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The prognosis of severe bronchial asthma in childhood on the basis of late reexaminations

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Fourhundred and forty one patients treated for asthma between 1954 and 1978 were reexamined. Their age ranged from 15 to 36 years at the time of reexamination. To regard a case as severe, at least four factors out of the following six had to be present:

1. Attacks more frequent than one every week;
2. attacks lasting for more than one day;
3. six or more hospitalizations;
4. absence from school exceeding one month per school-year;
5. drop-out from school for at least one school-year;
6. steroid treatment for more than one week.

59 patients (13.3%) fulfilled the criteria. The sex ratio within the severe group was 1:1 although there was a male preponderance of all asthmatics. The recovery rate for the severe group was lower (40.6%) than for all patients (75.0%). Prognosis was less favourable in female than in male patients.

In the severe group the disease appeared earlier, eczema during infancy occurred more frequently and allergic disorders had a higher incidence in the family than in the group as a whole. Chest deformities were observed in 48.7% of severe patients while its incidence was only 18.6% for all patients with asthma. Acetylcholine-induced bronchial hyperreactivity was more frequent in the severe patients than in all patients irrespective of the degree of severity while the prevalence of exercise induced asthma showed no relationship to the degree of severity. Among the severe cases 31% failed to cope with a standardized physical load.

Childhood asthma varies greatly in severity. The life-style of slightly ill patients hardly differs from that of healthy age-mates, and to these children only slight changes in the way of life, reduction of exposure to environmental allergens and occasional treatment with symptomatic drugs have to be recommended. Severe cases need concentrated medical and social help, have a high drop-out rate at school, and a reduced working capacity narrowing the quality of their life. In this study we have attempted to define severe asthma and to examine the prognostic value of certain factors occurring during childhood.

Judgment of the severity of asthma is not uniform in the literature. The term severe asthma is used for different clinical conditions. The most important factor is the frequency of attacks. Table I shows the classifications used by many authors; it is seen that the criterion of severe asthma varies from three attacks per year up to one or even more per week.

TABLE I

Criteria of severe asthma

Reference	Criteria
Blair 1977	More than 3 attacks/year
Ryssing 1963	More than 10 attacks/year
Dawson 1969	More than 10 attacks/year
Leveque 1972	More than 12 attacks/year
Kraepelien 1963	More than 25 attacks/year
Osváth 1976	More than 25 attacks/year
Vialatte 1972	More than 50 attacks/year
Charpin 1972	More than 60 attacks/year

TABLE II

Incidence of severe asthma in all cases of asthma

	Proportion of severe asthma per cent	Total No. of asthmatic	Note
Leveque 1972	16.0	206	Children
Antonsen 1974	20.0	331	Children
Editorial 1978	20.0	?	Children
Charpin 1972	25.9	589	Children
Pearson 1958	28.0	625	Adults
Vialatte 1972	33.3	741	Children
Mukoyama 1975	35.4	1000	Children
Ryssing 1963	42.0	442	Children

The criteria of Kraepelien [10] are widely accepted; in his classification mild means less than five attacks per year, moderate is characterized by six to ten, severe by eleven to twenty-four and very severe by twentyfive or more attacks per year. In the score system of Osváth [16] not only the frequency of attacks is taken into consideration but also their duration, the severity of wheezing and the number of days with dyspnoea per year; on this basis patients with scores between sixteen and twenty-one are regarded as very severe cases. The annual frequency of attacks has a primary role in this system too, as 12 of the possible 21 points reflect this factor.

It is thus not surprising that the proportion of severe cases shows wide variations. Table II illustrates the discrepancies in the literature: the lowest proportion is 16% and the

highest one 42%. Other factors too influence the proportion of severe cases, thus the ratio of children and adults in the material, whether the patients are collected from a geographic area or from a special hospital department [2], and whether they are hospitalized or out-patients [11].

