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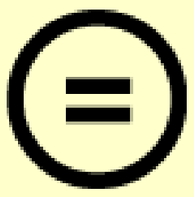

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DEVELOPMENT OF A 10 METRE SHUTTLE WALKING TEST TO ASSESS PATIENTS WITH CHRONIC AIRWAYS LIMITATION

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By

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A Doctoral Thesis

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ABSTRACT

The purpose of this study was to develop an incremental field exercise test of disability to use in the assessment of functional capacity in patients with chronic airways limitation (CAL). The test was modified from the 20m shuttle running test, employed to predict the maximal oxygen uptake of sporting individuals. The protocol devised for the patients was adapted from the running speeds proposed by Léger and Lambert (1982). The shuttle walking test requires patients to walk up and down a 10m course at speeds dictated by a series of audio signals played from a tape cassette, increasing each minute to a symptom limited maximum performance. Examination of the reproducibility of the test revealed strong test/retest reliability, after just one practice walk. The mean between trial difference (test 2 vs test 3) was -2m,(n=10), (95% CI -21.9 to 17.9m).

The shuttle walking test was validated against the traditional measurement of peak oxygen uptake ($\dot{V}O_{2\ peak}$) measured conventionally during an incremental maximal treadmill test with Douglas bags (n=19). The results from this exercise test were compared against the patients' performance (distance achieved) on the shuttle walking test (after one practice walk) and revealed a strong relationship between the two variables (r=0.88).

The validity and the resistance to breathing, of a portable oxygen consumption meter was examined. Validation, again in comparison to Douglas bag measurements, involved four cohorts (two healthy and two patient groups). After some modifications to the equipment, measurements of $\dot{V}O_2$ by the two different methods were not significantly different. The patients' response to the shuttle walking test was examined (n=10). The heart rate, ventilation and $\dot{V}O_2$ increased gradually in response to the increasing intensity of the shuttle walking test. Again $\dot{V}O_{2\ peak}$ measurements related strongly to the patients performance (r=0.81).

A further study employing a treadmill test and shuttle walking test confirmed that the latter provided a comparable metabolic and physiological challenge to the patients as the conventional treadmill test.

Comparison with the 6 minute walking test (6MWT), one of the most commonly employed field exercise tests in this patient population) revealed that the heart rate response was significantly higher in the shuttle walking test than the 6 MWT and graded, a response not observed in the 6MWT. The shuttle test reflected the true extent of the patients disability more accurately than the 6MWT.

The shuttle walking test provides a simple, reproducible exercise test of disability in patients with CAL that relates well to $\dot{V}O_{2\ peak}$. The external pacing of the test allows more valid intra- and inter- subject comparison than has previously been possible with field tests alone.

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PUBLICATIONS

Unless otherwise acknowledged or referenced to the published literature the work reported in this thesis is that of the author. Parts of this work have been reported in the following publications:

1. A progressive shuttle walking test of functional capacity in patients with chronic airways obstruction. Scott SM Walters DA Singh SJ Morgan MDL Hardman AE. Thorax 1990,**45**,781a.

2. A comparison of patients performance on the shuttle walking test and the six minute walking test. Singh SJ Morgan MDL Hardman AE. Thorax 1992,**47**,236p.

3. A comparison of patients performance on the shuttle walking test and maximal oxygen uptake in patients with chronic airways limitation. Singh SJ Hardman AE Bardsley PA Morgan MDL. Am Rev Resp Dis 1992,**145**:4,765a.

4. The development of the shuttle walking test of disability in patients with chronic airways obstruction. Singh SJ Morgan MDL Scott SC Walters D Hardman AE. Thorax 1992,**47**:1019-1024.

5. Patients performance on the shuttle walking test and the six minute walking test: a comparison. Singh SJ Morgan MDL Hardman AE. Clinical Rehabilitation 1992;**6**:348.

6. The ventilatory response of patients with COPD to the shuttle walking test. Singh SJ Rowe C Hardman AE Morgan MDL. Proceedings of the 2nd international conference on advances in pulmonary rehabilitation and management of chronic respiratory failure, Venice. 1992.

7. Does the shuttle walking test provoke a symptom limited maximal performance. Thorax 1993,48:446a.

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1. INTRODUCTION

Objective measures of disability are important in the assessment and clinical management of patients with chronic airways limitation (CAL). It is well documented that lung function values, the most commonly used being the forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) do not relate well to a patient's functional capacity. Consequently exercise tests are employed to evaluate more precisely a patient's level of disability and can subsequently be employed to assess a patients response to treatment.

Two modes of testing exist, formal laboratory assessment or perhaps more commonly field exercise tests. Laboratory assessment requires the patients to perform a treadmill or cycle ergometer test with detailed gas analysis measurements requiring the patient to wear either a face mask or mouthpiece and nose clips. This form of testing is not widely available, being confined to large teaching hospitals were the technical support exists. Added to which the equipment (treadmills and gas analysis equipment) is expensive and the procedures involved quite intimidating to the patient. As a consequence of these limitations field exercise tests were developed as a cheap, simple but effective alternative assessment of disability. Field tests of walking ability are most frequently employed and usually comprise a self paced test where the patient is required to walk as far as possible in either twelve or six minutes (McGavin et al 1976, Butland et al 1982). These protocols re difficult to standardise and may be overly influenced by motivation and encouragement (Guyatt et al 1987). In addition their very simplicity limits the information which can be obtained from them about the physiological and symptomatic changes that occur during exercise (Beaumont et al 1985).

The most accurate measure of exercise capacity is to

directly measure maximal oxygen uptake ($\dot{V}O_{2\,max}$) (Astrand & Rodahl 1986). In patients with respiratory disorders the $\dot{V}O_2$ is limited due to ventilatory abnormalities and consequently the maximal $\dot{V}O_2$ that a patient attains is often described as the symptom limited $\dot{V}O_{2\,max}$ or $\dot{V}O_{2\,peak}$. A $\dot{V}O_{2\,max}$ is traditionally defined as the point at which, despite an increase in the gradient of the treadmill there is no accompanying increase in oxygen uptake (less than 150ml O_2/min), ie a plateau effect. This point is rarely seen in patients with CAL, primarily attributable to different mechanisms causing the cessation of exercise in healthy subjects compared to patients with CAL. In patients with CAL the limitation to exercise is due to the inability of the lungs to meet the demand for increasing ventilation. In healthy trained subjects the limit to continued exercise is the cardio-vascular system.

There is a paucity of data relating existing field test performance to $\dot{V}O_{2\,peak}$ in patients and consequently their validity in assessing exercise tolerance is questioned. McGavin et al (1976) proposed the original 12 minute walking test to assess patients with CAL. The authors identified a moderate relationship between the two variables, ie distance walked versus $\dot{V}O_{2\,max}$. Subsequent work examining the relationship between these two variables for this test or any subsequent field exercise test is sparse. There is also a scarcity of data regarding the cardio-respiratory response to these field tests. Moreover, the data that has been presented focuses on the end points or maximal values rather than the overall response to exercise in these patients (Swinburn et al 1985).

Considerably more data are available examining patients' exercise tolerance in the laboratory environment, observing the ventilatory and physiological responses to exercise. Again authors tend to concentrate on maximal values rather than the response to various intensities of exercise (Matthews et al 1989).

The purpose of the series of studies presented in this thesis, was to develop an incremental externally paced field walking test to assess functional capacity in patients with CAL. The principle for the test, a 10m shuttle walking test, is based upon the 20m shuttle running test (Léger and Lambert 1982). The aim would be to offer this test as a more objective and standardised alternative to the currently available field exercise tests rather than to replace the more detailed measurements obtained by formal laboratory assessment.

1.1 Organisation of the thesis

There are six experimental chapters included in this thesis. The first study involves the development of a shuttle walking test protocol with suitable walking speeds and incremental increase in the speed that would allow range of patients to be stressed to a symptom limited maximum performance. The proposed protocol was initially assessed for reproducibility.

