Ventilatory Function in Subjects with Childhood Asthma who have Become Symptom Free

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Blackhall, M. I. (1970). *Archives of Disease in Childhood*, 45, 363. **Ventilatory function in subjects with childhood asthma who have become symptom free.**

Ventilatory function was studied in 12 males who suffered from asthma in childhood, but who had been free of symptoms for an average period of 11 years. Though resting levels of FEV₁ and the FEV₁/FVC ratio were in most cases normal, an abnormal degree of bronchial lability was found in 7 subjects. An increase in RV was noted in the majority of subjects.

The paediatrician who looks after children with asthma is clearly concerned with the long-term prognosis, as it is one of the commonest questions asked by parents. There is considerable evidence that the severe childhood asthmatic tends to continue to suffer from attacks in adult life (Unger, Unger, and Wolf, 1952; Ogilvie, 1962), but it is the clinical impression that the milder the asthma the more likely it is to disappear during adolescence.

Follow-up studies of subjects with childhood asthma indicate that a variable, but considerable, number become symptom free (Bullen, 1929; Rackemann and Edwards, 1952; Ryssing and Flensburg, 1963; Barr and Logan, 1964; Buffum and Settupane, 1966). Yet many subjects who have had an appreciable period of freedom from symptoms experience a recurrence of asthma (Rackemann, 1932; Pearson, 1958; Ryssing, 1959), suggesting that an abnormal mechanism continues to operate even during the symptom-free interval. The finding of an abnormal degree of bronchial lability 4-10 years after cessation of symptoms by Jones and Jones (1966) supports this theory. The present study concerns mainly the milder group of asthmatics, and presents evidence of persisting abnormalities of ventilatory function after a prolonged period of freedom from symptoms.

Subjects and Methods

Twelve males with childhood asthma who had been free of symptoms for a minimum period of 2 years were studied. 3 had attended the asthma clinic at Alder Hey

Children's Hospital, 5 were traced in the course of a follow-up study of adults who had attended the asthma clinic run by Professor C. A. Clarke, at the David Lewis Northern Hospital, Liverpool, 14-20 years previously, and the remaining 4 were members of the hospital staff.

Ventilatory studies. In all, the lability index was measured according to the method described by Jones (1966). The forced expiratory volume in one second (FEV₁) and the forced vital capacity (FVC) were measured by means of a Lode spirometer, the average value of three attempts, after practice, being used. Exercise lasting 8 minutes was then carried out, with the subject running on a treadmill. The speed and slope of the treadmill were adjusted during the early part of the 8-minute period so that a level of exercise was obtained for each subject which could be continued uninterrupted for the remainder of the period without producing undue stress. FEV₁ and FVC were measured in the post-exercise period at 2-minute intervals for 10 minutes, and the lowest value obtained was noted. Isoprenaline sulphate 1% was then given for 2 minutes, in divided doses, by a Wright's nebulizer with an air flow of 10 l./min. This was followed immediately by brisk exercise on the treadmill for 1 minute. The FEV₁ was then measured every minute for 5-6 minutes until a maximum value was reached. The lability index was then calculated according to the formula:

$$\text{Lability Index} = \left(\frac{\text{Fall in FEV}_1 + \text{Rise in FEV}_1}{\text{Predicted Normal FEV}_1} \right) \times 100$$

where Fall in FEV₁ = fall from resting level and where Rise in FEV₁ = rise from resting level

The predicted normal FEV₁ for subjects up to and including 18 years was obtained from the values given by Strang (1959), and for those over 18 years the formula of Cotes *et al.* (1966) was used.

Received 26 November 1969.

Lung volume and its subdivisions were measured using a closed-circuit helium-dilution technique (Gilson and Hugh-Jones, 1949). Preliminary studies were done to determine the accuracy of results using this method, duplicate estimations being made on 12 subjects. The mean change between first and second estimations was -0.013 ± 0.117 in the case of the Functional Residual Capacity (FRC), 0.051 ± 0.068 for the Residual Volume (RV), and -0.035 ± 0.102 for the Total Lung Capacity (TLC), indicating a satisfactory degree of repeatability.

A control series of normal subjects had lung volume estimations made and the data obtained from these were used to provide predicted normal values for the asthmatics. The results obtained from these normal subjects are reported elsewhere (Blackhall, 1969a).

Daily checks were made on the spirometers for leaks. All volumes were corrected to BTPS using the correction factors obtained from standard tables.

Results

It can be seen in Table I that all the subjects had originally had mild or moderate symptoms—none had severe asthma. The mean age of the group was 26.2 years (range 16–44 years) and the mean period of freedom from symptoms 10.6 years (range 2–32 years).

TABLE I
Clinical Details of Subjects

Case No.	Severity of Symptoms in Childhood	Present Age (yr.)	Period of Freedom from Symptoms (yr.)
1	Mild	16	9
2	Moderate	16	3
3	Moderate	18	2
4	Moderate	18	4
5	Moderate	22	11
6	Moderate	22	6
7	Mild	24	10
8	Mild	27	10
9	Moderate	30	16
10	Mild	33	20
11	Moderate	44	32
12	Mild	44	4
Mean		26.2	10.6
SD		9.5	8.3

The mean observed FEV_1 was 3.48 l., the predicted value being 3.93 l. (Table II). The difference between these values is not significant (see Table IV). The mean FEV_1/FVC ratio (Table II) is also in the normal range. The mean lability index, however, was 16.8%, which is somewhat higher than that obtained from most normal subjects, the majority of whom have values of < 15%. A minority of normal subjects lies in the 15–20% range, in which a number of mild asthmatics are also found.

