Exercise-induced airway obstruction in relation to chronic obstructive lung disease

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Thorax, **29**, 16–20. **Exercise-induced airway obstruction in relation to chronic obstructive
lung disease.** Forty-two patients with chronic obstructive lung disease and clinically suspected
exercise-induced airway obstruction were studied to ascertain whether those with proven
exercise-induced airway obstruction had specific distinguishing features. Exercise-induced
airway obstruction (defined as a fall of FEV_1 of at least 10% of the pre-exercise values) was
detected in 20 of the 42 patients. These 20 were found to have a lower elastic recoil but
were otherwise identical with the remainder as regards clinical and physiological abnormality.
It is postulated that exercise-induced airway obstruction can be a manifestation of chronic
obstructive lung disease.

Previous studies by a number of investigators have
documented the effects of exercise on various
aspects of pulmonary function in exercise-induced
airway obstruction. Some investigators reported
this phenomenon in a large percentage of young
patients with uncomplicated asthma as defined by
the CIBA Foundation Symposium (1959). Other
studies (Fisher, Holton, Buxton, and Nadel, 1970;
Vasallo, Gee, and Domm, 1972) were undertaken
to define more fully the nature of the abnormal
response to exercise.

In adult patients exercise may be the only factor
which precipitates airway obstruction (Crompton,
1968; Stanescu and Teculescu, 1970). Unfortu-
nately, it has been difficult from most reports to
deduce the extent of chronic obstructive lung
disease, as defined by Orie, Sluiter, de Vries, and
Tammeling (1961) and Fletcher (1961) in these
patients with exercise-induced airway obstruction.
The present study was undertaken to delineate
further this category of patients in relation to
chronic obstructive lung disease and to some of
the symptoms of this disease.

SUBJECTS AND METHODS

Patients in hospital with chronic obstructive lung
disease who had experienced breathlessness after exer-

tion were referred to the laboratory for routine pul-
monary function tests. The special procedures outlined
below were explained to each subject in detail before
participation in this study. All tests were made while
the subjects were in a steady-state phase of their
chronic lung disease. The tests were completed within
a few days and no subject was clinically ill on the days
of the study. The severity of the chronic obstructive
lung disease was graded from 0 to 4 according to the
prevalence of the following respiratory symptoms:
cough, phlegm production, attacks of dyspnoea at
rest, and breathlessness during exertion. The gradation
was based on the history and clinical observation
(Tammeling, Sluiter, Hilvering, and Berg, 1971). The
age of onset of the disease was also included. The
subjects were examined and inquiry was made con-
cerning symptoms and signs of nasal disease. The
results of allergy skin testing, histamine threshold
concentration indicating bronchial hyperreactivity (de
Vries *et al.*, 1964), blood and sputum eosinophil
counts, and smoking habits were recorded.

Measurement of vital capacity (VC), one second
forced expiratory volume (FEV_1), and maximum
voluntary ventilation (MVV) was performed with a
Lode D 53R spirometer. Residual volume (RV) was
determined by the closed-circuit helium dilution
method. Total lung capacity (TLC) was calculated as
the sum of VC and RV. Using the method of
Hilvering (1963), transpulmonary pressure was
measured as the pressure difference between the
mouth and oesophagus with the subject in the sitting

position. Transpulmonary pressure at full inspiration (P_{TLC}) was measured after a very slow maximal inspiration. Using a slow vital capacity manoeuvre, the quasistatic compliance was calculated from the rectilinear part of the expiratory volume-pressure curve above the level of the functional residual capacity.

The mean pressure (Pvisc), as the expression of mechanical work during spontaneous breathing, was derived from the volume pressure loop at rest (Pvisc = surface area of the volume pressure loop divided by the corresponding tidal volume). Bronchodilatation was induced by intramuscular administration of 25 mg of thiazinamium[1]. This is a drug with antihistaminic and anticholinergic properties (Booy-Noord *et al.*, 1957), and the effect was measured 30 minutes after injection. Blood gas tensions were measured with Radiometer glass and membrane electrodes.