The second study addresses the validity of the shuttle walking test against a traditional, maximal oxygen uptake. To explore this patients were required to perform a symptom limited incremental treadmill walking test and their $\dot{V}O_{2\,peak}$ was directly measured. In comparing patients performance on the shuttle walking test against the Douglas bag measurements of $\dot{V}O_{2\,max}$, it was possible to reveal if the shuttle walking test was in fact a valid indicator of functional capacity.

One of the subsequent aims of the project was to examine patients' respiratory response during the shuttle walking test. In order to do this it was necessary to examine the reliability of a portable oxygen consumption and ventilation meter, the 'Oxylog'. The Oxylog carried in a backpack enabled ambulatory measurements of ventilation and oxygen uptake during exercise in the field to be made. Chapter six scrutinises the usefulness of the Oxylog in a cohort of healthy volunteers and a two separate patient groups. The final section of this chapter examines the resistance to breathing of the Oxylog equipment compared to the conventional Douglas bags.

The following study examines the physiological responses to the shuttle walking test employing the Oxylog. This made it possible to investigate patients' respiratory responses throughout the shuttle walking test. Blood lactate concentration measurements were employed to assess the metabolic response to exercise in this patient group.

During this study the opportunity was taken to make the corresponding resting measurements.

The penultimate study investigates further, the patients' metabolic response to exercise, again using blood lactate measurements. For this study the performance of a group of patients with an age matched control group was compared. This allowed the examination of patients' response to exercise and explore the relationship with the control group.

The final study compares patients' response and performance on the self paced six minute walking test (Butland et al 1982) with their performance on the externally paced shuttle walking test.

2.0 REVIEW OF THE LITERATURE

This review is divided into seven sections. The first section defines and describes the pathological state of CAL and its associated clinical manifestations. The second section outlines some of the commonly employed tools of assessment (both objective and subjective) used in an attempt to quantify the degree of disability in the patient.

The third section discusses the usefulness of the exercise testing and its clinical relevance. The section is concerned primarily with the development of the argument supporting the proposal of another field exercise test, documenting the development of the currently available field exercise tests and the problems associated with them.

The final three sections examine the response to exercise firstly in the healthy individual and secondly in the patient with CAL. The normal response is important to understand when examining the abnormal response of patients with CAL. The response to exercise in patients with CAL focuses on the limitations imposed by the respiratory system, and examines published data on the measured values of exercise tolerance. The final section of this review examines the measurements of blood lactate concentrations and metabolic acidosis in this patient group.

2.1 DEFINITION AND PATHOLOGY OF CAL

The aim of this project was to develop a simple exercise test to be used in the assessment of patients with respiratory conditions. The spectrum of diseases affecting the chest is enormous and can be divided into two broad categories ie, those affecting the conducting airways and secondly those affecting the lung parenchyma. This project was confined to evaluate the suitability of the shuttle walking test in patients with pathology affecting the conducting airways, ie, chronic airways limitation. Within this broad diagnostic category however lies a vast spectrum of patients.

Definition

The definitions commonly used today are based upon those agreed in 1959 (Ciba symposium). In 1965 the Lancet (Editorial) published a statement outlining the definition and classification of chronic bronchitis which brought together work from this 1959 symposium and from the previous decade attempting to define this respiratory condition; ' Simple chronic bronchitis is defined as chronic or recurrent increase in the volume of mucoid bronchial secretion sufficient to cause expectoration. (This definition is in essential agreement with other published definitions but is simpler and shorter)'. This definition is based upon clinical and functional abnormalities and proceeds to outline diagnostic criteria. This work also described subclassifications of chronic bronchitis-

a. Simple chronic bronchitis (as described above)
b. Chronic or recurrent mucopurulent bronchitis
c. Chronic obstructive bronchitis, chronic bronchitis associated with persistent irreversible widespread narrowing of the airways (Lancet 1965, Pride 1990a).

The working party of 1965 did not attempt to define asthma or emphysema. The definition of emphysema has tended to be based more upon pathological terms describing the anatomical abnormality unlike the definition of chronic bronchitis based upon patients symptoms and history - 'Emphysema is defined pathologically as a condition characterised by destruction and dilation of air spaces distal to the terminal bronchioles'. Both emphysema and chronic bronchitis may occur in the same patient (Petty 1990).

Recently there has been a trend towards a collective label for these lung conditions, in part due to trans-atlantic anomalies. The diagnosis of chronic airways limitation (alternatively, chronic obstructive pulmonary disease (COPD) or chronic airways obstruction) embraces emphysema and chronic bronchitis,

' A disorder characterised by abnormal tests of expiratory flow that do not change markedly over periods of several months observations' [American Thoracic Society (ATS) 1987].

This describes the dominant functional defect, a slowing of the lung emptying on forced expiration. The pathology of CAL can be explained in terms of the disease processes or in terms of the resulting mechanisms of the particular lesions such, as loss of elastic recoil and airway narrowing. Petty (1990) suggests that by the time the patient has advanced and irreversible airways obstruction, particularly at an older age, there is little point in seeking a more specific diagnosis than COPD.

2.1.1 Pathogenesis of CAL

The cause of chronic bronchitis and emphysema is not clearly understood but certain relevant factors have been identified in epidemiological studies (Cole & Mackay 1990). CAL is most likely to be observed in smokers (CAL is diagnosed in 4% of non-smokers (Pride 1990a)), the cigarette smoke having a number of toxic effects including immediate increase in airways resistance, inhibition of ciliary action and release of proteolytic enzymes from neutrophils (Cole & Mackay 1990, Wanner 1990). Other risk factors include environmental pollution, particularly prior to the Clean Air Act (1952-68), working environments ie, dust, smoke or industrial fumes, gender and deficiency of the enzyme alpha 1-antitrypsin. Overall males appear to be at an increased risk. Alpha 1-antitrypsin is a proteolytic enzyme inhibitor believed to protect the lung from the powerful effects of elastase released from neutrophil leucocytes (Cole & Mackay 1990) and appears to be associated with the development of emphysema particularly in the 30-40 age group (Hopkin 1991).

Chronic bronchitis

This disease is characterised by excessive mucus production of the bronchial tree. This hypersecretion

causes coughing and excessive sputum production. Excessive expectoration is defined as occurring on most days during at least three consecutive months for more than two successive years (Lancet 1965). The functional importance of mucus hypersecretion is unclear it shows no clear relationship to persistent airway narrowing (Lamb 1990).

The pathological changes that occur are characterised by the hypertrophy of the mucous glands in the large bronchi and evidence of chronic inflammatory changes in the small airways (West 1987). The mucous gland enlargement is due to hyperplasia and hypertrophy accompanied by an increased proportion of mucous (goblet) to serous cells and can be quantified using the 'Reid' index , the ratio of gland thickness to wall thickness (Thurlbeck 1991a). In normal lungs this ratio is normally less than 0.4 (West 1987) but in chronic bronchitis it may exceed 0.7.

A decrease in the number of ciliated cells and the mean ciliary length in the larger airways may also contribute to the accumulation of mucus in the conducting airways (Wanner 1990). The presence of smooth muscle hypertrophy in the large airways is a controversial issue. Thurlbeck (1991a) suggests that the role of smooth muscle hypertrophy and its contribution to airflow obstruction is unclear, but adds that it is unclear if this is a typical presentation. Jeffery (1991) proposed that the percentage of the bronchial wall occupied by smooth muscle fell within the normal range. Reid (1960) stated that inflammatory changes were not characteristic of chronic bronchitis.

