

Pulmonary rehabilitation in chronic respiratory insufficiency · 2

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Exercise in patients with chronic obstructive pulmonary disease

Michael J Belman

Exercise is widely promoted as a means of improving physical endurance. It is recommended, not only for the healthy, but also for individuals with various disabilities and disease. In respiratory medicine we have witnessed several decades of investigation directed not only at the pathophysiology of exercise in patients with chronic obstructive pulmonary disease (COPD), but also at the effects of exercise training in improving function. As was initially the case with coronary artery disease, many physicians of the mid 20th century adopted a very conservative approach and generally discouraged exercise in patients with significant COPD. Despite the pleas for greater physical exercise for patients with chronic lung disease by Barach, a pioneer of pulmonary medicine,¹ it was only in the late 1960s and early 1970s that his ideas were aggressively pursued. In the USA there is now widespread support for pulmonary rehabilitation programmes which, almost without exception, include a liberal dose of exercise training. The transfer of the standard recommendations for exercise training to healthy subjects and even cardiac patients has not been easy. The pattern of exercise response in patients with COPD presents some unusual and, in some cases,

unique features that require radical rethinking of the traditional advice given to the normal subject and those with heart disease. The purpose of this review is to highlight key features of the pathophysiology of this exercise pattern in patients with COPD and to analyse the evidence which supports exercise training.

Exercise limitation in COPD

Abnormalities of ventilatory mechanics, respiratory muscles, alveolar gas exchange, and cardiac function are present to varying degrees in patients with COPD. Delineation of the major mechanisms underlying exercise limitation has obvious value in that treatment aimed at reducing the severity of a major limiting factor would be beneficial in improving exercise function. This process has not always been easy and it is likely that the importance of limiting factors is not the same in every patient. The discussion below deals with each of these factors separately, although they are probably interrelated in most patients.

VENTILATION AND PULMONARY MECHANICS

This is one of the most important factors that limits exercise performance. Expiratory air flow obstruction is the main pathophysiological result of the alveolar wall destruction and bronchiolar narrowing which characterises this disease. In moderate to severe obstructive lung disease resting expiratory airflows approach or are equal to maximal airflow.^{2,3} In contrast to normal subjects in whom expiratory flow limitation may only occur during expiration at the highest work rates, patients with COPD show flow limitation over most or all of expiration at low exercise levels (fig 1). In patients with severe disease flow limitation is present at rest.⁴ The prolongation of expiration together with a higher than normal exercise breathing frequency leads inexorably to dynamic hyperinflation with an increase in end expiratory lung volume.⁵ The dynamic hyperinflation causes an increase in inspiratory loading and work through (1) a decrease in static compliance as patients now breathe along a shallower portion of the pressure-volume curve; (2) a high inspiratory threshold load caused by the need to generate additional pressure required to overcome elastic recoil pressure before inspiratory flow can begin (this increased threshold pressure has been referred to as intrinsic positive end

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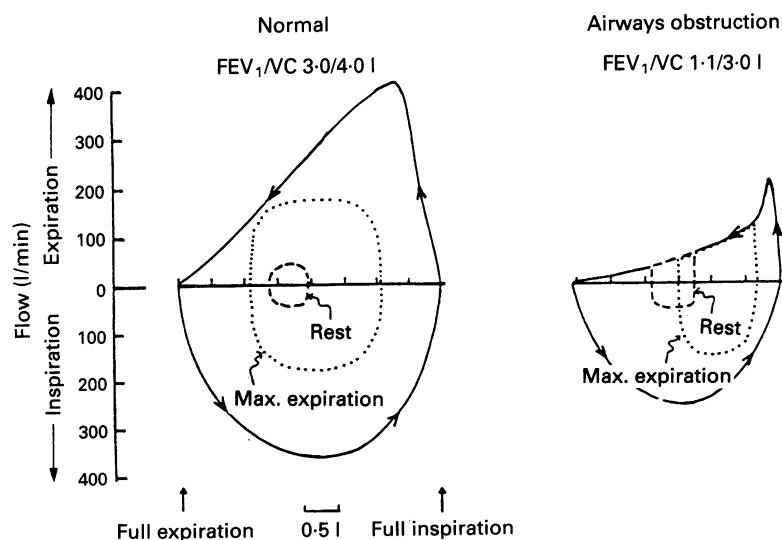


Figure 1 Spontaneous flow-volume curves at rest (dotted lines) and maximum exercise (dashed lines) as well as maximum flow-volume curves at rest (outer solid line) in a normal subject and a patient with chronic airways obstruction. Reproduced with permission from ref 2.

expiratory pressure); and (3) an exaggeration of dependence of compliance on frequency. As Younes⁵ has stated: "While the mechanical defect is primarily resistive in nature in expiration, the mechanical consequences are encountered in inspiration and are primarily restrictive in nature." The more severe the reduction in the forced expiratory volume in one second (FEV_1), the greater the increase in end expiratory lung volume.⁶ The dynamic hyperinflation brings with it an increase in inspiratory load, but it is a necessary evil for without it the patients with COPD would not be able to increase ventilation to meet the demands of exercise. As end expiratory lung volume rises the patient is able to increase maximum expiratory airflow by breathing along a higher portion of the expiratory flow-volume curve.^{4,7}

The importance of end expiratory lung volume in patients with mild COPD (FEV_1/FVC ratios of approximately 60%) has recently been emphasised.⁸ In these patients it was thought that ventilatory limitation plays only a minor part in contrast to patients with more severe disease. In a recent study, however, it was shown that, although the ratio of maximum exercise ventilation (\dot{V}_{Emax}) to the maximum voluntary ventilation at peak exercise was considerably less than 70%—a value traditionally used to rule out a ventilatory limitation—these patients demonstrated a rise in end expiratory lung volume and flow limitation during exercise. In contrast, age matched control subjects maintained or reduced their resting end expiratory lung volume and achieved a maximum oxygen consumption ($\dot{V}O_{2,max}$) which was 30% higher than the patients. These investigators concluded that, despite the mild degree of COPD, there was a significant impact on pulmonary mechanics during exercise.⁸

Because the respiratory system in the exercising patient with COPD fails to reach its relaxation volume, inspiration can only occur after respiratory muscles develop sufficient

force to overcome the recoil pressure of the hyperinflated chest. Preliminary studies have now examined the effect of applying continuous positive airway pressure as a means of providing inspiratory assistance.^{9,10} The results of this work showed that continuous positive airway pressure reduced the work of breathing and dyspnoea. In the study by O'Donnell and colleagues⁹ the exercise endurance was prolonged. This response emphasises the importance of negating the loading effect of the intrinsic positive end expiratory pressure.

