Ventilatory Capacity in Young Adults with a History of Asthma in Childhood

R. H. TREFOR JONES,* M.B., CH.B., D.C.H. ; R. S. JONES,† M.D., M.R.C.P., D.C.H.

Brit. med. J., 1966, 2, 976-978

This study was carried out in order to determine the ventilatory capacity of a group of young adults who had suffered from asthma in childhood but who had been free of symptoms for an average period of six years at the time of the study (range from four to ten years).

The results were compared with those of a group of 24 healthy adults of similar age who were divided into smokers and non-smokers, and also with a group of young adults who had continued to suffer from asthma since childhood.

Method

Selection.—The normal subjects were medical students who had no history of asthma or hay-fever. The group studied were university students who were interviewed with the co-operation of the University of Liverpool Student Health Service. All those who were recorded as having suffered from asthma as children and who had been free from symptoms for a period of at least three years were asked to participate. The adults with asthma were referred from a chest clinic in the city and were considered clinically to have moderately severe asthma.

Ventilatory capacity was assessed by determining the forced expiratory volume in one second (F.E.V.₁) and the forced vital capacity (F.V.C.) (Tiffneau *et al.*, 1947). The effects on the F.E.V.₁ of long exercise (8 to 10 minutes) and subsequently of isoprenaline inhalation was observed (Jones *et al.*, 1962, 1963).

Eight resting values of F.E.V.₁ and F.V.C. were first determined with a modified Gaensler spirometer (Gaensler, 1951 ; McKerrow *et al.*, 1960). The mean value of the last five estimations was taken as the resting level.

The subjects then exercised by running along a covered corridor for a period of 8 to 10 minutes. At the end of this time the F.E.V.₁ and F.V.C. were determined at one-minute intervals in order to observe the fall. (We have found that the maximum fall in F.E.V.₁ occurs usually during the first 10 minutes after the end of exercise.)

When the post-exercise F.E.V.₁ approximated the resting level the subject inhaled a solution of 1% isoprenaline sulphate by the method outlined by Jones (1966). At the end of this time the F.E.V.₁ was determined at intervals of one minute until the maximum rise was obtained.

The subject then sprinted for one minute and the F.E.V.₁ was repeated at one-minute intervals for 5 to 10 minutes or until an obvious maximum level had been obtained.

Results

The fall in F.E.V.₁ after long exercise and the rise after isoprenaline inhalation and short exercise serve as an indication of the degree of both bronchoconstriction and bronchodilatation which occurs under these circumstances (Drutel and Dechoux, 1952 ; Engström *et al.*, 1959 ; Capel, 1959 ; Jones *et al.*, 1962, 1963 ; Capel and Fletcher, 1964).

The sum of these values in litres, when expressed as a percentage of the predicted normal F.E.V.₁ (determined from a nomogram—Kory *et al.*, 1961), is an index of bronchial lability and may be termed the lability index.

$$\text{Lability index} = \frac{\text{Fall in F.E.V.} + \text{Rise in F.E.V.}}{\text{Predicted normal F.E.V.}} \times 100$$

Normal Group

The mean resting F.E.V.₁ for this group was slightly higher than that predicted from the nomogram used (mean F.E.V.₁ = 4.51 litres, predicted normal = 4.19 l.). After long exercise the mean F.E.V.₁ fell by 140 ml. (3.4%). After isoprenaline and short exercise it rose to a level 240 ml. (5.8%) above the resting level. This gives a lability index of 9.2 for this group.

When the results in those who smoked were compared with those in the non-smokers certain slight differences were noted. Both groups had the same mean age and height and hence the same predicted normal F.E.V.₁ (4.19 l.). The mean resting F.E.V.₁ in the smokers was 120 ml. less (2.9%) than in the non-smokers, and on long exercise the F.E.V.₁ fell by 180 ml. as compared with 100 ml. in the non-smokers. The rise above the resting level after isoprenaline and short exercise was 220 ml. in the non-smokers and 240 ml. in the smokers. Hence the lability index in the smoker was slightly higher than in the non-smoker.

The lability index of the group as a whole is similar to that found in normal children. One of the smokers had a lability index of 20, but all the others were below 15. The highest index in the non-smokers was 15, and the remainder, except for two with an index of 11 and 12, were below 10.

The F.E.V.₁/F.V.C. ratio in this group was above 85% in all phases of the experiment.