The changes in the small airways (less than 2mm diameter) are thought to be the most important in mild airflow obstruction and not associated with any physical impairment (ATS 1987) and may represent pre-clinical or early CAL (Wright et al 1984). Considerable obstructive changes can occur here without appreciable changes in airways resistance (Pride & Macklem 1986). The characteristic pathology here is one of inflammation, the changes are

relatively subtle and appears as an infiltrate containing mainly lymphocytes and macrophages (Thurlbeck 1991a), which ultimately leads to airway narrowing. The presence of the inflammatory exudate itself can result in the displacement of the surfactant layer of these peripheral airways and destabilise the airway allowing it to close too easily and not reopen effortlessly. Alternatively the inflammatory process may release mediators that cause the smooth muscle walls to contract, regardless of the mechanism the effect is to cause fibrosis and narrowing of the small airways (Thurlbeck 1990a). Severe CAL is identified by marked narrowing of these small airways although inflammation at this stage may not be the primary cause, there appears to be an increase in goblet cells and the small airways may be more distorted leading to a large increase in airflow obstruction.

Emphysema

Emphysema is characterised by abnormal permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls and without obvious fibrosis (ATS 1986). It is sub-divided into further clinical groups according to their effect on the acinus, (emphysema itself is forms a sub-category of the diagnosis 'respiratory space enlargement')-

a. centrilobular
b. panacinar
c. distal acinar

It should be noted that enlargement of the acinus and loss of alveolar wall are normal features of increasing age (Thurlbeck 1991a). The emphysematous lung shows loss of alveolar wall and destruction of part of the capillary beds (West 1987). The small airways are narrow and tortuous and reduced in number and those that do exist have thin atrophied walls.

a. Centrilobular emphysema

The destruction is limited to the central part of the lobe the more peripheral alveolar ducts and alveoli remain undamaged (West 1987). It is related to cigarette smoking and inflammation induced (Thurlbeck 1990b). It is the most common presentation of emphysema and is more common and more severe in the upper lobes but spreads down the lung as the disease progresses (West 1987). The respiratory bronchioles and corresponding alveoli contain excess macrophages which are highly active and excrete high levels of proteases. The effect of proteolytic enzymes is heightened in smokers by the partial inhibition of alpha 1-antitrypsin [this globular protein inhibits the excessive action of neutrophils and macrophage elastase which cigarette smoking promotes (Hopkin 1991)], which results in the digestion of elastic tissue.

b. Panacinar emphysema

The acinus is more or less uniformly involved, identical lesions may be found in different situations and again may also result from the inflammation caused by smoking. There is one distinct group of patients which is particularly susceptible to the effect of cigarette smoking. They have a deficiency of alpha 1-anti-trypsin (Hopkin 1991). It may occur maximally in the bases of lungs in patients with centrilobar emphysema (ATS 1987), in association with the enzyme deficiency (Lamb 1990) and as an incidental finding in older patients.

c. Distal acinar emphysema

The alveolar sacs and ducts are predominately affected. It is usually accompanied by fibrosis and inflammation and is probably infective in origin (Thurlbeck 1991) and is uncommon (Thurlbeck 1990b). Because of its location it is often sited adjacent to lobular septa or the pleura and consequently associated with pneumothoraces (Thurlbeck 1991b).

2.1.2 Pathophysiology

CAL is a functional disturbance caused by pathological changes in the lung. Airflow is determined either by the

pressure applied or the resistance encountered. Applying this to the lung, the pressure is derived from the elastic recoil of the lungs, the chief defect in emphysema, and the resistance encountered is in the form of airway narrowing (Thurlbeck 1990a). In the normal lung the major site of resistance lies in the large conducting airways and a small reduction of the diameter would lead to a noticeable increase in airways resistance. Hogg et al (1968) drew attention to the changes occurring in the small airways suggesting that their initially smaller diameter makes them more vulnerable to significant narrowing or even closure. This narrowing due to intrinsic disease and loss of elastic recoil leads to an increased resistance in flow in the more peripheral units, noticed at low driving pressures and flow and appears to be the major site of fixed airway narrowing in CAL.

In the emphysematous lung there is a loss of elastic recoil and therefore a reduction in the expiratory pressures and increased resistance as a loss of support for the surrounding lung tissue which then encroaches upon the lumen of the airway (Pare et al 1991). Emphysema can also lead to air trapping and associated with the loss of elastic recoil results in an increase in total lung capacity. These increases in functional residual capacity (FRC),the gas remaining after tidal breathing and total lung capacity (TLC) places the inspiratory muscles at a mechanical disadvantage due to their increase in resting length (Pride 1990b). FRC in normals is about 50% of the predicted TLC whilst in patients with CAL it may increase to possibly as much as 80% of TLC which may in turn increase by 10-20% (Rochester 1984).

The loss of alveoli results in decreased gas transfer (Kumar & Clark 1987) and the lung becomes an inefficient gas exchange organ. Ventilation perfusion (V/Q) mismatching consequently occurs . In chronic bronchitis there are areas with a low V/Q value (1.0 represents an ideal match) ie, less than 1.0, the airways in this situation are

compromised by mucus, inflammation or bronchospasm. In predominately emphysematous patients the V/Q ratio is higher as destruction of the alveolar walls and the capillary beds results in a greater loss of perfusion than ventilation (Dantzker 1987). Perfusion can also be limited by active vasoconstriction in areas of severe hypoxia (Aitkenhead & Smith 1990). Usually this V/Q mismatching leads to an increase in the $PaCO_2$ and a fall in the PaO_2. Carbon dioxide is the predominant stimulus to respiration in the healthy individual (Ganong 1987) and in CAL the $PaCO_2$ is chronically elevated and the sensitivity of the central chemoreceptors is dampened and hypoxaemia becomes the chief stimulus to respiration. The carotid bodies mount their major action in response to hypoxia. In patients with CAL this chronic hypoxia can cause the carotid bodies to hypertrophy to ten times their original size (Flenley 1990).

The increase in airways resistance and increased FRC obviously leads to an increase in the work of breathing which limits the oxygen available for peripheral activity (Cole & Mackay 1990). Total respiratory muscle consumption may be 10-20 times normal values (Rochester 1984) (normal value - ventilation at 6 $l.min^{-1}$ O_2 uptake would be up to 6 ml Astrand & Rodahl 1986). The pressure change required to maintain tidal breathing is increased and the decreased resting length of the respiratory muscles confers a mechanical disadvantage. Fortunately the inspiratory muscles are able to adapt to chronic hyperinflation (Pride 1990b).. Due to the alteration in lung pathology and respiratory muscle activity the pattern of breathing in patients with CAL is altered from the norm. A higher negative inspiratory pressure is required to overcome these limitations and may require the recruitment of accessory muscles of respiration. This may result in relatively less movement of the abdomen. The inspiratory time is also shortened in some patients allowing a greater proportion of the total breath duration for expiration. Although the

limits to respiration in CAL are predominately expiratory it is the inspiratory muscles that compensate to a greater degree. The inspiratory muscles are also subject to increased activation to maintain a normal minute ventilation. This compensates for the inefficiency of gaseous exchange and increased dead space.

2.1.3 Symptoms of CAL

The principal symptoms are cough, sputum, breathlessness and wheezing. There may be associated chest discomfort but rarely pain (Howard 1990). Symptoms can be worsened by non-specific factors eg. cold and the weather (Kumar & Clark 1987). Breathlessness is the most common reason that patients seek medical advice and is usually first noticed on activities such as climbing the stairs or walking uphill. Severely incapacitated patients may notice increased breathlessness when they lie flat due to the limitation of diaphragmatic movement in this position (Cole & Mackay 1990). Carbon dioxide retention may give rise to disturbed sleep and early morning headaches and a further increase can cause drowsiness and confusion (Partridge 1982).

2.1.4 Physical signs

CAL tends to affect the middle aged and elderly person (ATS 1986), commonly with a history of smoking (Kumar & Clark 1987). On examination the patient may present with a normal, kyphotic or barrel shaped chest (increase in the antero-posterior diameter due to the hyperinflation of the lungs). Airflow obstruction is indicated by excessive use of accessory muscles of respiration, pursing the lips during expiration and by alteration of the respiratory rhythm increasing the time of the cycle for expiration and abnormal breath sounds.