For the exercise test a Lode electric bicycle ergometer was used. The external work load given to the subjects was determined by their pre-exercise FEV_1 and by their sex and age. The exercise test was preceded by a warming-up period of one minute and its duration was six minutes in all studies. The six-minute exercise period was considered necessary for adjustment of respiration and circulation to the work load (Åstrand and Rodahl, 1970). The heart rate was monitored electrocardiographically and was recorded at the end of six minutes' exercise. The FEV_1 was measured before exercise. Statistical analysis for significant differences between groups was performed using Student's *t* test for lung function and laboratory data and the chi-square test for clinical data. We tested the hypothesis that there was no significant difference between group 1 and group 2.

RESULTS

Twenty of the 42 patients studied had a post-exercise decrease in excess of 10% of the pre-exercise FEV_1 value and were allocated to group 1, while the remaining 22 patients were placed in group 2.

HISTORY AND CLINICAL FINDINGS (Table I) The two groups did not differ significantly with respect to age of onset of the complaints, incidence of cough and phlegm production, severity of dyspnoea and breathlessness during exertion, family history, smoking habits or presence of nasal disease. The mean age was the same in both groups (30 years) with a range of 14 to 59 years in group 1, and 14 to 54 years in group 2. There were 15 men and 5 women in group 1 and 18 men and 4 women in group 2. There was also no difference in the mean height and weight. The results of allergy testing, including skin tests and, in the case of positive

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results, of inhalation tests with house dust, fungi or pollen, were not significantly different in either group, as was the case with the histamine threshold concentrations and blood and sputum eosinophil counts. The individual data may be obtained from the authors on request.

TABLE I
HISTORY AND CLINICAL FINDINGS

	Group 1 (Total 20 Patients)		Group 2 (Total 22 Patients)	
	Mean ± SEM		Mean ± SEM	
Age (years)	30	3·15	29·5	2·59
Height (cm)	174	0·02	174	0·01
Weight (kg)	67	2·71	71	2·40
Age onset	14	2·55	18	2·85
Blood eosinophils (mm³) ..	580	70·56	373	62·20
Histamine threshold (mg/ml)	21	2·69	24	2·22
	No. of Patients	%	No. of Patients	%
Family history	14	70	15	68
Smoking	8	40	9	40
Nasal disease	12	60	7	32
Cough				
Grade 0	7	35	10	45
,, 1 or 2	9	45	10	45
,, 3 or 4	4	20	2	10
Phlegm production				
Grade 0	14	70	14	63
,, 1 or 2	4	20	6	27
,, 3 or 4	2	10	2	10
Attacks of dyspnoea at rest				
Grade 0	9	45	8	37
,, 1 or 2	0	0	1	5
,, 3 or 4	11	55	13	69
Breathlessness during exertion				
Grade 0	6	30	4	18
,, 1 or 2	5	25	10	45
,, 3 or 4	9	45	8	37

SEM = standard error of mean.

RESPIRATORY FUNCTION AND BLOOD GASES (Table II) The means of total lung capacity (TLC) and vital capacity (VC) as a percentage of the predicted values (Group 1: TLC = 109% and VC = 102%; Group 2: TLC = 100% and VC = 98%) were normal and similar in both groups. After bronchodilatation the means were about the same as before. The FEV_1 and MVV before bronchodilatation tended to be lower in group 1 although there were no significant differences between the means of the two groups. In both, the means of FEV_1 and MVV became normal after bronchodilatation. The mean of the pressure (Pvisc) to overcome the mechanical work during quiet breathing tended to be higher in group 1 ($p < 0.05$); however, after bronchodilatation, all mean values were within the normal range. The quasistatic compliance was normal in both groups, but after bronchodilatation was slightly increased in group 1 ($p < 0.05$); the values indicated abnormally compliant lungs. In group 1, the transpulmonary pressure at full inspiration (P_{TLC}) was less than in group 2 ($p <$