The clinical characteristics, the long-term course and the late prognosis of severe asthmatics were investigated by several authors. Severe asthma usually has an early onset [4, 5, 18], simultaneous or previous eczema foretells a bad prognosis [5], chest deformities, especially barrel chest and pigeon chest, develop more frequently in severe patients [18].

Growth and weight development may be impaired either by the disease itself or by the prolonged steroid treatment [7, 17, 18]. Asthmatics with severe complaints, are practically never free of symptoms [8] and they are usually on long-term steroid treatment [13, 17]. In this group of asthmatics the positive skin test, especially that for house-dust, frequently persists into adulthood [3, 5].

The relationship between the severity of asthma and the gender of patients is not clear. Some authors [1] believe that the overwhelming majority of severe cases are males while others [2] found a better recovery trend in males. Pearson [14] observed no difference in severity between the two sexes.

Similar differences prevail in the recovery outlook of severe asthmatics. In a study [3] checking the childhood cases twenty years later, the recovery rate was 69% in mild cases and 33% in the severe group of patients. Cases classified as severe during childhood exhibit a reduced tendency to recovery during puberty, and so the relative proportion of severe cases increases with age. A high frequency of attacks predicts a bad prognosis in adulthood [11, 14].

Death from asthma occurs nearly exclusively among severe patients. In a series of 11,646 mild and moderate cases collected in Japan [12] there was a single fatal case while eleven of 354 severe cases in the same series died of the disease.

Among severe asthmatics exercise induced asthma has a higher incidence but the severity of the latter and that of the disease itself shows no close relationship [7, 9].

In this work we have studied the severe cases of our material by comparing their anamnestic, clinical and prognostic findings with an unselected group of asthmatic children treated over the same period of time.

Material

During the twenty-five years 1954–1978, more than 1200 asthmatic children were treated in our Department. Of these, we selected those who had completed 14 years of age in 1979; they were adolescents or young adults with their age ranging from 15 to 36 years. The home address of 525 such patients was available and 441 of them (84%) answered our letter; 381 reported for examination an ients or their parents completed a questionnaire. In the latter case eventual dubious answers were clarified by correspondence. The rea-

sons for their absence were as follows: 5 patients had died, the others were lactating or doing military service or were abroad. In the patients reporting at our clinic the tests described in detail below were carried out. In some exceptional cases not all examinations were performed, physical loading and the acetylcholine provocation test had to be omitted in some pregnant mothers, physical loading was omitted in two men who had been injured or had an ankylosed knee. Six patients refused to have skin tests.

Methods

Every patient had to complete a questionnaire. The answers given were thoroughly examined in the presence of the patient, anamnestic data were checked by comparison with the original history and eventual corrections were made. We had the opportunity to talk to one or both parents of 40% of the patients.

Physical examination was performed and the eventual chest deformity noted. Prick tests were carried out with Bencard allergens, in the evaluation of results the prescriptions of the makers were observed. The following allergens were used: A_1 and A_2 mixed inhalants, house-dust, house-dust mite, feathers, horse, cat and dog hairs, hay-dust, straw-dust, mixed threshing powder, cotton flakes, grass pollen B_2, tree pollen B_3, flower and shrub pollen B_5, nettle, plantain, mixed moulds A_{13}, M_{10}, and M_{11}. The acetylcholine provocation test was performed by three minute inhalation of 1% nebulized acetylcholine. Vital capacity (VC) and forced expiration volume during 1 sec (FEV_1) were registered with a Spiroscreen 11 device before and three, five and 10 minutes after provocation.