On auscultation in these patients the chest may sound wheezy with decreased breath sounds (ATS 1986). Wheeze is more common at the bases and is an indication of excessive mucus secretion in the airways. Flenley (1990) suggests

that decreased breath sounds is an unreliable indicator of hyperinflation as is hyperresonance on percussion as the disease effects both sides of the chest and the value of comparison between the two sides is lost. Partridge (1982) proposes that auscultation in these patients is performed largely to exclude co-existing disease.

Central cyanosis may be detected by examination of the tongue and inside the lips (Croft & Douglas 1989) but is difficult to detect until the saturation falls below 85% (Flenley 1990). It may be the case that some patients only desaturate on exercise. Examination of the hands may reveal peripheral cyanosis which always accompanies central cyanosis. If the patient has a chronically high $PaCO_2$ the veins may be dilated and if the arms are stretched out a flapping tremor may be observed (Cummings & Semple 1973).

Two patterns of CAL can be distinguished clinically the 'pink puffer' and the 'blue bloaters'. Most patients display some features of both manifestations. It was originally felt that the 'pink puffers' suffered predominately from emphysema and therefore a pathological difference existed between the two groups (Burrows 1966). It is now believed that generalised emphysema may occur in 'blue bloaters'. Flenley (1990) suggests that the differences, although based upon clinical assessment, may be due to inherent differences in the ventilatory response to hypoxia. The 'blue bloaters' have a congenitally poor response to hypoxia, whereas the 'pink puffer' has a very brisk response.

The 'pink puffers' tend to present late in life around 70 years old (Howard 1990) following a history of increasing dyspnoea, the patient is always breathless with a hyperinflated chest and characteristically thin but is not usually cyanosed (Kumar & Clark 1987). Arterial blood gases show mild hypoxia (Flenley 1990). The 'pink puffer' has an excessive respiratory drive causing intractable dyspnoea

(Howard 1990) which becomes severe after only mild exercise (Cochrane 1984). The 'blue bloater' presents commonly at around 60 years of age (male to female ratio 5:1) and is usually obese with a history of smoking. The patient may not be particularly breathless, has severe central cyanosis, is oedematous and hypoventilates with little respiratory effort (Flenley 1990). As a consequence these patients have arterial blood gases which demonstrate hypercapnia. In some 'blue bloaters' the normal stimulus to respiration (increased CO_2) is replaced by a hypoxic drive, it is thought that this may be due not to insensitivity to the increased levels but to the inability of the lung to increase the rate of ventilation. The 'blue bloater' often has cor pulmonale, a term defined as right heart hypertrophy associated with parenchymal lung disease (unlike the 'pink puffer') (Howard 1990).

Many patient with CAL cannot be categorised into one of these groups but demonstrate some features from each. The two groups tend to represent opposite ends of the spectrum.

2.2 THE ASSESSMENT OF PATIENTS WITH CAL

Lung function tests are used to identify or exclude respiratory disorders and to quantify the impairment (Spiro & Roberts 1991). The simplest test of lung function is a forced expiration requiring minimal equipment and calculations but it also provides considerable information (West 1987). The forced expiratory volume is the volume of gas that can be exhaled in one second (FEV_1) after a full inspiration. This measurement and the forced vital capacity (FVC) can be measured by spirometry. The FEV_1 depends on several factors including the size and elastic properties of the lung, the diameter of the airways and collapsibility of the airways walls (Gibson 1990). In CAL the reduction in the spirometry values is due a combination of obstructive changes in the small airways and destructive changes in the acinus (Pride 1990b). Consequently, loss of lung recoil associated in particular with emphysema reduces the

distending force on all the airways and, in conjunction with intrinsic narrowing enhances dynamic airways compression, resulting in expiratory flow limitation occurring at lower pressures and flow rates. The FEV_1/FVC ratio is again lower than the 70-80% predicted normal value (Spiro & Roberts 1991). In health it is the upper airways that contribute to airways resistance whereas in CAL it tends to be the small airways that make the major contribution to airways resistance (Pride & Macklem 1986). The FEV_1 values are mainly influenced by the large airways of the lung and in the early stages of CAL the disease in the small airways may not influence the FEV_1 values, in fact quite considerable obstruction can be present before a drop in lung function is observed (Pride 1990b). If the patient has severe obstruction there may be changes in the central airways that contribute to expiratory flow limitations when combined with dynamic compression during the FEV_1 manoeuvre, and may even occur on tidal breathing (Pride 1990b). When the patient develops abnormal breathlessness on exertion standard tests of lung function including the FEV_1 values are abnormal. Many other parameters can be calculated from the spirometry but there is no evidence that they provide any more useful information than the FEV_1 and the FVC (ATS 1986). Repeat spirometric readings are useful in the assessment of airways reversibility and after the administration of drug therapies to assess their effectiveness (ATS 1986).

The peak expiratory flow (PEF) is also a widely used lung function test It measures the maximum expiratory flow rate over the first 100 milli-seconds (Gibson 1984). Patients with CAL demonstrate a persistently lowered PEF, this test is dependent on the patient's effort. Spiro & Roberts (1991) suggests that the FEV_1 and FVC are relatively independent of effort.

Flow volume curves are useful in detecting mild changes in airway function. The inspiratory and expiratory flow

rates are plotted against volume. Pride (1990b) proposes that the peripheral narrowing occurring in CAL should become apparent in the final stages of the expiratory flow/volume curve towards residual volume (RV), the gas remaining in the lungs after maximal expiration. This has not been conclusively demonstrated in clinical practice. In chronic bronchitis the expiratory flow rate is decreased throughout the expiratory curve. In emphysema the flow is reduced because of the airways' tendency to close which results in a dramatic reduction in flow (Spiro 1991).

Spirometry does not allow the measurement of RV or the FRC or TLC. These can be measured using a body plethysmograph or helium dilution techniques. Both techniques demonstrate an increase in RV, FRC and TLC in patients with CAL (Clausen 1990). Plethysmography appears to reveal a larger increase in FRC and TLC than helium dilution techniques. Pride (1990b) suggests that the former may overestimate lung volumes as the technique measures trapped gas whereas the latter only measures the gas that communicates with the airways. Changes in the elastic properties of the lung allow the lung to achieve greater lung volumes despite a normal chest wall (Spiro & Roberts 1991). This occurs particularly in patients with emphysema where the elastic support of the lungs is lost and the airways close at abnormally high volumes (West 1987). Elevated FRC may play an important role in the development of respiratory muscle weakness, fatigue and dyspnoea (Clausen 1990). The RV is a result of the force generated by the expiratory muscles and the opposing tendency of the thorax to recoil outwards at low lung volumes. In CAL airway narrowing and/or the loss of elastic recoil, allowing dynamic compression allows gas trapping and an increase in the RV, commonly an early feature of CAL.

CAL is frequently associated with a reduction in the diffusing capacity for carbon monoxide (DLco) (ATS 1986). The value of this depends on the ventilation/perfusion match and provides an estimate of the surface area

available for gas exchange. The transfer factor is dependent upon gas passing from the alveoli to the capillaries and in turn this is dependent upon the gas reaching the alveoli. In any patient with airflow limitation this will be reduced and is compensated for by using an inert gas (helium) to facilitate the measurement of alveolar volume. The division of the alveolar volume into the transfer factor gives the transfer coefficient (Kco). The Kco is normal in patients with mainly irreversible airflow limitation but is reduced in patients with predominately emphysema (Partridge 1982). Clausen (1990) cites evidence to suggest that the measurement of DLco correlates well to the pathological assessment of emphysema. The American Thoracic Society suggest that the measurement of DLco in conjunction with the measurement of lung volumes may be useful in the initial assessment of those patients suspected of having CAL, but for follow-ups FEV_1 and FVC is adequate.

Other commonly used laboratory based methods of assessment and diagnosis of this patient group include blood gas analysis, chest x-rays and sometimes sputum analysis.