Adults with a History of Asthma

The results in this group are given in Table I. The mean resting F.E.V.₁ was 3.93 l., while the predicted normal for their mean age and height was 4.38 l. The mean resting F.E.V.₁ was therefore within the normal range at 88% of normal. The mean resting F.E.V.₁/F.V.C. ratio was 75%.

After long exercise there was a considerable fall in F.E.V.₁ to a mean of 2.69 l., indicating a drop of 1.24 l. below the resting

TABLE I.—Adults with a History of Asthma in Childhood

No.	Age	Height		N. F.E.V. ₁ (l.)	Resting		After Exercise		After Iso- prenaline		Lability Index (%)
		in.	cm.		F.E.V. ₁ (l.)	%N	F.E.V. ₁ (l.)	%N	F.E.V. ₁ (l.)	%N	
1	18	71	180	4.50	3.94	88	2.42	53.7	4.32	96	42
2	20	66	168	4.05	3.37	83	1.95	48.1	4.15	102	52
3	20	70½	179.3	4.50	3.84	85	2.82	62.6	4.30	95	55
4	20	68	173	4.22	3.60	85	3.30	78.2	3.94	93	15
5	19	72	183	4.70	4.08	87	3.08	65.5	4.19	89	23
6	20	68	173	4.25	3.79	89	1.95	45.8	4.11	97	51
7	31	74	188	4.45	3.96	89	2.86	64.2	4.19	94	30
8	29	72½	184.3	4.40	4.89	111	3.20	72.7	5.00	114	42

* Research Fellow in Child Health.

† Alder Hey Children's Hospital and the Department of Child Health, University of Liverpool.

level. There was also at this stage a fall in the F.E.V.₁/F.V.C. ratio to 60%.

Following isoprenaline and short exercise there was a rise to 4.27 l., which was 340 ml. above the resting F.E.V.₁. Hence the maximum F.E.V.₁ attained at the end of the experiment was about 97% of normal. The F.E.V.₁/F.V.C. ratio at this time was 78%. The lability index for the whole group was 38.

Adults with Asthma

The mean predicted normal F.E.V.₁ for this group was 4.19 l. However, the mean resting F.E.V.₁ was only 2.39 l. (57% of normal). After exercise the mean F.E.V.₁ fell to 1.35 l. (actual fall of 1.04 l.) and after isoprenaline and short exercise rose to 3.27 l., which was 880 ml. above the resting level.

The F.E.V.₁/F.V.C. ratio at rest was 65%, but after long exercise it fell to 50%. At the end of the experiment the mean ratio was 72.5%.

The lability index for this group was 46.

TABLE II.—Adults with Asthma

No.	Age	Height		N. FEV ₁ (l.)	Resting		After Exercise		After Iso- prenaline		Lability Index (%)
		in.	cm.		FEV ₁ (l.)	%N	FEV ₁ (l.)	%N	FEV ₁ (l.)	%N	
1	20	65	165	3.95	2.27	57	1.30	33	3.20	81	48
2	28	68	173	4.00	2.04	51	1.19	29.7	2.45	61	31
3	24	72	183	4.45	1.96	44	1.49	33	3.10	69	37
4	23	69	175	4.25	3.06	72	1.20	28	3.95	87	60
5	21	71½	181.3	4.50	3.45	74	1.69	37	3.66	86	57
6	18	66	168	4.00	2.45	61	1.69	42	3.45	86	42
7	19	69	175	4.30	2.95	69	1.30	30	3.71	86	56
8	30	69½	176.3	4.10	2.85	69	2.10	51	3.20	78	28
9	29	74	188	4.50	1.63	36	1.05	23	3.65	81	58
10	30	67½	171.3	3.90	2.05	52	0.90	23	3.05	78	55
11	28	68	173	4.20	1.66	39	0.96	23	2.62	62	40

TABLE III.—Mean Values for F.E.V.₁ in the Three Groups

Group	Age	Height		Pre- dicted FEV ₁ (l.)	Resting FEV ₁ (l.)	After Exercise FEV ₁ (l.)	After Iso- prenaline FEV ₁ (l.)	Lability Index (%)
		in.	cm.					
Normal ..	23.8	68.7	174	4.19	4.51	4.37	4.75	9
History of asthma ..	22.1	70.2	178	4.38	3.93	2.69	4.27	38
Asthma ..	24.5	69.0	175	4.19	2.39	1.35	3.27	46

FIG. 1.—F.E.V.₁ at rest (A), after long exercise (B), and after isoprenaline and short exercise (C). Mean and range.