TABLE II
RESPIRATORY FUNCTION, BLOOD GASES, AND pH BEFORE AND AFTER THIAZINAMIUM

	Group I Mean	Group I ±SEM	Group II Mean	Group II ±SEM	Significance of Difference of Means
TLC (l. BTPS):					
Predicted	6·3	0·26	6·4	0·21	ns
Before 25 mg i.m. of thiazinamium	6·9	0·44	6·4	0·21	ns
After	7·0	0·43	6·5	0·22	ns
VC (l. BTPS):					
Predicted	4·8	0·22	4·9	0·15	ns
Before	4·9	0·31	4·8	0·18	ns
After	5·1	0·32	5·0	0·16	ns
FEV_1 (l. BTPS):					
Predicted	3·6	0·19	3·7	0·13	ns
Before	3·0	0·22	3·5	0·18	ns
After	3·8	0·23	4·0	0·18	ns
MVV (l. BTPS/min):					
Predicted	95	4·74	94	4·97	ns
Before	87	6·66	96	6·12	ns
After	105	7·11	108	6·93	ns
P visc. (cmH_2O):					
Before	3·4	0·40	2·5	0·12	$P < 0·05$
After	1·9	0·24	1·7	0·12	ns
Compliance (l./cmH_2O):					
Before	0·34	0·02	0·27	0·02	ns
After	0·44	0·04	0·32	0·05	$P < 0·05$
P_{TLC} (cmH_2O):					
Before	14	1·77	21	1·70	$P < 0·05$
After	14	1·40	21	2·10	$P < 0·05$
pH (units)	7·41	0·005	7·40	0·002	ns
$Paco_2$ (mmHg)	34	1·14	34	0·72	ns
Pao_2 (mmHg)	92	1·50	94	1·82	ns

TLC=total lung capacity; VC=vital capacity; FEV_1=one-second forced expiratory volume; MVV=maximum voluntary ventilation; Pvisc=mean pressure to overcome viscous resistance; P_{TLC}=transpulmonary pressure at full inspiration; Pao_2=arterial oxygen tension; $Paco_2$=arterial carbon dioxide tension; BTPS=body temperature and pressure saturated with water vapour; SEM=standard error of mean.

TABLE III
EFFECT OF EXERCISE ON FEV_1 (l. BTPS) IN 42 PATIENTS WITH CHRONIC NONSPECIFIC LUNG DISEASE WITH (GROUP I) OR WITHOUT (GROUP II) EXERCISE-INDUCED AIRWAY OBSTRUCTION

	Group I Mean±SEM	Group I	Group II Mean±SEM	Group II
FEV_1 normal values	3·63	0·19	3·67	0·13
before exercise	3·33	0·24	3·54	0·16
Exercise work (Watts)	142	7·65	138	4·11
Heart rate, at six minutes work	172	3·86	170	4·03
FEV_1 after exercise, minutes 1..	3·09	0·26	3·58	0·16
,, ,, ,, 2..	2·89	0·28	3·58	0·17
,, ,, ,, 3..	2·73	0·22	3·57	0·16
,, ,, ,, 10..	2·75	0·24	3·59	0·16
,, ,, ,, 12..	2·65	0·22	3·63	0·17
,, ,, ,, 14..	2·75	0·21	3·64	0·17
,, ,, ,, 28..	2·83	0·22	3·66	0·17
,, ,, ,, 30..	2·98	0·24	3·68	0·17

SEM=standard error of mean.

cise was between 10 and 14 minutes and recovery began within the next 14 minutes. In the present study, 10 patients showed a maximal decrease of FEV_1 of 10 to 20% of its pre-exercise value, in six patients it was 20 to 40%, and in only four patients was it more than 40%. Patients in group 2 showed no decrease in FEV_1 after exercise. An increase of FEV_1 occurred, although in the majority it was small. No correlation was noted between the decreased FEV_1 and clinical features.