An impairment in the efficiency of the lungs to deliver oxygen or eliminate carbon dioxide becomes apparent when analyzing a sample of arterial blood. Patients with CAL demonstrate hypoxaemia and with increasing severity of the disease, hypercapnia. Pride (1990b) states that there is considerable potential for the arterial blood gases to vary independent of the severity of the airways obstruction. This variation depends upon primarily on the V/Q mismatch and also alveolar hypoventilation. In this situation the alveolar oxygen partial pressure drops due to the development of raised partial pressure of arterial (Pa) and alveolar(PA) carbon dioxide (CO_2). Flenley (1990) suggests that blood gas analysis confirms the diagnosis of 'pink puffers' and 'blue bloaters'. The former demonstrating mild

hypoxaemia (8.0 - 10.0 KPa) and a low or normal arterial PCO_2 (4.0 - 5.3 KPa), the latter tending to have a low PaO_2 (5.3 - 8.0 KPa) and high $PaCO_2$ (6.0 - 8.6 KPa). Normal values for the partial pressure of arterial oxygen and carbon dioxide are 12.6 and 5.3 KPa respectively (Aitkenhead & Smith 1990).

There is a thought to be a link between the reduction in the FEV_1 and declining PaO_2. The $PaCO_2$ is thought to remain within normal limits until the FEV_1 falls below 1.2 - 1.5 litres (Lane 1968). The blood analysis may also reveal secondary polycythaemia, particularly in the patients categorised as 'blue bloaters'.

A chest x-ray is an important investigation in the overall management of patients with CAL although they do not always show distinct features. They are often used to exclude other diagnoses of airways limitation. The most common features of this patient group are seen in the 'pink puffers'. These patients tend to have hyperinflation of the lungs associated with a low flattened diaphragm and bullous lesions are quite common (ATS 1986). Irregular patchy shadowing may occur in patients with CAL representing areas of fibrosis and possible bronchopneumonia (Cole & Mackay 1990). The characteristic x-ray of the 'blue bloater' with cor pulmonale will show an enlarged heart and prominent vascular markings at both hila. Hyperinflation is not as obvious in this group as those patients with predominately emphysema (Flenley 1990). However these x-ray findings do not correlate well with patients' symptoms and the severity of the airflow limitation (ATS 1986, Clausen 1990).

All the above tests rely on objective findings assessed by the medical practitioner. To judge how the patient is affected both physically and psychologically by his respiratory disease, questionnaires are frequently employed. An alternative subjective assessment of the airways limitation is to ask the patient about their

perceived breathlessness.

Breathlessness/dyspnoea can be defined as 'an awareness of the act of breathing, usually occurring when ventilation or the effort required to ventilate the lungs is excessive'(Howell 1990), or alternatively 'occurring when the demand for ventilation exceeds the patient's ability to respond' (West 1987). The feeling of breathlessness can manifest itself to the patient in a variety of ways, ie the patient could complain of 'chest tightness', 'an inability to fill the lungs' or simply 'difficulty in breathing'. The feeling is a personal sensation which is strongly influenced by the individual's psychological state at the time of assessment and not a physical phenomenon that can be quantified objectively, (Sweer & Zwillich 1990). There is no one simple explanation of the cause of dyspnoea, however a number of contributing factors have been suggested. Altose (1985) proposed a variety of signals that may be responsible for mediating the sensation of breathlessness including the chemoreceptors in the blood and brain, mechanoreceptors in the thorax and outgoing CNS respiratory motor commands.

An increase in the ventilatory drive is produced by hypoxaemia, hypercapnia, acidaemia and exercise in patients with CAL. Leblanc et al (1986) suggested that respiratory effort may be linked to dyspnoea, and he demonstrated that in general the sensation of dyspnoea increased when ventilation reached a high percentage of the maximum voluntary ventilation. The length-tension relationship of the respiratory muscles is thought to influence dyspnoea. The muscle spindles lie parallel to the muscle bundles and signal whether or not the expected change in muscle length has taken place following a central motor command to the respiratory muscles. If breathing is limited due to increased resistance or the lungs are hyperinflated as in CAL the expected amount of shortening may not occur for a given motor command, consequently the sensation of dyspnoea may be generated due to this 'length-tension

inappropriateness' (Howell 1990, Sweer & Zwillich 1990). This has been disputed by Freedman et al (1987) who noted that the reflexly stimulated increases in ventilation to the point of breathlessness was not matched by the same sensation when the increase in ventilation were volitional. Adams & Guz (1991) suggests that this may indicate breathlessness depends upon a degree of reflex stimulation of the respiratory muscles.

Hypoxaemia and hypercapnia evoke the sensation of dyspnoea but produce shortness of breath due to the stimulation of the carotid bodies in hypoxic patients and via direct stimulation of the brain stem in patients with a high $PaCO_2$. Swinburn et al (1984) demonstrated the effect of hypoxia on breathlessness in patients with CAL. He found that the administration of O_2 during exercise prevented the previous falls in oxygen saturation and also an improvement in the breathlessness.

In patients with CAL the sensation of breathlessness is multi-factorial. The predominant factor is thought to be related to the hyperinflation of the lungs (Howell 1990) and the influence this has upon the respiratory muscles (Sweer & Zwillich 1990). Lung hyperinflation results in the diaphragm being flatter than normal and therefore forced to operate within a non-optimal portion of the length-tension curve. In the normal lung the optimal position for diaphragm contraction is at FRC but in CAL the muscle is shortened and requires a greater motor input to evoke a satisfactory shortening (Rochester 1991). The actual configuration of the diaphragm is altered, normally the diaphragm increases in both the transverse and anterio-posterior diameters of the chest when contracting, but in the hyperinflated chest the lower ribs may in fact be drawn in (Howell 1990). [It is thought that when a patient leans forwards in an attempt to relieve the dyspnoea the diaphragm is pushed proximally into a more efficient position (Cielsa 1989)]. The hyperinflated lung also

disadvantages the inspiratory muscles as they too have a reduced resting length as compared to normal which reduces the maximum tension they can develop (Folgering et al 1991).

Altose (1985) states that the sensation of breathlessness can be represented as a function of the conscious awareness of the outgoing motor commands to the muscles of respiration as the afferent signals are responsible for the evaluation of muscle tension but the efferent signal is responsible for the sense of effort.

The assessment of dyspnoea is difficult because it is something that the patient feels and is affected by both emotional and environmental factors and cannot be measured accurately. One of the earliest approaches was to relate exercise ventilation to a maximal voluntary ventilation. This ratio $\dot{V}_E$/MVV was termed the 'dyspnoea index'. More recently this relationship has been used to describe the ventilatory reserve during exercise rather than dyspnoea (Clarke 1991). An easily applied scale is required that can reveal the functional impairment experienced as a result of the breathlessness (Sweer et al 1990). There are a handful of commonly used scales that are applied in a clinical environment to assess the severity of the sensation and its limitations, alternatively an exercise test can be used to formally assess the degree to which dyspnoea limits function. The commonly used scales that can be easily administered in clinics include the Medical Research Council (MRC) breathlessness scale (1966) and the Oxygen cost diagram (McGavin et al 1978).

The first scale requires the patient to choose a verbal description that describes their sensation of breathlessness and the associated functional limitations ie, indicate the point were breathlessness would be present. The descriptions are divided into categories, for example (using the MRC scale) the patient may choose from one of three options (eg, '3. have to stop for breath when

walking at own pace on level ground'). The Oxygen cost diagram requires the patient to mark on a line the level which corresponds to the point where their breathlessness would not allow them to continue. Along side this line is a list of daily activities. McGavin et al (1978) found that the distance that patients were able to walk on the 12-minute walking test correlated well with the point marked on the Oxygen cost diagram. An alternative to this 'categorical' assessment is to use a visual analogue scale (VAS). A 10 cm line labelled from 0 to 10 is commonly used and the patient marks along the line the intensity if the sensation. For this method the stimulus-response is treated in a linear fashion (Jones 1988) and the patient assigns a numerical value to a sensation.