Dodd and colleagues¹¹ have shown that patients with airflow obstruction attempt to compensate for the increase in end expiratory lung volume by actively recruiting abdominal and expiratory rib cage muscles during expiration. At the onset of inspiration the patients rapidly relaxed these muscles, an effect which allows them to exploit the outward recoil of the chest wall and gravitational descent of the diaphragm at the onset of inspiration. This reaction functions as a form of inspiratory assistance. On the other hand, excessive use of expiratory musculature during expiration increases oxygen utilisation of the expiratory muscles, further reducing the overall efficiency of breathing in these patients.¹²

It is well recognised that in moderate to severe COPD maximal exercise ventilation reaches a high percentage of the maximum ventilatory ventilation (MVV) at rest. This \dot{V}_{Emax}/MVV ratio may in fact even exceed 100% in patients with severe airflow obstruction.¹³ There are significant correlations between measures of expiratory airflow such as the FEV_1 and MVV on the one hand, and \dot{V}_{Emax} and $\dot{V}O_{2,max}$ on the other.^{14,15} Because of the relatively large scatter of the data, however, the confidence intervals of individual predictions are large and it is not possible to predict peak minute ventilation with great accuracy in an individual patient. For example, the 95% confidence interval of one equation is ± 18 l/min despite a correlation coefficient of 0.97.¹⁴ Factors other than mechanical ventilatory limitation also have a role (see below).

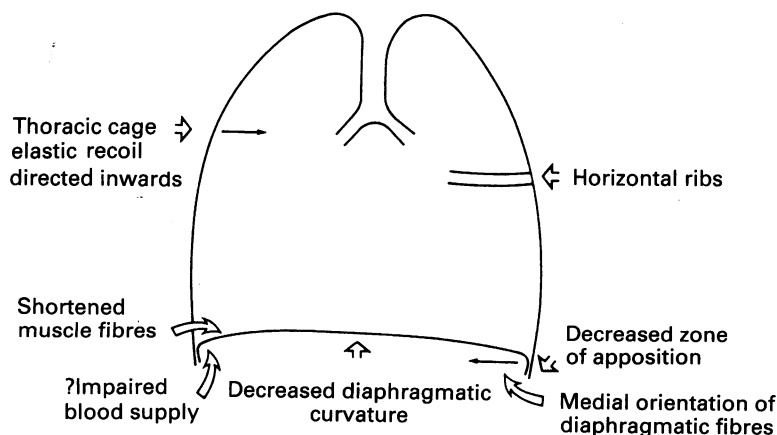
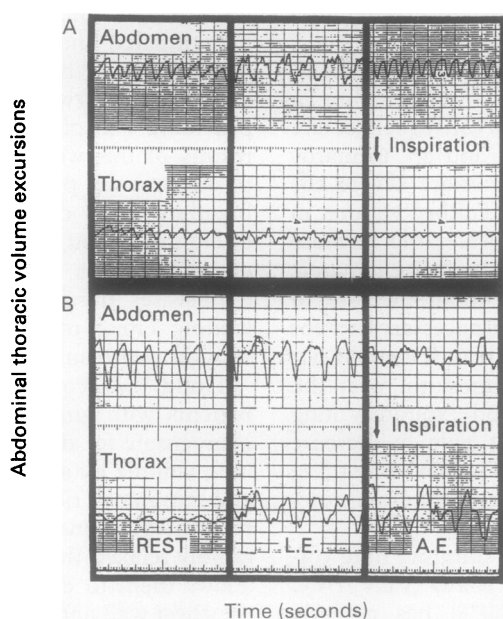


Figure 2 Detrimental effect of hyperinflation on respiratory muscle function. Reproduced with permission from ref 16.

RESPIRATORY MUSCLE DYSFUNCTION

Patients with COPD exhibit respiratory muscle weakness (see Tobin for review¹⁶). Intrinsic factors such as hypoxia, hypercapnia, acidemia, and malnutrition impair respiratory muscle contractility. Superimposed on this are the mechanical derangements which further weaken diaphragmatic function. Hyperinflation shortens the diaphragm, moving it to a disadvantageous portion of its length-tension curve. Moreover, the zone of apposition is reduced and this impairs the optimal inspiratory action of the muscle (fig 2).¹⁶ Although patients with COPD show compensatory changes in the diaphragm which allow for relative preservation of function even at the limits of hyperinflation,¹⁷ these inspiratory pressures are still well below those of normal subjects at functional residual capacity (FRC).¹⁸ Activity of the upper

Figure 3 Tracings of abdominal and thoracic excursions. Panel A shows excursions in a patient with synchronous thoracoabdominal movements at rest during leg exercise (LE) and arm exercise (AE). Panel B shows that the synchronous pattern observed at rest and during LE changes to dyssynchronous during AE. Full inward retraction during inspiration is seen in the last two breaths of the arm exercise tracing. Reproduced with permission from ref 19.



limbs^{19,20} is an additional aggravating factor which hampers diaphragmatic function. During arm work the stabilising effect of the shoulder girdle on the thorax is lost and the inspiratory load is shifted onto the diaphragm and muscles of expiration. In these circumstances the diaphragm is required to assume a greater load and, as noted above, is ill prepared to do so (fig 3).^{19,20} The net result is a greater limitation of arm than of leg exercise associated with the earlier onset of dyspnoea in many patients with severe airflow obstruction. As performance of most activities of daily living require repetitive upper extremity movement, this phenomenon has important implications for patients with COPD (see section on upper extremity training below).