DISCUSSION

Investigations comparing two groups of patients suffering from chronic obstructive airway disease are difficult to standardize. We attempted to avoid the variability due to the disease by studying patients while they were in hospital and in a steady state of their disease. The data show that both groups of patients were relatively well, as can be seen from respiratory, blood, and exercise studies.

In this study, the subjects with exercise-induced airway obstruction did not differ from the control group in incidence or severity of respiratory symptoms and clinical findings. The present data show that both groups had similar pulmonary function and blood gases. The most significant differences were found in the elastic recoil estimated from the P_{TLC} when compared with the group 2 values. In group 1 a decreased elastic recoil occurred with little expiratory airway obstruction at the time of the investigation. Penman, O'Neill, and Begley (1970) demonstrated that several patients with loss of lung recoil had no appreciable limitation of forced expiratory flow. Woolcock and Read (1968) suggested that long periods of marked hyperinflation with permanent stretching of the elastic

0·05). The abnormally low pressure after bronchodilatation occurred without increased total lung capacity. The mean values of arterial pH, carbon dioxide tension, and oxygen tension were not significantly different in the two groups and were all within normal limits.

EXERCISE TESTS (Table III) There were no significant differences between the means of FEV_1 before exercise, level of exercise work, and heart rate after six minutes' work, indicating that probably there was no difference in training in cycling or fitness between the groups. In fact the only significant difference in all the data shown in Table III were the FEV_1 values after exercise. The probability of the differences being due to chance was less than 0·05 and 0·01 in the first and second minute after exercise. In seven patients the maximal decrease in FEV_1 occurred between 1 and 3 minutes, in 10 patients it was between 10 and 14 minutes, and in only four between 28 and 30 minutes. The mean maximal decrease after exer-

elements of the lung tissue might have been responsible for the loss of elastic recoil. The investigations of Anderson, McEvoy, and Bianco (1972) have recently demonstrated that a marked hyperinflation occurs in patients with exercise-induced airway obstruction after exercise, and that it seems to be spontaneously reversible. Thus, it is possible that the loss of elasticity in the patients of group 1 is secondary to repeated lung hyper-inflation after exercise.

In the present investigation no connection could be demonstrated between post-exercise airway obstruction and an increase in airway responsiveness as detected by the histamine threshold. However, the coincidence of post-exercise airway obstruction and a concomitant increase in airway responsiveness to cold air, forced expirations or hyperventilation has recently been emphasized by Simonsson, Skoogh, and Ekström-Jodal (1972). Differences in technique and probably also in the patient's condition at the moment of investigation make it difficult to compare our results with those of Simonsson and co-workers. It is generally accepted that exercise-induced airway obstruction occurs after exercise in a large percentage of asthmatic patients, as defined by the Ciba Foundation Symposium (1959), and particularly in the younger age groups (Katz, 1970). In our experience, this phenomenon can also occur in older age groups and in patients belonging to the group of chronic obstructive lung diseases, as defined by Orie *et al.* (1961) and Fletcher (1961). The report of Simonsson and associates (1972) points in the same direction.

In our experience, the clinical condition of the patient influences the presence of post-exercise airway obstruction: when investigated during absence of complaints, it is often not possible to reproduce the phenomenon. In one patient we were able to demonstrate the obstruction after exercise only when he had a bacterial bronchitis. A second patient only showed exercise-induced airway obstruction 24 hours after a positive reaction to the inhalation of house dust. Thus, it is possible that the inconsistency of the reports in the literature may be due at least partly to these concomitant factors.

CONCLUSION

After exercise a certain number of patients with chronic obstructive lung disease increase their airway resistance to a greater extent than do healthy individuals. The same can be said about the bronchial obstructing activity (de Vries *et al.*,

1964) of various physical and chemical stimuli. It is consistent with reports from the literature that the increased 'responsiveness' of the airways to exercise in this group of patients may be considered a manifestation of the obstructive lung disease and that exercise may act as a triggering mechanism.

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