The modified Borg scale (1982) is commonly used to assess patients perceived breathlessness in response to clinical exercise testing. The adjectives range from 'nothing at all' to 'maximal' and are assigned a value ranging from 0 to 10. The scale presents a combined category and ratio scale and has been suggested possess interval properties (Appendix B) allowing analysis using parametric statistical tests. This however may not be an entirely valid assumption and the use of non-parametric statistical tests may be more valid. This discrepancy has lead to the divergence of analysis of results; Belman et al (1991) Silverman et al (1988) and Wolkove et al (1989) applied rank transformation to their Borg data whilst Killian (1985) applied tests appropriate to interval data. However, if patients were asked to adjust their level of exercise so that their perceived rate of breathlessness was halved, the level of exercise may not coincide with the level chosen. Borg (1982) proposed that the scale allows a inter-individual comparison to be made. The category scale increases linearly as exercise intensity increases and is closely correlated to physiological responses that also increase linearly such as heart rate (ACSM 1991). This was demonstrated by Muza et al (1990) on patients with CAL. They compared the VAS(30 cm) with the unmodified Borg scale

(numbers ranged from 6-20 and described the sense of effort associated with breathing) during incremental exercise in patients with CAL, the results showed that both test scores increased linearly with oxygen consumption. They also suggested that the VAS was more sensitive than the Borg, possibly a reflection on the categories of the Borg scale and the fact that the line was 30 cm for the VAS.

The reproducibility of the Borg scale was assessed in patients with CAL by Belman et al (1991). They found that the Borg rating decreased progressively with repeated testing at sub-maximal levels. Silverman et al (1988) concluded that the Borg scale was highly reproducible in patients with stable CAL. For this project the patients were required to repeat maximal exercise tests which decreased the variability of the Borg score seen during repeated sub-maximal tests (Belman et al 1991). Wolkove et al (1989) investigated the relationship between the scoring on the Borg scale and the spirometry results before and after bronchodilators for a large number of patients with CAL. They concluded that the Borg scale related poorly to the spirometry. The Borg scale did however identify a reduced sensation of dyspnoea post-treatment not shown in the FEV_1 values.

Breathlessness can also be assessed from an alternative perspective, the employment of quality of life measures. These can indicate the impact that the patients breathlessness and other manifestations of respiratory disorders have upon their daily life, and therefore relate to the quality of life. Questionnaires were developed to aid the overall evaluation of functional status and to reveal any hidden links between directly measured pathophysiological parameters and a patients quality of life. It is well recognised that disability does not relate well to conventional lung function tests (McGavin et al 1978).

The first quality of life measure designed for the specific assessment of patients with chronic respiratory disorders was the Chronic Respiratory Disease Questionnaire (CRDQ)(Guyatt et al 1987)(Appendix C). This questionnaire based upon previously identified areas (Guyatt et al 1987) examines four aspects of patients lives; dyspnoea, fatigue, emotion and mastery (the feeling of control over the disease). The questionnaire consists of 19 questions. Dyspnoea is evaluated by asking the patient to identify the five most important activities which they do frequently and are limited by dyspnoea. These can be volunteered independently or taken from a list. These activities are identified on the first administration and used for repeating the CRDQ. The responses for all the questions are based upon a seven point Likert scale. The questionnaire is both reproducible and responsive. The responsiveness of the CRDQ was confirmed by examining patients taking part in a rehabilitation programme. For the validity study patients' results on the CRDQ were compared with several other measures, including FEV_1, the six minute walking test and the Oxygen cost diagram (McGavin et al 1987). In general moderate correlations were found between the changes in the CRDQ and changes in the other measures. It was found that there was a moderate relationship between the dyspnoea score and the six minute walking test but the six minute walking test was less well correlated with the 'emotion' score. Guyatt et al (1987) concluded that the CRDQ was highly reproducible and responsive enough to detect changes in the quality of life in small sample groups. It should be noted that the data generated from this study was examined using parametric statistical analysis, primarily, according to the authors because this was the most familiar form of analysis to the readers.

In 1989 Guyatt et al used the CRDQ and other outcome measures (including Oxygen cost diagram) to assess the effectiveness of bronchodilators in CAL. The CRDQ dyspnoea score presented the highest correlation values for the

change in the measures and the changes in the variables (spirometry, six minute walking test and a breathlessness VAS post walking test).

Jones (1991) highlights some of the problems associated with the CRDQ. He proposes that by allowing an individual to choose activities which make them feel short of breath the questionnaire is not standardised and does not allow a score to be calculated.

Weir et al (1991) identified a problem when using the CRDQ in patients with cystic fibrosis. They found that this group of patient identified fewer activities that induced breathlessness and had to alter the scores to allow a comparison to be made between these patients and patients with CAL. However when using the CRDQ to assess patients with CAL it is sensitive to change, reproducible in stable patients, allows for statistical comparisons to be made on repeat questioning and is easy to administer (Morgan 1991).

The St Georges Respiratory Questionnaire (SGRQ) has recently been introduced to assess both CAL and asthma patients (Jones et al 1991). It is proposed that this test is more standardised than previous questionnaires and consists of seventy-six items divided into three sections (symptoms, activity and impacts). The questionnaire it was reported, correlated well to other reference values [including spirometry, FEV_1 r=0.22 and the six minute walking test r=0.36 (Jones et al 1990)] and was related to more general measures of health eg. The Sickness Impact Profile (Bergner et al 1981), although the former appeared to be more sensitive to a wider range of diseases (Jones 1991).

2.3 EXERCISE TESTS FOR THE ASSESSMENT OF FUNCTIONAL CAPACITY IN PATIENTS WITH CAL.

2.3.1 Introduction

The assessment of exercise tolerance in patients with CAL provides an objective index of their disability and reveals functional abnormalities not present in measurements made at rest. However, laboratory assessment is not always available. In addition, formal laboratory testing requires skilled technicians, is expensive in terms of the equipment required (eg. treadmills, cycle ergometer and gas analysis equipment) and can be quite intimidating to the patient. As a consequence of these limitations field tests were developed as a cheap, simple and effective alternative method of assessing disability. Field tests are frequently employed by physiotherapists in the assessment of a number respiratory conditions including CAL.

Exercise testing in patients with CAL is an important tool in the assessment of functional capacity. A well recognised problem is that spirometric values from these patients do not match their ability to exercise. It would seem reasonable to suggest that a patient's static lung function test results should relate well to their exercise tolerance, but this is not the case and most studies reveal a poor relationship between the two (McGavin et al 1978, Swinburn et al 1985). Simple exercise tests are therefore employed to reveal the true extent of disability and assess a patient's ability to perform day to day activities. Secondly an exercise test can objectively characterise the true extent of a patient's disability. Patients accounts of their own functional capacity is notoriously under/over exaggerated and an exercise test can help to distinguish dyspnoea associated with anxiety from cardio-respiratory disease (Spiro 1977). Health service workers also need to assess a patient's response to treatment (drugs/physiotherapy) and in the case of exercise rehabilitation for these patients it has been shown that lung function values alter very little (Simpson et al 1992)

and in these situation it is more appropriate to use an exercise test to gauge a patient's response to treatment.

Research examining 'traditional' chest physiotherapy for these patients has also documented very little change in these reference values (Gallon 1991, Sutton et al 1985). However a change may be apparent by exercise testing and consequently more credibility assigned to these 'custom & practice' modalities of treatment. Many drug interventions may also appear to have an enhanced effect if the researches combined the traditional lung function values with exercise testing. An exercise test can also indicate the limitations to exercise, ie respiratory or cardiovascular and therefore be of use in the differential diagnosis of a patients condition. Despite field testing being considered a relatively crude form of testing it is possible to differentiate between cardiac, respiratory or peripheral limitations (eg muscle fatigue) to exercise. However a more specific diagnosis can be made with laboratory testing.

2.3.2 Requirements of a simple exercise test

An exercise test should be simple for both the operator and patient to use and based upon an activity familiar to the patient. For this reason walking tests are preferred to cycle ergometry and step tests. To assess patients' disability the exercise test should stress the cardio-respiratory system to a symptom limited maximum (see below).