RESPIRATORY MUSCLE FATIGUE

Whether or not respiratory muscle fatigue occurs during exercise in patients with COPD is not clear. Preliminary evidence from Pardy and coworkers²¹ showed that in some patients a decrease in the high to low ratio—an electromyographic index of fatigue—occurred in only some patients during exercise. The fact that the high to low ratio has proved useful in carefully controlled laboratory experiments does not imply that it can be transferred to use in individuals during exercise. As Younes has stated,²² a change in the ratio may occur between rest and exercise because of changes in breathing pattern and changes in the spatial relationship of the electromyographic electrode and the muscle. Moreover, other muscles recruited at higher exercise intensities may contaminate the signal. The presence of thoracoabdominal asynchrony during breathing has also been cited as support for the presence of inspiratory muscle fatigue. More recent evidence^{23,24} indicates, however, that asynchrony of the thorax and abdomen during inspiration is not pathognomonic of fatigue, but may be seen in circumstances in which an individual breathes against a high inspiratory load. With cessation of the loading the breathing pattern returns to normal, even

though presumably the low frequency fatigue induced by the loading persists for several additional hours. Definitive proof of fatigue would require documentation of decreased muscle contractility after performance of work. Rochester has emphasised that inspiratory muscle weakness is more important than fatigue.^{18,25} He emphasises the ratio of the pressure required per breath to the maximum inspiratory pressure ($P_{\text{breath}}/P_{\text{max}}$) as an index of the weakness. During exercise P_{breath} rises as inspiratory work increases while the rise in end expiratory lung volume and configurational changes in the diaphragm reduce the P_{max} . The net effect is a reduction in functional diaphragmatic strength during exercise.

IMPAIRED GAS EXCHANGE

Hypoxaemia, a common feature of COPD, frequently shows further reductions during exercise. A low diffusing capacity (<55% of the predicted value) has been used as a predictor of those patients in whom exercise desaturation will occur.²⁶ The hypoxaemia of exercise is largely due to the effects of a reduction in mixed venous PO_2 on low ventilation diffusion lung units²⁷ aggravated in some cases by hypoventilation. On the other hand, some patients do show an improvement in PaO_2 with exercise which must reflect an improvement in intrapulmonary ventilation perfusion matching.²⁸ There is little evidence for diffusion limitation. The absence of the normal exercise decrease in the physiological dead space to tidal volume ratio (V_D/V_T) further aggravates the ventilatory limitation in COPD. In order to maintain efficient carbon dioxide output in the presence of a reduced alveolar ventilation, greater than normal increases in total minute ventilation are required as exercise intensity increases²⁹ (see section on Lactic acidosis and exercise training below).

CARDIOVASCULAR FUNCTION

Remodelling of the muscular arteries and arterioles is the main cause of the increase in pulmonary vascular resistance.³⁰ These changes lead to thickening of the intima and narrowing of the arterial and arteriolar lumens and are more extensive than the increase in muscle seen in the media of medium and small arteries in people exposed to high altitude hypoxia. Other factors that play a part in the elevated pulmonary vascular pressures include emphysematous destruction of the vascular bed, alveolar hypoxia, increased alveolar pressure, increased haematocrit and acidosis.³¹

Commonly observed abnormalities of cardiovascular function during exercise are an increased heart rate/ $\dot{V}O_2$ ratio related to a shift upwards and to the left of the heart rate/ $\dot{V}O_2$ slope which itself, however, may be normal.^{2,32} In other words, at a comparable $\dot{V}O_2$ the heart rate in a patient with COPD is increased with a corresponding decrease in the oxygen pulse. This means that estimation of exercise intensity in these patients by

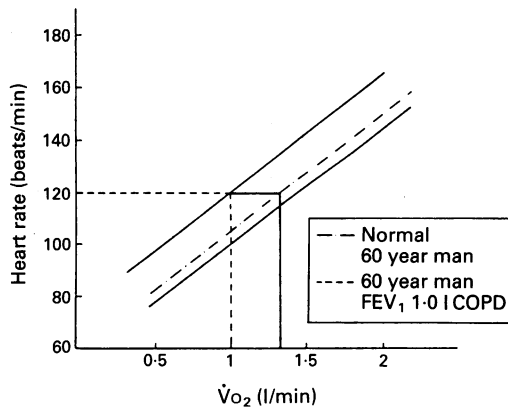


Figure 4 Normal heart rate response to exercise is illustrated by the parallel solid lines. In the patient with COPD, in whom the heart response is generally at the upper limit of normal, the $\dot{V}O_2$ achieved at a heart rate of 120 beats/min (1.0 l/min) would be less than a normal subject (1.33 l/min).

means of heart rate can be erroneous (fig 4).³³ A heart rate of 120–130 beats/min in a normal individual reflects a $\dot{V}O_2$ of greater than 1 litre/min while in a patient with COPD this may represent a significantly lower $\dot{V}O_2$. This phenomenon has implications for the intensity of exercise training which will be discussed later. The reduction in heart rates achieved at peak exercise are proportionately less than the reduction in peak $\dot{V}O_2$, and the maximal oxygen pulse at peak exercise is therefore smaller. The rise in the cardiac output/ $\dot{V}O_2$ relationship is considered generally to be normal² despite the fact that pulmonary vascular resistance is increased and there is a higher than normal rise in pulmonary artery pressure. The increased afterload on the right ventricle can cause right ventricular dysfunction, but whether or not this actually limits exercise is unclear.³¹