Physical loading was performed by the help of an ergometer; 1 Watt/kg was applied over 6 minutes. VC and FEV_1 values were registered before and three, five and ten minutes after loading. Some patients did not tolerate the load and gave

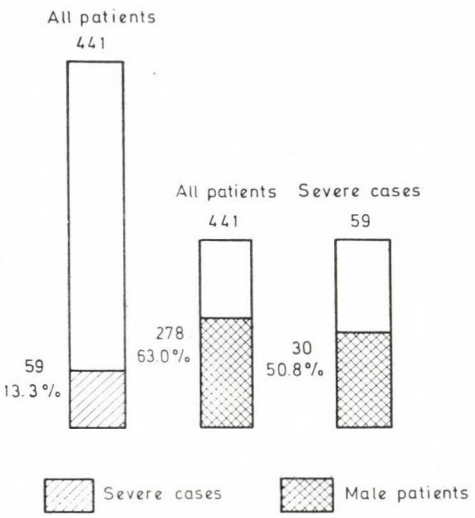

Fig. 1. Prevalence of severe asthma among all patients with asthma. Criteria of severity: 1. Attacks once per week or more frequent. 2. Attacks persisting for more than 24 hours. 3. Six or more hospital admissions. 4. Absence from school for more than one month. 5. Drop-out from school for at least one school-year. 6. Steroid treatment for a period exceeding one week. At least four criteria were present

up before completion of the six minutes period; the fact and time were then noted. In both loading tests a decrease of FEV_1 exceeding 10% of the initial value was regarded as a sign of bronchospasm.

The severe cases were selected by the following method. From the data registered the criteria listed in Figure 1 were examined, taking into consideration the duration of attacks and the frequency of complaints. The following events were also considered to indicate a high degree of severity. Six or more hospital admissions, long absence or drop-out from school for a whole year or more. Since we apply steroids according to very strict indications, steroid treatment over a period exceeding one week could also be regarded as a sign of severity. The presence of at least four of the six criteria led us to classify the patient as severe.

Results

Of the 441 patients available for follow-up 59 (13,3%) were classified as severe (Fig .1). As mentioned above, five patients had died (2 from a cause other than asthma, 2 others from asthma and in the fifth fatal case asthma was complicated by chronic myocarditis). The asthmatic deaths were classified into the severe group.

The unselected asthmatics showed a 2:1 male-female ratio (278 men and 163 women), in accordance with the literature. On the other hand, the severe group contained a comparable number of men and women, 30 and 29 respectively.

The criterion of recovery was a complete freedom from asthmatic symptoms without any treatment over a period exceeding one year. Fig. 2 shows the data. The overall recovery rate was 75% while in the severe group only 40.6% recovered; the difference was significant statistically. Separate analysis for the two sexes showed that the unfavourable outcome of severe asthma was due largely to the low recovery rate in

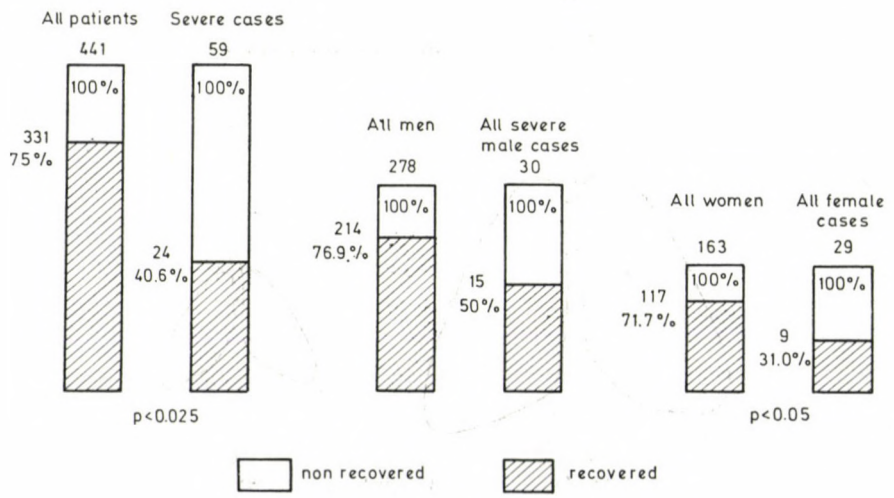

Fig. 2. Recovery rates in asthmatic patients

TABLE III

Data of the history, per cents

	Overall	Severe	
Onset before two years of age	37.9	49.2	NS
Infantile eczema	22.2	28.8	NS
Positive skin test at follow-up	38.9	48.7	NS

NS (Non significant)

women. The proportion of recovery was 50% in severe asthma while the overall recovery rate for men was 76.9%. The corresponding figures for women were 31 and 71.7%, respectively.