Any protocol used must also be reproducible and, consequently, capable of providing meaningful results. At least one practice test is required, often more (Mungall & Hainsworth 1979), to familiarise the patient to the test and minimise any training or learning effect. For a test to be reproducible the protocol and conduct should be both standardised and consistent.

Both walking and step tests represent a form of exercise

testing that can be performed outside of the laboratory environment. The former is often the preferred mode of testing being an activity familiar to the patient. Nevertheless step testing is frequently used to assess cardiac function. A number of step test protocols are employed which the changes of work rate can be made by altering the step height and the frequency (Nagle et al 1965). The disadvantages associated with step tests relate mainly to the fact that the amount of work done is difficult to measure and is dependent on the patient's weight (Wilmore 1984). Jones (1988) suggests that it is also difficult to measure the power because of the difficulty in gauging the work done in stepping down. The patients for whom stepping is an unfamiliar activity the limitation to exercise may be caused by local muscular fatigue rather than due to a symptom of their respiratory disorder. A small area of space is required to perform the test may make it preferable to a walking test in some situations. A variety of opinions exist as to whether it is relatively easy to make physiological measurements (eg HR) as the patient is confined to a small area or alternatively because of the considerable vertical displacement the results have to be viewed with caution (Wilmore 1984).

Swinburn et al (1985) assessed the usefulness of step testing in patients with CAL and he found a 96% improvement in performance from test one to test four. He also found that the maximum ventilation (V_E) and oxygen consumption Vo_2 were significantly greater in the paced fixed height step test than in the self paced walking test (12 MWT - see below).

2.3.3 Development of the field walking test

One of the first field tests proposed that was not a step test was developed by Cooper (1968). The twelve minute running test was used to assess the fitness of male air force officers. Performance on the field test had a strong relationship with laboratory determined maximal oxygen

consumption ($\dot{V}O_{2\ max}$) data (correlation coefficient of r=0.897) considered to be the traditional indicator of cardio-vascular fitness. An individuals' maximal aerobic power plays a decisive role in his/her physical performance (Astrand & Rodahl 1986) and is regarded as the best physiological measurement of endurance performance. McGavin et al (1976) suggested that a downgrading of this test to a twelve minute walking test (12 MWT) would be appropriate in the assessment of patients with CAL. The reproducibility of the test was assessed on twelve in-patients over a three day period. This test, conducted along a hospital corridor, advises patients to " Cover as much ground as you can in twelve minutes. Keep going continuously if possible, but don't be concerned if you have to slow down to stop and rest. The aim is to feel that at the end of the test you could not have covered any more ground in the time." A doctor accompanied the patient acting as a time keeper and gave encouragement as necessary. Taking into account the variation in spirometry (the test was not conducted during a period of clinical stability) McGavin and colleagues (1976) found that there was a significant difference between test 1 and 2 but a further increase on test 3 was not significant. The mean percentage improvement in distance walked for test 1 vs 2 was not documented but the mean change for test 2 vs 3 was 7.33%. The 12 MWT exhibited only moderate relationship with the peak oxygen uptake ($\dot{V}O_{2\ peak}$) (r=0.52) (McGavin et al 1976). Therefore only 25% of the variation recorded in the walking distance was explained by the variation in the $\dot{V}O_{2\ peak}$. The latter was measured during a progressive exercise test performed on an electrically braked cycle ergometer, and the $\dot{V}O_{2\ peak}$ reached during this form of exercise can be up to 10% lower than that obtained during treadmill walking (Astrand & Rodahl 1986). This need not decrease the strength of the relationship if the difference between the cycle $\dot{V}O_{2\ peak}$ and treadmill $\dot{V}O_{2\ peak}$ is systematic, but it may not always be. In conclusion, it was suggested that the 12 minute walking test must be carried out twice before the distances

recorded are reproducible (McGavin et al 1976).

A six minute walk (6 MWT) was presented by Butland et al (1982). The group initially studied the usefulness of 2, 6 and 12 minute walks in patients with CAL. The tests were conducted in a similar manner to the 12 MWT except that encouragement was standardised. Two practice 12 MWT's walks were required before entry into the study. They found that performance on the 6 MWT related well the performance on the 12 MWT distance (r=0.95). Although the implication is the 6 minute walk is reproducible no direct evaluation of the reproducibility of the 6 MWT was performed in this study. These 6 and 12 minute walking tests are the most commonly used self paced walking field tests for the assessment of various drug and therapeutic interventions.

There have been a few additions to these two most popular walking tests to measure disability in patients with CAL. One is the 100 m walk proposed by Morrice and Smithies (1984). The authors felt that the 'traditional' corridor tests could be too challenging for the more severely affected patient. Patients were therefore required to walk 300 m in total, by walking successive 50 m lengths of corridor. The authors found that the time taken to complete the third 100 m correlated well with the 12 minute walk distance. The mean distance that the patients walked for the 12 MWT was 778 m, it could be that for some of the patients this 300 m walk may confer little time benefit over the 6 MWT. Davidson et al (1988) suggested an endurance walk, for this the subject is instructed to walk as far as possible (at a pace as though late for an appointment) and to stop when unable to go any further. The endurance time and distance covered is recorded. Recording two variables can cause some difficulty when trying to make inter-subject comparison. This test was introduced as part of a study examining the affect of supplemental oxygen on exercise ability in patients with CAL. They also used the 6 MWT as an outcome measure (after 3 practice walks). Their results showed that the endurance walk (distance and time)

revealed a greater effect of the treatment than the 6 MWT (17% vs 59% improvement of distance) although the number of practice walks performed for the endurance walk is not documented.

The most recent development in this area is the use of the 20m shuttle running test to examine the incidence of exercise induced asthma and concurrently reveal levels physical fitness in school children (Freeman et al 1990). This field test is based upon the 20m shuttle running test (Léger and Lambert 1982) now widely used to assess the functional capacity of sportsmen and women. There was a strong relationship between the athletes' shuttle running performance and $\dot{V}O_{2\,max}$ (r=0.84) (Léger and Lambert 1982). This test represents a new direction in field testing. The speed of running is externally paced and progressive, being dictated by audio-signals played on a tape recorder. As the speed of running is dictated by the tape, the influence of encouragement and motivation is limited.

2.3.4 Problems associated with field walking tests

There has been extensive work using the six and twelve minute walking test as a research tool in the assessment of various therapeutic interventions. However its reliability does remain in question. The details of the protocols are not standardised and the lack of uniform instructions for the operator or the patient results in a variety of test procedures being adopted. This lack of standardisation is apparent in several aspects in the conduct of the test, for example the variables a) whether the doctor/physiotherapist walks alongside the patient throughout the test, which it could argued is in itself a form of pacing and b) what if any form of encouragement is offered. An obvious practical dilemma is locating a corridor of adequate length to perform the 6 or 12 minute walk that is free from obstacles and the outside influence by visitors or other hospital personnel.

Reproducibility also presents a problem for these self paced tests, as a measurement that is totally unrepeatable clearly has no validity (Chinn 1991). It has been suggested that 1, 2, or 3 practice walks may be necessary to counteract any learning or training effect (Knox et al 1988, Mungall & Hainsworth 1979 Swinburn et al 1985). Knox et al (1988) identified a 33% increase in the 12 MWT distance over walks 1 to 12 performed over three consecutive days, half of this increase occurred during the first three walks. An 8.5% increase was observed in repeat testing that occurred over a four week period. In the conclusion it is suggested that five practice walks are required before the learning effect appears to plateau when testing at short intervals and four practice walks are required if the testing interval is greater.

Swinburn et al (1985) identified a similar magnitude of improvement of 16% for the first four tests performed during consecutive days and although a placebo was administered between test three and four no effect on the exercise was detected. This work suggested that three practice 12 MWT are necessary before the effect of any intervention can be measured and even then it may be important to consider the effects of repeat testing.

Mungall and Hainsworth (1979) also identified a significant increase in the 12 MWT distance in 13 patients with CAL tested six times at intervals of two or three weeks (no numerical value was assigned to the increase). At the same time a variety of standard respiratory tests were completed and these values did not alter significantly. Again it was conclude that three practice walks were required to obtain reproducible values.