LACTIC ACIDOSIS

Lactic acid is produced during incremental exercise although the time at which it appears in arterial blood varies and is dependent on circulatory function and level of fitness. The point at which blood lactate rises has been termed the lactic acid threshold and precedes, by approximately 150 ml of $\dot{V}O_2$, the increase in minute ventilation related to the increased carbon dioxide output.^{34,35} This increase in ventilation can be detected by one of many indices as described by Wasserman and coworkers but, most recently, they have emphasised the use of the "V slope criterion."³⁶ In this index the rate of rise in carbon dioxide output is plotted against oxygen uptake. While oxygen uptake remains linear at the onset of lactic acid production, carbon dioxide output increases and so a break point can be discerned. This inflection point has been termed the "anaerobic threshold" by Wasserman and colleagues, while other investigators have used the term "ventilation threshold." This difference in terminology symbolises a heated controversy. Wasserman *et al* feel that the appearance of lactic acid truly indicates a transition to anaerobic glycolysis because of tissue

hypoxia.³⁷ Their critics disagree and consider that, while lactic acid certainly does rise during exercise, it does not necessarily imply anaerobiosis but merely an imbalance between lactate production on the one hand and its utilisation on the other.³⁸ In patients with COPD lactic acid and anaerobic thresholds can be determined even in those with moderately severe disease³⁹ although, clearly, peak lactate levels will be considerably reduced in these patients because of their overall reduction in exercise capacity.^{39,40} It should be noted that the lactic acid in these patients probably arises from working limb muscles since it is those patients who reach the highest work rates who show the highest lactate levels.⁴⁰ Conversely, patients with very severe obstructive disease in whom respiratory muscle work is high have low lactate levels and, moreover, lactate levels during isocapnic hyperpnoea are only marginally increased.⁴¹

Sue *et al*³⁹ feel that the V slope criterion is useful in detecting metabolic acidosis in these patients (fig 5) but recognition of V slope may not always be easy, as was shown in a recent study⁴² in which not only was there considerable interobserver variability in V slope detection but a significant number of patients with exercise induced metabolic acidosis did not develop inflection points. Conversely, inflection points were found in patients without metabolic acidosis. This finding detracts from the value of the V slope in detecting metabolic acidosis in patients with COPD (see section on Exercise training intensity below).

PERIPHERAL MUSCLE FATIGUE

Despite the emphasis on impaired ventilatory mechanics and dyspnoea it is now well documented that a significant number of patients with COPD will stop exercising because of peripheral muscle fatigue.⁴³ In a recent study about one third of patients stopped for this reason. In addition, both limb and respiratory

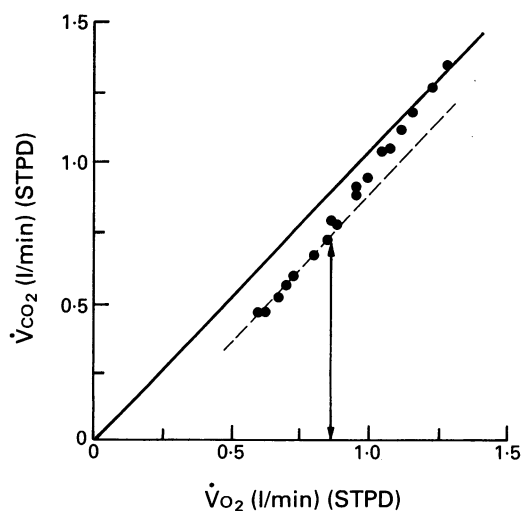


Figure 5 Carbon dioxide output ($\dot{V}CO_2$) plotted against oxygen uptake ($\dot{V}O_2$). When the anaerobic threshold is reached, $\dot{V}CO_2$ accelerates compared with $\dot{V}O_2$. The inflection point marking this acceleration is shown by the arrow. Reproduced with permission from ref 39.

muscle show parallel decrements in strength and contribute independently to reduced exercise capacity.

These are the major pathophysiological abnormalities seen in COPD, but other factors do play a part in limiting exercise. Their recognition is important as treatment aimed at improving functional capacity must take them into account. Additional factors include nutritional status through its effect on both limb and respiratory muscle strength and endurance,⁴⁴ perception of and response to breathlessness which varies amongst patients,^{45 46} and psychological factors such as depression, anxiety, and fear of exercise.⁴⁷ Furthermore, the role of deconditioning—a common problem in these patients because of their chronic inactivity—can aggravate the impaired exercise tolerance.⁴⁰ Although breathlessness is clearly related to the severity of abnormalities in expiratory air flow this is not the only factor, as recently emphasised by O'Donnell *et al*⁴⁸ who showed that patients with comparable levels of airway obstruction may have varying degrees of breathlessness. The major differences between mildly and severely breathless patients were the presence of hypoxaemia during exercise and an abnormally low diffusing capacity in the latter group. Other investigators have shown an additional effect of psychological and psychosocial factors on functional capacity over and above that of lung function. Their analyses showed that dyspnoea, respiratory muscle strength, and spirometry each contributed independently to functional limitation and emphasised that each of them should be assessed separately.⁴⁵

Exercise training in COPD

Pulmonary rehabilitation programmes vary in their complexity and may include several therapeutic components^{49 50} including (1) patient and family education; (2) treatment of bronchospasm by means of bronchodilators or reduction in bronchial secretions; (3) treatment of bronchial infections; (4) treatment of congestive heart failure; (5) oxygen therapy; (6) chest physical therapy including breathing technique training; (7) exercise reconditioning; and (8) psychosocial therapy and vocational rehabilitation.

CONTROLLED EXERCISE STUDIES

Although exercise reconditioning has long been considered an essential component of the rehabilitation process it is only very recently that a randomised study has confirmed this belief.⁵¹ In this eight week study 119 patients with COPD were randomised either to a comprehensive rehabilitation programme including exercise reconditioning or, alternatively, to an education control programme. The investigators provided education, physical and respiratory therapy, psychosocial support, and supervised exercise training to the treated group while the control group received twice weekly classroom instruction in respiratory therapy, lung

disease, pharmacology, and diet but did not exercise. Before and after the treatment and after an additional six months both groups underwent extensive physiological and psychosocial tests. The major finding of this study was that at eight weeks the improvement in exercise endurance as measured by treadmill walking showed a mean increase in treadmill time from 12.5 minutes to 23 minutes compared with an insignificant change from 12 to 13 minutes in the control group. At six months the treated group still maintained a comparable advantage with a treadmill endurance of approximately 21 minutes compared with 12 minutes in the control group. No difference in the quality of well-being scale—a measure of health related quality of life—was noted. This well designed randomised controlled study definitively established exercise therapy as an essential component of the pulmonary rehabilitation process.