Table III presents the data in the history. A higher proportion of severe asthma patients had experienced the onset of the disease before completion of the second year of life and had had eczema during infancy. Positive skin

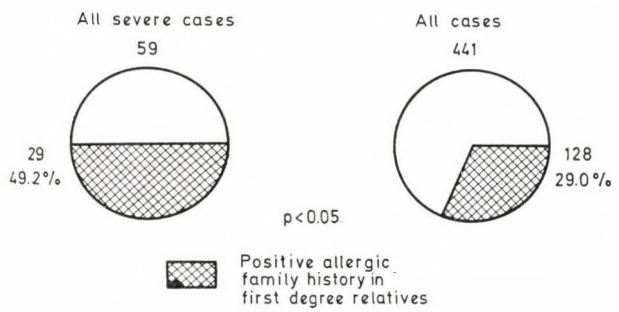

FIG. 3. Family history of asthmatic patients

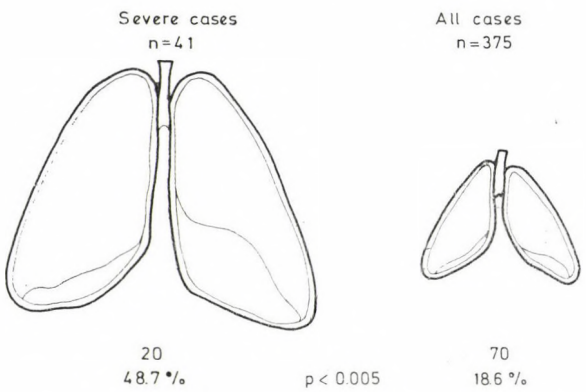

FIG. 4. Incidence of chest deformities

tests at follow-up in adult or adolescent age were more frequently encountered in the severe group. These differences were, however, not significant statistically.

The incidence of allergic diseases in close relatives (Fig. 3) was higher in the severe than in the moderate group. No distinction was made between the atopic (asthma, pollinosis, eczema, etc.) and non atopic (urticaria, drug hypersensitivity, etc.) forms of allergy.

Within the severe group a much higher proportion of the patients exhibited chest deformity than in the whole material (Fig. 4). Among the 375 patients appearing at follow-up, 55 had a slight and 15 a grave chest deformity while among the 41 severe