TABLE II
 FEV_1 , FEV_1/FVC , and Lability Index

Case No.	FEV_1 (L)		FEV_1/FVC %	Lability Index %
	Observed	Predicted		
1	3.22	3.21	89	17
2	3.19	3.86	80	7
3	4.88	4.70	81	14
4	3.26	4.20	76	28
5	3.02	4.03	72	17
6	4.09	4.30	72	13
7	4.86	4.52	75	19
8	3.11	3.71	75	17
9	2.84	4.05	56	28
10	3.22	3.96	73	8
11	3.09	3.25	71	19
12	2.98	3.39	67	14
Mean	3.48	3.93	73.9	16.8
SD	0.69	0.46	7.7	6.2

It can be seen in Table II that though most subjects have good levels of FEV_1 at rest, only 5 subjects have completely normal values for lability index (Cases 2, 3, 6, 10, and 12). Two subjects have high values (Cases 4 and 9), and the remaining 5 are in the 15–20% range.

The results of lung volume estimations are shown in Table III. The striking fact is that only 2 subjects have values of RV which are less than the predicted levels (Cases 4 and 11). The mean value for RV is 1.64 l., the predicted value being 1.33 l. The difference between these means is significant (Table IV). The FRC and TLC are only marginally greater than the predicted values, and the differences are not significant.

Only one subject (Case 12) shows normal values for FEV_1 , RV, and lability index.

Discussion

The finding of an abnormal degree of bronchial lability with normal levels of FEV_1 and FEV_1/FVC is in agreement with the results of Jones and Jones (1966). The mean lability index here is considerably lower than the value of 39% found by these workers. There is, however, a difference in the length of time during which no symptoms have occurred—6 years in the case of the 1966 study, 11 years in the present study. Possibly of even greater significance is the difference in the mean age of the groups—22 years in the first study, 26 years in the present one. We have reported elsewhere a decrease with age in the labile component of airways resistance in asthmatics (Blackhall, 1969b), and this may explain the lower values in this series. Yet the fact remains that an increased degree of lability still exists in over half these subjects, and

TABLE III
Details of Lung Volume and its Subdivisions

Case No.	FRC (L)		RV (L)		TLC (L)	
	Observed	Predicted	Observed	Predicted	Observed	Predicted
1	2.77	2.13	1.27	0.88	5.34	4.95
2	2.96	2.66	1.68	1.08	5.78	6.16
3	3.82	3.83	2.03	1.64	8.50	8.03
4	2.64	2.89	1.07	1.29	6.03	6.42
5	3.11	2.76	1.68	1.23	6.01	6.30
6	3.70	3.27	1.66	1.43	7.60	7.18
7	4.33	3.72	2.13	1.60	8.36	8.01
8	2.97	2.43	1.37	1.10	6.16	5.88
9	3.23	3.13	1.73	1.36	7.47	7.16
10	2.68	2.63	2.00	1.30	6.85	6.47
11	2.57	2.95	1.40	1.48	5.90	6.46
12	3.30	3.00	1.62	1.58	6.69	6.71
Mean	3.17	2.95	1.64	1.33	6.72	6.64
SD	0.52	0.47	0.31	0.22	1.00	0.83

TABLE IV
Significance of Results

	t	Probability
FEV ₁	1.82	0.1 > p > 0.05
FRC	1.06	0.5 > p > 0.2
RV	2.68	0.02 > p > 0.01
TLC	0.20	p > 0.5

this may result in their being liable to experience further attacks of asthma if the appropriate stimuli required to trigger off an attack are encountered.

Of interest is the finding of raised values of RV in the majority of these patients, in association with a normal FEV₁. Briscoe (1965) has pointed out that the important effect on lung volume of obstructive airway disease is that the RV is increased in absolute amount above its predicted value. Cotes (1968) has remarked on the apparently irreconcilable findings of increased RV without an associated rise in airway resistance, and work by Gough (1952) has shown that no permanent anatomical changes occur in asthma, which could account for the raised RV. The observations of Tammeling, Berg, and Sluiter (1966) may shed some light on this. By examining spiograms, they found that there was little change in the FEV₁ until after FRC level was reached, when constriction became obvious. High transmural pressures applied during forced expiration could, by causing premature collapse of small peripheral air passages, lead to an increase in RV without affecting the FEV₁.

The length of time after cessation of symptoms for which these abnormalities persist is at present uncertain. The present series shows that one

individual free of symptoms for 20 years has retained a considerable increase in RV, and one 16 years after his last attack has a high lability index. It is possible that abnormalities may persist for the rest of the individual's life.

I wish to thank Professor J. D. Hay for making available to me the facilities of the Department of Child Health, Dr. R. S. Jones for advice and encouragement throughout this work, Professor C. A. Clarke for permission to study his patients, and Mrs. S. Dulson for technical assistance.

This work was supported by a Research Fellowship from the Department of Child Health, University of Liverpool, augmented by a grant from the Children's Research Fund.

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