Relatively few other studies have compared treated and control groups. In the study by Cockcroft and colleagues⁵² a treated group of 19 patients was compared with a control group of 20 patients. During training the patients used cycle exercise, rowing machines, and swimming and, in addition, free range walking was performed. This treatment was carried out for six weeks in a rehabilitation centre; patients were subsequently discharged and encouraged to continue walking and stair climbing. The control group was given no special instructions to exercise. The findings showed an increase in 12 minute walking distance and peak exercise $\dot{V}O_2$ and $\dot{V}E$ in the treated group at two months and these differences were significantly greater than those in the control group. The treated group also showed improvement in general wellbeing and dyspnoea. In a study by McGavin and coworkers⁵³ training was carried out by stair climbing at home, but the patients were tested with a 12 minute walk. In this study of 24 patients (12 in the exercise group and 12 in a control group) a significant, albeit small, improvement in the 12 minute walking distance was noted. Other notable findings were an increase in stride length in the exercise group but no change in peak $\dot{V}O_2$, heart rate, or minute ventilation as measured during an incremental cycle ergometer test. Additional studies comparing treated and control groups are summarised elsewhere.⁴⁹

UNCONTROLLED EXERCISE STUDIES

Numerous uncontrolled studies of exercise training have been performed during the past three decades, the results of which have been summarised in recent publications.^{3 33 49 50 54} In this review several more recent studies will be dealt with in detail. Apart from the study of Casaburi and coworkers⁴⁰ the findings are similar to those in previous work. These studies do, however, effectively highlight the methods of testing and training and discuss unresolved issues, including mode and intensity of exercise training.

LACTIC ACIDOSIS AND EXERCISE TRAINING

In an editorial published in 1986 Casaburi and Wasserman⁵⁵ emphasised the role of carbon dioxide output as the major drive to ventilation during exercise. Recognising the well known relationships between \dot{V}_E on the one hand and \dot{V}_{CO_2} , arterial P_{CO_2} , and V_D/V_T ratio on the other, they suggested that aerobic training in patients with COPD would reduce carbon dioxide output and the ventilatory stimulus. The interrelationship of these variables is expressed in the equation

$$\dot{V}_E = \frac{k \times \dot{V}_{CO_2}}{P_{aCO_2} (1 - V_D/V_T)}$$

where \dot{V}_E is expired minute ventilation, \dot{V}_{CO_2} is carbon dioxide output, P_{aCO_2} is partial pressure of arterial carbon dioxide, V_D/V_T is the physiological dead space to tidal volume ratio, and k is a constant.

The lactic acid produced during exercise is buffered mainly by bicarbonate with the generation of carbonic acid which dissociates to carbon dioxide and water. The carbon dioxide produced by the buffering of lactic acid must be excreted by the lungs in addition to carbon dioxide produced by muscle metabolism during exercise. Exercise training delays the rise in blood lactate levels so any delay in lactic acid production will, by reducing the carbon dioxide load, decrease the ventilatory requirements during exercise. The effect of aerobic training and reduction in \dot{V}_E during exercise has been well documented in normal subjects by these investigators. At high levels of work near peak \dot{V}_{O_2} , large reductions of 30–40 l/min in \dot{V}_E can be achieved in normal individuals.⁴⁰

With this rationale in mind, Casaburi and Wasserman from the USA, in conjunction with a group of Italian investigators,⁴⁰ performed a study in which high and low intensity training was performed in patients with

COPD and the effects on lactate production were examined in detail. Exercise testing was performed on a cycle ergometer with breath by breath measurements of gas exchange before and after the training. Arterial blood gas measurements and arterial lactate measurements were also made. The anaerobic threshold was determined by means of the modified V slope technique.³⁶ Training was performed on a calibrated cycle ergometer five days a week for eight weeks. The high intensity group performed exercise at 45 min/day at an intensity 60% of the difference between the anaerobic threshold and the \dot{V}_{O_2max} . The low intensity group exercised at 90% of this level, but the duration was increased so that total work performed in the two groups was similar.

The major results of Casaburi's study were a reduction in the peak \dot{V}_{CO_2} and the maximal ventilatory equivalent for oxygen (\dot{V}_E/\dot{V}_{O_2}) in the high intensity group. In a high work rate, constant load test, the high intensity trained group showed significant reductions in blood lactate, \dot{V}_E , \dot{V}_{CO_2} , \dot{V}_{O_2} , and the \dot{V}_E/\dot{V}_{O_2} ratio. Heart rate at comparable work rates was reduced. All these findings confirm the development of a true aerobic training effect (fig 6). On the other hand, the group who trained at the low intensity, even though the total work performed was similar, showed smaller changes in these variables. In this group, although the lactate decrease was significant (10%), the decreases in \dot{V}_E , \dot{V}_{CO_2} , and \dot{V}_{O_2} were not significantly different. Furthermore, a significant increase in endurance of exercise at the higher work rate seen in the high intensity trained group (6.6–11.4 min) was not seen in the low intensity trained group (6.9–7.5 min).

There was a significant relationship between the decrease in minute ventilation during exercise and the decrease in blood lactate ($r = 0.73$, $\Delta\dot{V}_E = 2.46$ l/min/mEq lactate). The slope of the relationship $\Delta\dot{V}_E/\Delta\text{lactate}$ in these patients (fig 7) was considerably lower than that recorded in a previous study in normal subjects in whom the \dot{V}_E decreased by 7.2 l/min/mEq lactate. This study clearly shows that (1) significant lactic acidemia occurs in patients with mild to moderate chronic airways obstruction, and in some cases this may develop at low work rates (pedalling at 0 W); (2) both high and low intensity training reduce the rise in lactate but the effect with high intensity training is considerably greater; (3) although lactate levels and \dot{V}_E are lower after training in patients with COPD, the reduction in ventilation in patients is only about a third as large as that seen in normal subjects. The explanation for this difference is related to the fact that these patients show a reduced ventilatory response to the lactic acidosis of exercise and therefore a decrease in lactic acid after training produces a comparably smaller decrease in \dot{V}_E .