The results in this group are shown in Table II. Table III summarizes the mean values found in all the groups. A diagrammatic comparison is shown in Fig. 1 and in Fig. 2, one individual from each group has been selected and matched for age, height, and predicted normal F.E.V.₁.

FIG. 2.—Changes in F.E.V.₁ occurring in one subject from each group. (Predicted normal = 4.5 litres $\pm$ 0.8 l.)

Discussion

Normal Group

It will be seen from the results that the lability index in this group was 8 for the non-smoker and 10 for the smoker.

The resting F.E.V.₁ in the smokers was slightly lower than in the non-smokers, although the mean was above the predicted normal. There was a greater fall in F.E.V.₁ after long exercise in the smoker and a correspondingly higher rise after isoprenaline and short exercise.

The lability index for the two groups as a whole was 9, with a range of 5 to 15 in non-smokers and 5 to 20 in smokers. These values are similar to those that have been found in normal children.

Adults with a History of Asthma but Symptom-free

Many follow-up studies of asthma from childhood into adult life have been carried out, and the number of patients who were symptom-free at the time the studies were undertaken varied from 30 to 50% (Bullen, 1929; Rackemann and Edwards, 1952; Engström and Kræpelien, 1957; Ryssing, 1959; Johnstone and Crump, 1961; Ogilvie, 1962; Ryssing and Flensburg, 1963).

Some of these studies were retrospective surveys and gave an indication of the prognosis of asthma; others were performed to assess the benefit of therapy. A physiological assessment of young adults who have either "grown out" of their asthma or who have improved after treatment does not seem to be recorded in the literature.

In the series carried out by Ryssing and Flensburg (1963), of 442 asthmatic children 37% had been symptom-free for at least one year. They subdivided these into those who developed dyspnoea on effort easily and those who did not. This appears to be the only attempt to determine the status of the child cured or having grown out of his asthma, and this with regard only to dyspnoea and exercise tolerance. The absence or presence of

dyspnoea is not in itself a reliable indication of the degree of ventilatory defect that may be present (Leiner *et al.*, 1965).

There appears to be reasonable agreement between different workers regarding the classification of asthma with respect to the severity of symptoms, but there is as yet no satisfactory method of correlating this physiologically. The use of F.E.V.₁ or the F.E.V.₁/F.V.C. ratio (Engström *et al.*, 1959), or the determination of peak-flow rate (Pearson, 1963), would have produced normal results in this group had they been studied at rest.

However, the determination of the airways lability by the method suggested in this article demonstrates that in this group there is a gross abnormality present which would otherwise not have been discovered.

The lability index in this group appears to bear no relation to the agents (allergy, infection, or emotion) which were thought to have precipitated the attacks of asthma. It is also unaffected by the length of history or the period of freedom from symptoms. There appears to be, however, a direct relation between the severity of the asthma as expressed by the frequency of attacks and the present ventilatory capacity as determined by the lability index—that is, the subjects who had the greatest fall in F.E.V.₁ on exercise were in fact those with the greatest degree of incapacity as children.

Pearson (1958), in an analysis of 625 cases, found that 47 had had periods of freedom from one to 40 years before developing a recurrence of symptoms. Rackemann (1958), in a study of 272 patients with "intrinsic" asthma, found 18 cases in which allergic asthma in young people was followed by a clear interval lasting from 10 to 30 years, during which time they were symptom-free. This period was followed later by asthma of the "intrinsic" type. In this paper and in an earlier one (Rackemann and Edwards, 1952) it is suggested that in those individuals who are not free of symptoms or who, after a period of freedom, develop a recurrence of their asthma an abnormal basic mechanism of some kind is still operating. They further suggest that the fact of long intervals of freedom between attacks makes the concept of a fundamental defect hard to justify.

Our findings have shown that the mechanism which was present during the time the asthma was active can still be demonstrated, despite the absence of symptoms. A comparison of the results in these adults with those in the children in groups 1 and 2 (Jones, 1966) shows that they conform physiologically and that their airways exhibit the same degree of lability. Engström *et al.* (1959) have shown that in the child with asthma the ventilatory defect persists despite the absence of symptoms. If the symptom-free period is therefore extended from a few weeks, as it is in the child, to years, as it is in the adult, the same abnormality persists, the only difference being that the child continues to have attacks.

It appears, therefore, that these individuals are in a latent phase of asthma and that the potential to develop a recurrence of symptoms (or the fundamental defect) is still present and may or may not be "triggered off" at a later stage by some aggravating factor.

