless, that remains a potential limitation in this analysis of cross-sectional data. It is well known that boys are more likely than girls to have had asthma in childhood, so the higher proportion of boys in the subgroup with a history of childhood asthma is not surprising. Similar inversions of sex ratios between childhood and adulthood have been observed in several studies (14, 21).

This study suggests that relapsing asthma in adulthood is potentially more "severe" than new-onset asthma at the same age. It was generally thought that the airway obstruction that occurs in childhood asthma is completely reversible. However, several studies have demonstrated persistent pulmonary abnormalities in both children and adults (22-25). We found that FEV₁ and especially FEF₂₅₋₇₅ were extremely low in adult asthmatics reporting childhood asthma, and that the impairment was related to severity of childhood asthma. Reduced flow indicates narrowing of the small airways and is considered to be a measure of the severity of airflow obstruction in asthmatics (14). It now seems that significant functional disturbances persist during apparent clinical remission (23), and the presence of various functional abnormalities may be the rule rather than the exception during asthma remission.

As expected, a personal history of allergy diseases was frequent in both subgroups of adult asthmatics. The prevalences of the various allergies were similar, although perennial rhinitis was slightly but not significantly more frequent in the subjects reporting childhood asthma. The age at onset of allergy was clearly lower for the patients reporting childhood asthma. Allergy was more often recognized by patients reporting childhood asthma as the trigger of asthma attacks. Prick tests were more frequently positive in patients reporting childhood asthma for all allergens tested except cat hair and fungi. Families with children with allergy to cat hair are very unlikely to keep a pet cat. Most studies have shown a negative association between atopy and the outcome of asthma (15), although some studies have shown no association at all (9). It is therefore not surprising that most atopic subjects begin to suffer from asthma in childhood, and that intrinsic asthma is more prevalent in adulthood than in childhood.

The number of asthmatic subjects with parents suffering from allergies was high, as reported previously (26–30). Only the proportion of patients with a maternal history of allergy differed between the two groups, the proportion of patients with paternal and

sibling allergy histories being similar for the two groups. In our study, paternal asthma, eczema, and perennial and seasonal rhinitis had similar frequencies in the two groups, whereas the subgroup with a history of childhood asthma more frequently had mothers suffering from atopic dermatitis and, to some extent, perennial rhinitis. It is possible that sex may influence the atopic condition (31).

This study supports the phenotypic heterogeneity of asthma, as several characteristics are different between adult-onset asthma and a subgroup of childhood-onset asthma. The description of these phenotypes is useful in etiologic research and to classify subjects in genetic studies (32).

In conclusion, this study conducted in young adults, with its highly internally consistent results, highlights differences in the characteristics of asthma beginning in childhood and relapsing in adulthood, and adult-onset asthma: especially the greater frequency of asthma attacks and earlier onset of allergy in patients with a history of childhood asthma. It also confirms that, even after a remission of at least 5 years as teenagers, subjects who had asthma in childhood and relapsed in adulthood have more obstructed airflow than patients with adult-onset asthma.

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