Although this study clearly shows the generation of a true aerobic training response, this was accomplished in a group of relatively

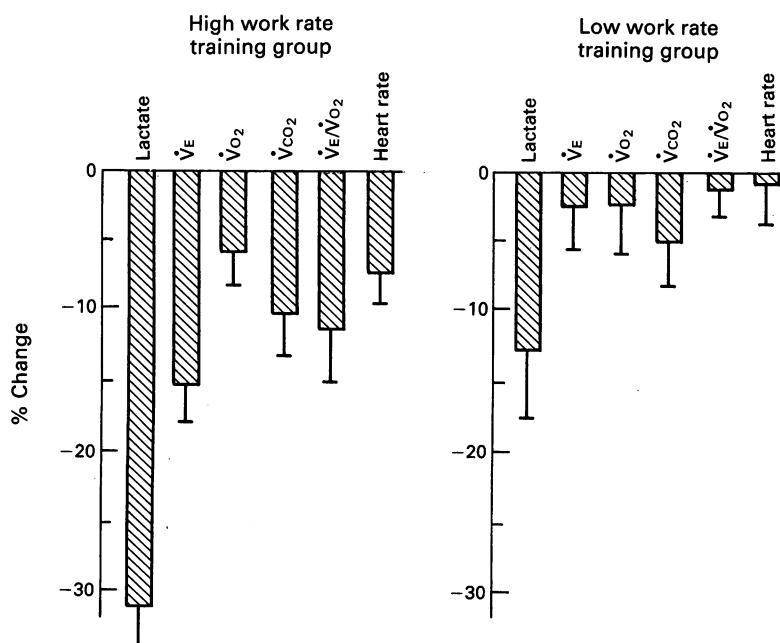
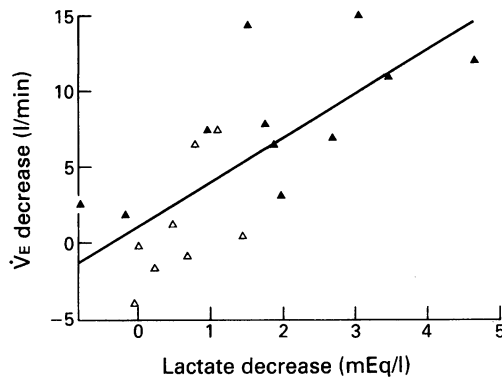


Figure 6 Changes in physiological responses to identical exercise tasks in high and low work rate training groups. Reproduced with permission from ref 40.

Figure 7 Relation between the decrease in ventilation and the decrease in arterial lactate in response to a high constant work rate test as a result of a programme of exercise training: ▲, high work rate trained group; △, low work rate trained group. Solid line is obtained by linear regression. $\Delta\dot{V}_E = 2.84$, $\Delta \text{lactate} = 1.19$. Reproduced with permission from ref 40.



young patients (mean age 49) with rather mild disease (FEV_1 percentage predicted 56% and FEV_1/FVC ratio 58%). These are not the type of patients commonly found in most rehabilitation programmes. In the past most studies examined patients in whom the FEV_1 was considerably lower. In the USA it is not unusual to find patients participating in exercise programmes with FEV_1 values < 1.01 .⁴⁹ Moreover, before the training these patients were relatively unfit as shown by the lactate threshold which was found to be at oxygen consumptions below 1 l/min. It is not surprising, therefore, that they responded dramatically to the exercise programmes. The fact that the ventilatory response to exercise acidosis is blunted in patients with COPD further detracts from the practical benefit of lactate reduction. Casaburi *et al*⁴⁰ document a $\Delta\dot{V}_E/\Delta\text{lactate}$ change of only one third of that in normal subjects. This, however, was in mildly affected patients. In severely affected patients one would anticipate an even smaller reduction in lactate levels and consequently a smaller decrease in exercise in ventilation. Most studies other than that of Casaburi *et al* have treated patients with moderate to severe disease.⁴⁹ In many patients the average FEV_1 is lower, generally about 1 litre, and in some cases less than that. Similar results in a more severely affected group of patients would be helpful before these exercise recommendations could be generalised.⁵⁶

EXERCISE TRAINING TO TOLERANCE

Exercise testing and training directed at manipulation of blood lactate levels involves complex measurements and should be contrasted with the more unstructured approach of exercising to tolerance, an approach which has been used in a large number of studies.⁴⁹ These studies, despite the fact that they have not necessarily documented reductions in lactate levels, have shown that even severely obstructed patients (some with extreme hypercapnia⁵⁷) can be exercised safely and show impressive gains in submaximal exercise endurance. This is particularly striking in the study of Niederman *et al*⁵⁸ who showed the greatest percentage improvement in those patients with the lowest FEV_1 values and low pretraining exercise endurance. In that study the training was done without emphasis on

intensity, patients being allowed to choose their own exercise level. Exercise sessions were conducted three times a week for two hours for a total of nine weeks. During each session the time was divided among cycling, treadmill walking, and lifting weights. The most impressive gains were in cycle endurance which increased from 129.5 to 726.1 W/min. Similar results were obtained by Holle *et al*⁵⁹ who showed large increases in treadmill endurance.