Whether or not this mechanism was present before the onset of symptoms is of course difficult to postulate, but this could be determined by a follow-up study of children with hay-fever. It is known that 43% of hay-fever subjects will eventually develop asthma (Frankland and Gorrill, 1953). Thirteen children with hay-fever have been studied in this department and their lability index has been determined. Six were found to have an abnormally high figure. Further studies may show that those with a high lability index may be the ones who will develop asthma at a later date.

Asthma Group

In adult asthmatics the mean resting F.E.V.₁ was only 57% of normal. This confirms the fact that most of the individuals in this group had moderate-to-severe asthma and possibly also some degree of emphysema. The actual fall and rise in F.E.V.₁ in this group were similar to those found in the symptom-free group, the only difference being that the F.E.V.₁ was at a lower level.

The adults with asthma conform physiologically to those children found in group 3 (Jones, 1966)—that is, the resting F.E.V.₁ is below the normal range, the amount depending on the severity of the asthma, and the lability index is high.

Summary

Ventilatory capacity in a group of young adults who had a history of asthma in childhood but who had been symptom-free for an average period of four years was assessed by determining the changes in F.E.V.₁ which followed long exercise and subsequently isoprenaline inhalation and short exercise.

The results of this group are compared with a normal group and with a group of adults with asthma.

The changes which occur in F.E.V.₁ under these circumstances indicate the airways lability, and when expressed as a percentage of the predicted normal F.E.V.₁ may be termed the lability index.

The group under study were found to have an abnormally high lability index, indicating that some abnormal mechanism was still operating despite the absence of symptoms.

The implications of these changes are discussed, and it is suggested that adults who suffered from asthma as children but who have become symptom-free are in a latent phase of asthma. They may remain in this phase indefinitely, but they still have the potential to develop a recurrence of their symptoms.

We would like to thank Professor J. D. Hay for facilities provided in the Department of Child Health; Dr. Blair Macaulay for referring some of the adults with asthma; Dr. W. E. Smellie and the staff of the University of Liverpool Student Health Service; and Mr. J. C. Kay for his assistance with the experimental work. We would also like to thank the medical students and students of other faculties at the University of Liverpool for participating in this work.

REFERENCES

- Bullen, S. S. (1929). *N.Y. St. J. Med.*, **29**, 545.
- Capel, L. H. (1959). In *Bronchial Asthma*, p. 45. Chest and Heart Association, London.
- and Fletcher, E. C. (1964). *Brit. J. Dis. Chest*, **58**, 174.
- Drutel, P., and Dechoux, J. (1952). *J. franç. Méd. Chir. thor.*, **6**, 517.
- Engström, I., and Kræpelien, S. (1957). *Acta paediat. (Uppsala)*, **46**, 81.
- Escardó, F. E., Karlberg, P., and Kræpelien, S. (1959). *Ibid.*, **48**, 114.
- Frankland, A. W., and Gorrill, R. H. (1953). *Brit. med. J.*, **1**, 761.
- Gaensler, E. A. (1951). *Amer. Rev. Tuberc.*, **64**, 256.
- Johnstone, D. E., and Crump, L. (1961). *Pediatrics*, **27**, 39.
- Jones, R. S. (1966). *Brit. med. J.*, **2**.
- Buston, M. H., and Wharton, M. J. (1962). *Brit. J. Dis. Chest*, **56**, 78.
- Wharton, M. J., and Buston, M. H. (1963). *Arch. Dis. Childh.*, **38**, 539.
- Kory, R. C., Callahan, R., Boren, H. G., and Syner, J. C. (1961). *Amer. J. Med.*, **30**, 243.
- Leiner, G. C., Abramowitz, S., Lewis, W. A., and Small, M. J. (1965). *Amer. Rev. resp. Dis.*, **92**, 822.
- McKerrow, C. B., McDermott, M., and Gilson, J. C. (1960). *Lancet*, **1**, 149.
- Ogilvie, A. G. (1962). *Thorax*, **17**, 183.
- Pearson, R. S. B. (1958). *Acta allerg. (Kbh.)*, **12**, 277.
- (1963). *Folia allerg. (Roma)*, **10**, 421.
- Rackemann, F. M. (1958). *Acta allerg. (Kbh.)*, **12**, 407.
- and Edwards, M. C. (1952). *New Engl. J. Med.*, **246**, 815.
- Ryssing, E. (1959). *Acta paediat. (Uppsala)*, **48**, 255.
- and Flensburg, E. W. (1963). *Ibid.*, **52**, 97.
- Tiffineau, R., Bousser, J., and Drutel, P. (1947). *Paris méd.*, **37**, 624.