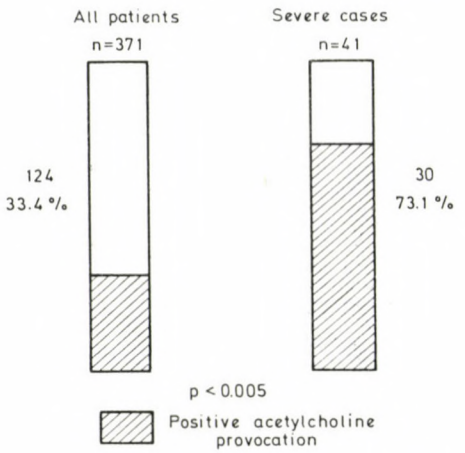

FIG. 5. Acetylcholine provocation

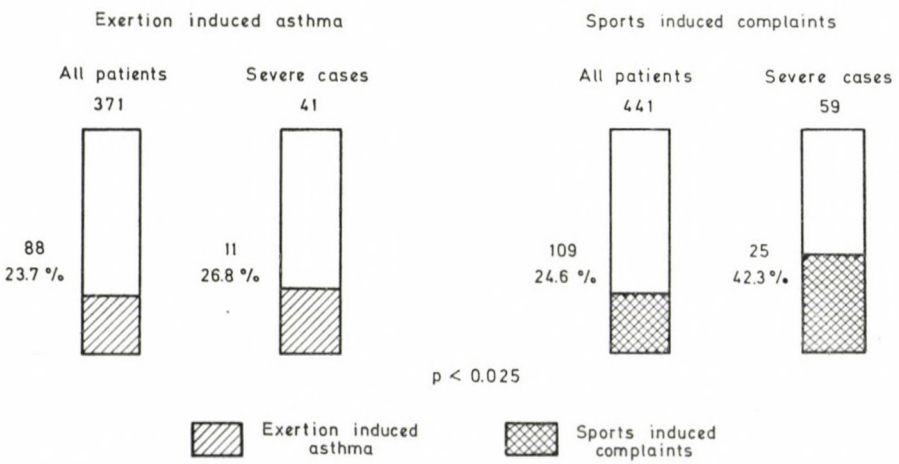

FIG. 6. Physical exertion. 13 severe cases could not complete the test

cases there were 15 with slight and 5 with severe chest deformity. The difference was significant statistically.

Fig. 5 shows the results of acetylcholine provocation at follow-up: again, a larger number of patients had a positive reaction in the severe than in the moderate group.

Physical exercise including sports caused complaints in a higher number of severe patients than in the whole material (Fig. 6). Out of the 441 patients 93 complained of dyspnoea and 16 of asthmatic attacks elicited by exercise while of the 59 severe patients 18 respectively 7 displayed such complaints. The bicycle ergometer test revealed that exercise induced asthma was hardly more frequent among the patients labelled as severe. It is noteworthy, however, that of the severe patients 13 (31.0%) were unable to complete the 6 minute load; they soon became tired and they also lacked the self-confidence needed for the task. For the overall data this proportion was 10% (38 cases).

Discussion

The main purpose of this study was to select the really severe cases of childhood asthma. Our principle of selection, the occurrence of at least four of the six criteria, can only be applied in a given material and for a given period of time. The frequency and severity of attacks has always been a good indicator of grave asthma. The other criteria such as the duration of absence or the drop-out from school and frequent hospitalisations prolonged steroid treatment have become comparatively unfrequent. Still, we feel that by our principle of selection all grave asthmatics in the material could be classified into the severe group, including all the children who had died of asthma and all the adults who were incapable to work. By the score system of Osváth [13], all our cases considered severe by our own criteria had a score exceeding 15, i.e. they would have been classified as very severe.

It may be argued that the patients' memory could fail in answering questions pertaining to events 10 or even 25 years back in the past. We are however certain that they did correctly remember their drop-out from school, their treatment in sanatoria and the long-term steroid treatment since these events must have left deep traces in their or their parents' memory.

Comparing the various parameters in the severe group with those observed in the whole asthmatic material, it turned out that the severe patients form a distinct group in several respects.

The proportion of severe cases amounted to 13.3%, with an equal representation of the two sexes. This markedly differed from the 2:1 male-female ratio found in our unselected asthmatics and in reports in the literature.

The long-term prognosis of severe asthma especially in female patients

is much worse than the average. An earlier onset, a higher incidence of infantile eczema in the patients, of allergic diseases in the close relatives, and of positive skin tests at follow-up are all characteristics of the severe group.

The consequences of asthma notably the chest deformity, especially its severe forms such as a barrel chest or a pigeon chest occur with a higher than normal frequency in patients having had severe asthma during childhood. In addition, bronchial hyperreactivity, as revealed by the acetylcholine provocation test, persists in a higher proportion of severe than of moderate asthmatics. Exercise induced asthma does not occur with increased frequency in the severe group but these persons cannot endure physical exercise and so they rarely participate in sports or other physical activities.

All this forces us to concentrate medical help and social assistance to the severe group. The criteria described in this study may help in selecting severely ill children from the patients affected by asthma in general. They must be advised concerning their way of life and the choice of profession [6]. The family members must be instructed about the importance of rational body exercise, holidays under a favourable climate, the avoidance of smoking by the patient and his environment, etc. Environmental antigens must be kept within reasonable borders, and pets like dogs, cats or guinea-pigs should not be kept by the child.

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