In two recent studies large gains in endurance were achieved, although high intensity training was used and patients were encouraged to reach maximal levels of ventilation during training.^{60,61} In the former study patients were initially separated into two groups based on whether an anaerobic threshold was reached. In those unable to reach an anaerobic threshold training was performed at the maximal work load achieved on the treadmill. In the patients who passed the anaerobic threshold training intensity was initially aimed at the threshold level itself. In both groups intensity and duration were increased as tolerated. Of interest was the finding that these patients could train at exercise ventilations close to or even exceeding the maximum level reached on initial testing. In contrast to the work of Casaburi *et al*⁴⁰ both groups showed significant and comparable improvements in endurance on the treadmill. The investigators were quick to point out that this does not mean that a high intensity training regimen is therefore desirable for patients with COPD. In fact, in comparison with the previously described study,⁵³ gains in endurance were similar. Clearly both approaches are successful in the moderate to severely affected patient; there does not appear to be an intrinsic benefit in demanding that training be performed at almost maximal ventilatory capacity. High intensity exercise may also be disadvantageous because of the higher risk of injury and because the discomfort of extreme exercise may reduce compliance with exercise programmes.⁶² These findings are summarised in the table.

UPPER LIMB EXERCISE TRAINING

The impact of upper extremity exercise has been discussed (see section on Respiratory muscle dysfunction). Ries and coworkers⁶³ performed a randomised study which compared a control group with two groups who used two different forms of upper arm training. Testing was done by means of cycle ergometry and unsupported arm exercise. In addition, three tests of activities of daily living were used, namely, dishwashing, dusting a blackboard, and placing grocery items on shelves. Training was performed for at least six weeks and showed that, although the patients who underwent the upper extremity training improved their performance on an arm cycle ergometer, they did not improve performance in arm activities of daily living. The specificity of limb training is emphasised by the findings of Lake *et al*⁶⁴ who randomised patients to one of three groups. The

first group was a control group who received no training; the second group received upper limb training only; and the third group performed combined upper and lower limb training. Upper limb training included cycle ergometry with varying resistances, throwing a ball against a wall with the arms above the horizontal, passing a bean bag over the head, and arm exercise with ropes and pulleys. Lower limb exercise was tested by cycle ergometry and a six minute walk distance. Training was continued for one hour, three times a week, for eight weeks. The results showed that limb training was limb specific. Thus it was only in the group that trained with the upper extremity that upper extremity endurance increased, while walk distance improved in the lower limb trained group. The combination trained group showed improvements in both upper and lower limb endurance. A modified quality of life questionnaire was also used but only produced significant changes in the group that received combined upper and lower limb training.

Two recent studies^{65,66} have confirmed the value of specific arm training. In both studies specific arm training resulted in increased arm endurance and a reduction in the metabolic cost for arm exercise. In the latter study the improvements in unsupported arm activity were seen only in the group who performed unsupported exercise and not in the group who did supported arm exercise.⁶⁶ The improved endurance in conjunction with the reduced metabolic cost is indicative of improved mechanical efficiency of movement of the arms and possibly breathing muscles during arm activity.

An interesting finding of previous studies^{63,64} was the lack of change in ventilatory muscle function. Before and after the upper extremity training these investigators examined ventilatory muscle endurance and neither found an improvement. Early work by Keens *et al*⁶⁷ in patients with cystic fibrosis suggested that upper extremity exercise may have a

crossover effect and improve respiratory muscle endurance but this was not confirmed in a study of patients with COPD by Belman and Kendregan,⁶⁸ in which a group of patients who performed upper extremity cycle ergometry did not improve their ventilatory muscle endurance. Similarly, in both these studies of upper extremity training no significant change in ventilatory muscle function was found.^{63,64}

Mechanisms of improvement

Improvements in exercise tolerance may be ascribed to one or more of the following factors: improved aerobic capacity, or muscle strength, or both; increased motivation; desensitisation to the sensation of dyspnoea; improved ventilatory muscle function; and improved technique of performance. Despite the multiplicity of studies performed there is, as yet, no clear consensus on the predominant mechanism of improvement.

IMPROVED AEROBIC CAPACITY

In normal subjects increased endurance has largely been ascribed to changes in the trained muscles.⁶⁹ These changes, which consist mainly of increased capillary and mitochondrial density together with increased concentrations of oxidative enzymes, occur concomitantly with training induced decreases in the exercise heart rate and constitute the major components of the aerobic training response in normal subjects.⁷⁰ Apart from the study by Casburi *et al*⁴⁰ this pattern has not been observed in patients with COPD so it is not possible to ascribe improved exercise endurance to improved aerobic performance. A striking feature of the results of exercise training in patients with COPD is the fact that, almost without exception, investigators have claimed success for their respective programmes despite the fact that training modes, intensity, and frequency have varied widely.⁴⁹ Moreover, in a study in which aerobic training effects were specifically examined by means of muscle biopsies from the trained limbs no significant improvement in oxidative enzymes was found.⁷¹ These authors concluded that patients with COPD were unable to exercise at the threshold intensity necessary to elicit a true aerobic response.

Although the emphasis on training has concentrated on endurance activities, recent evidence supports an important role for peripheral muscle strength. A third of patients with COPD implicated muscle fatigue as the limiting factor during exercise. A subsequent randomised study evaluated the effect of a weightlifting programme in these patients.⁷² The patients performed weight training three times a week for eight weeks. Both arm and leg strengthening exercises were done. The results showed an increase in cycle endurance and reduction in symptoms as assessed by a questionnaire. This study certainly reinforces the need not to neglect strength training as an important component of the training regimen.

Exercise training in chronic obstructive pulmonary disease

	Casaburi <i>et al</i> ⁴⁰	Punzal <i>et al</i> ⁶⁰	Niederman <i>et al</i> ⁵⁸
No. of patients	9	57	24
FEV ₁ /FVC	58%	44%	50%
Intensity	High (60% of difference between anaerobic threshold and $\dot{V}O_{2,max}$)	(1) $\dot{V}E_{max}$ (2) At anaerobic	Unstructured, laissez faire threshold
Frequency	5/week	Daily treadmill	3/week
Duration	8 weeks inpatient 45 min cycle	Supervised 2/week \times 4, then 1/week \times 4 free daily unsupervised walking	9 weeks 20 min on cycle, treadmill, upper extremity
Test	Cycle endurance 6.6–11.4 min Anaerobic threshold \uparrow	Treadmill endurance 12.1–22.0 min	Cycle endurance 5.0–12.0 min 12 min walk \uparrow
Peak $\dot{V}O_2$	10% \uparrow	10% \uparrow	19% \uparrow
Psychosocial	Not measured	Breathlessness \downarrow Fatigue \downarrow	Depression \downarrow Disability \downarrow

INCREASED MOTIVATION

Increased motivation might easily account for the improvement seen in some studies. This could be evaluated by noting an increase in the maximal \dot{V}_E or heart rate. However, neither of these variables has increased consistently in cases where there has been an increase in endurance. In submaximal steady state exercise tests, where exercise endurance time is the measure of improvement, motivation may be a factor.

REDUCTION IN DYSPNOEA

Research into the mechanisms of dyspnoea is complicated by the inherent problems with measurement of intensity of a symptom. This topic has been reviewed recently.⁷³ Various scales and questionnaires are in use including the Borg scale for perceived exertion, the baseline and transitional dyspnoea indices, and the chronic respiratory disease questionnaire.⁷⁴ Moreover, techniques are available which allow measurement of quality of life. Improved measurement in these areas is essential to gauge the impact of pulmonary rehabilitation programmes in general, and exercise training in particular.

Dudley *et al*⁴⁷ have reviewed the psychosocial aspects of pulmonary rehabilitation and cited several studies which have found correlations between improved exercise endurance and improved feeling of wellbeing. One study found that psychological improvement resulted from either pulmonary rehabilitation including exercises or psychotherapy alone. It has also been shown that there is a better correlation between mood and motivation and exercise endurance than between pulmonary function and exercise endurance.⁷⁵ Several studies of exercise training have shown improvements in wellbeing and reduction in breathlessness.^{49,50} In the study by Agle and coworkers⁷⁶ many of the patients also reported an improved sense of wellbeing and decreased sensation of breathlessness after exercise training. These authors speculated that the process of graduated exercise training in the presence of trained medical personnel "inadvertently functioned as a desensitising form of behaviour therapy." They felt, therefore, that progressive exercise led to a decrease in the unrealistic fear of activity and dyspnoea. A recent study by Belman and coworkers⁷⁷ showed that four repetitive episodes of treadmill walking over 10 days at a relatively high intensity resulted in a decrease in the perceived level of breathlessness over this short period of exercise and speculated that "desensitisation" may have played a part. In a study of ventilatory muscle training⁷⁸ a control group showed significant increases in exercise after participating in the testing sequence only. This evidence has given rise to the speculation that, when patients with dyspnoea experience their symptoms in a medically controlled environment while simultaneously receiving support and encouragement, they learn to overcome the anxiety and apprehension associated with their dyspnoea. This desensitisation to

dyspnoea may be a key component to improved endurance after exercise, but further investigation is necessary to prove this point.

VENTILATORY MUSCLE TRAINING

Ventilatory muscle training will be dealt with in a separate article in this series. Its role in improving endurance is as yet unclear. A recent meta analysis of ventilatory muscle training concluded that any effect, if present, is small and unlikely to contribute significantly to improved exercise tolerance in these patients.⁷⁹

IMPROVED MECHANICAL SKILL

Improved skill in performance has been found in several studies including the early studies by Paez and coworkers⁸⁰ who showed that skill in treadmill walking improved with repeated attempts. Clearly, skillful performance of the task decreases both the oxygen cost and the ventilatory requirements of work, although the actual work rate is unchanged.⁸¹ This effect constitutes training of technique and can be used to advantage in that these patients can be trained to perform specific tasks more efficiently. Although the technique of treadmill walking has been shown to improve in some studies, it is not known if this is indeed a component of improvement seen in walking other than on a treadmill.

From the large number of studies performed to date it is striking that there is no appreciable benefit on pulmonary function and gas exchange.^{33,49,50} As noted above, with the singular exception of the work of Casaburi *et al*⁴⁰ no true aerobic training effect has been found. Even in the absence of a training effect it is impressive that there is almost universal success shown for studies of exercise training when the outcome measure is increased exercise endurance. This includes studies in which the training intensity is low. The precise mechanism responsible for the improvement is not clear, but the absence of objective cardiopulmonary improvements raises the possibility that a reduction in dyspnoea perception is important. Further research to evaluate this mechanism is required. Moreover, additional research which combines measurements of exercise as well as valid measures of breathlessness and quality of life are indicated. The transfer of improved walking endurance to increased endurance for carrying out activities of daily living also requires improved documentation.

Summary

Sporadic visits to the local doctor followed sometimes by changes in oral and inhaled bronchodilators and occasionally by the addition of steroids frequently does little to significantly improve symptoms and function in the disabled patient with COPD. As in other chronic diseases, the management of these patients is facilitated by a team approach in conjunction with general rehabilitation principles.⁵⁰ The rationale and

practical implementation of such a programme has recently been outlined by the American Association of Cardiopulmonary Rehabilitation.⁵⁰ These are multifaceted programmes but a key component, as outlined above, is exercise training. In this brief review the various approaches available have been described. Controversy still reigns regarding the optimal modes of training and there are important differences among the several approaches. Two main groups can be delineated. One emphasises the detailed definition of the impaired physiology with therapeutic measures targeted to specific defects.⁴⁰ There is good documentation that, conversely, unstructured programmes that use treadmill and free range walking and cycling also improve endurance for walking.⁵⁹ Upper extremity training is of additional benefit. Programmes with as little as three sessions per week of 1–2 hours of low intensity activity have achieved success so we know that simple programmes can be helpful. Moreover, without the necessity for complex testing and training methods these programmes can be implemented with relatively low costs. Future investigations to examine the relationship between improved exercise capacity for walking and arm exercise on the one hand, and the ease of performance of activities of daily living on the other, will help to reinforce the effectiveness of exercise programmes.

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