If reproducibility of the test is in the order of 5-10% improvement with repeat testing, then it would only be possible to identify treatment effects that produce more than a 5-10% increase in performance. Consequently researchers may fail to identify real effects or

alternatively wrongly assign a treatment effect. Quite variable results have been recorded for the 12 MWT distance in the above and other clinical trials despite the patient groups being similar in their physical characteristics (Swerts et al 1990, Beaumont et al 1985, McGavin et al 1976).

Guyatt et al (1984) demonstrated that the effect of encouragement during the walk could significantly increase performance. He randomised 43 patients with either CAL or chronic heart failure or both to receive or not receive encouragement as they performed a series of 2 and 6 MWTs. The effect of encouragement constituted a 30.5 m increase in walking distance for the 6 MWT over tests three to six. The effect of repeat testing appeared also greater in the group receiving encouragement and the patients with CAL showed a greater improvement with repeat testing than did the cardiac patients. The administration of encouragement could in fact account for the 'positive' treatment effect in studies that used the 6 or 12 MWT as an outcome measure (Cockcroft et al 1981, Sinclair & Ingram 1980, Pardy et al 1981, Leitch et al 1981, Belman & Mittman 1980). Consequently when reviewing original research the protocol should be carefully scrutinised for standardisation and the verbal encouragement controlled. As an example, Pardy et al (1981) studied the effect of inspiratory muscle training and 'physiotherapy' in patients with CAL. The patients were required to perform just one practice 12 MWT prior to the intervention and no indication is provided regarding the conduct of the test. After inspiratory muscle training the 12 MWT distance increases by 59 m (10.4%). This apparent treatment effect could also be accounted for by either the effect of repeat testing as the learning curve will not have plateaued after just one attempt or due to the positive effect of encouragement. Physiotherapy appeared to have a 4 m (3.6%) improvement in walking distance which is an insignificant improvement.

Swinburn et al (1985) suggest that the habitual nature of

walking may prevent a self-paced walking test from demonstrating fully the possible beneficial effects of any treatment. In the same way that the operator can influence the outcome, so can the patient's mood, often affected by how he feels he should perform. As mentioned above, there is only a moderate relationship between $\dot{V}O_{2\,peak}$ and walking performance measured on these tests, in patients with CAL (McGavin et al 1976).

Day to day activities are mostly of an irregular nature with a steady state rarely being achieved. Most clinical problems and their associated symptoms lead to a premature limitation of exercise tolerance which is most likely to be revealed or identified during an increasing work rate test (Spiro 1977). An incremental test suitable for a wide range of patients and valid results are obtained regardless of how much exercise stress the patient is able to tolerate. Therefore an incremental test can provide an objective assessment for a range of patients, from those with severe CAL to those whose function is minimally effected. Because the pace is externally controlled the effect of motivation and encouragement is minimised.

External pacing also allows for valid inter-subject comparison. Patients who have completed 500 metres in an incremental field walking test have experienced an equivalent 'work rate'/stress. This however cannot be concluded from patients completing similar distance in the 6 or 12 MWT and any comparison made as to their respective functional capacity would be invalid. A standardised incremental walking test would allow for a more objective comparison of any intervention to be made. An improvement in a patient's exercise capacity is immediately apparent when a patient repeats an incremental test and easily recorded but the same improvement is often not as obvious in a self paced test. For example a patient on his first recorded walk (not including practice walks) may walk 500 metres. After a course of physiotherapy/drugs the repeated

walking test may again record 500 metres but the patient approach to the two walking tests could have been quite different. In the first test they may have sauntered along the course but for the second walk they could have walked considerably quicker for the first 4 minutes and slowed down for the last 2 making the overall distances comparable. To the operator it would have been apparent that the patient's ability to exercise at a higher capacity had improved but not at all obvious to a second person assessing the patient's results. The 12 and 6 MWTs can be time quite consuming as they require at least two practice walks.

2.3.5. Laboratory assessment

Laboratory assessment is both expensive in terms of the equipment required and quite intimidating to the patient and as a result of these limitations field exercise tests were developed. Field tests are easy to administer but have the disadvantage that usually the pulse, ECG and respiratory rate can only be measured after exercise or with telemetry devices. It is impossible or very difficult to measure $\dot{V}_E$, $\dot{V}o_2$ or $\dot{V}co_2$ (carbon dioxide). If this breadth of information is required it is usually necessary to perform a laboratory based test. This is usually performed using either a treadmill or a cycle ergometer.

In the mid-eighties a compromise between the self-paced field test and laboratory assessment was proposed, a self paced treadmill test (Beaumont et al 1985). The patients, as in the 12 MWT were allowed to control the speed of treadmill walking and during this test various physiological parameters were monitored. The distances covered for treadmill test two vs test three was not significantly different, nor was the distance between the corridor and treadmill test. However this distance did become significantly different for the treadmill test when measurements of gas exchange were made that required the patients to breathe through a mouthpiece. In conclusion it

was suggested that patients may prefer this type of testing over progressive treadmill tests which may be frightening to them and being able to quantifying the rest periods may be of use in assessing the limits to everyday activity. Contrary to the results of Beaumont et al (1985) Swerts et al (1990) identified that patients walked significantly further during the corridor test than during a self paced treadmill test (no equipment worn) although the maximal heart rate and breathlessness score were not significantly different. This suggests that the patients experienced a similar level of stress for the two protocols and were more familiar with the corridor walk.

There exists a wealth of incremental treadmill protocols that are varied in their speed, inclination or both to assess the breathless patient. They allow detailed cardio-respiratory measurements to be performed. The majority have their origins in the assessment of cardio-vascular disorders. The most widely used is the Bruce protocol (ACSM 1991). The protocol involves a change of speed and inclination every 3 minutes. These increases of exercise intensity are relatively large and consequently the test is usually quite brief. A disadvantage of this approach is the high oxygen cost of the initial stage and each increment (Jones 1988). The ACSM suggest a 10-20% error in the estimation of $\dot{V}O_{2\,peak}$ due to the large increments of the test exceeding the $\dot{V}O_2$ uptake mechanisms in most patients. The Balke protocol keeps the speed constant and the gradient is increased from zero by equal steps of 2.5% every minute. A modified Balke protocol (Balke 1959, Jones 1988) format again adopts a constant walking speed with increases of 2-3% every 2-3 minutes. This test is appropriate for the more severely disabled patient. The ACSM (1991) suggest that this protocol is more suitable to assess $\dot{V}O_{2\,peak}$ in patients because of the gradual rise in exercise intensity.

Very recently Myers et al (1992) recommend that the most appropriate treadmill test is indeed one that is

individualised to each patient. McKelvie and Jones (1989) propose that treadmill testing is the most appropriate form of exercise testing if a rehabilitation program constitutes fully or in part an exercise regimen based upon walking.

The treadmill offers a familiar activity to the patient ,perhaps unlike cycle ergometry. Jones (1988) suggests that some measurements are more easily taken during a cycle test. Blood pressure and blood sampling is easier for the operator and breathing through a mouthpiece is easier for the patient whilst on a cycle. This is because of the relative stability of the upper body. Practical disadvantages to the treadmill are the size, weight and cost of the equipment and some are quite noisy. The major difference between the two modes of testing is with the $\dot{V}O_{2max}$. In untrained subjects it is usually higher on the treadmill than on the cycle ergometer. On average this difference is 5-10% (ACSM 1991). The majority of these studies applies to a normal population and may not apply equally well to a patient population (McKelvie and Jones 1989). This difference is possibly related to the peripheral fatigue of the exercising thigh muscle. However some patients find it difficult to walk without holding on to the handrail and this reduces O_2 uptake (ACSM 1991).

Cycle ergometry has certain advantages over treadmill testing. The former is relatively inexpensive and quiet and the work rate is easy to control. Because the body weight is supported the work rate is definable although for some individuals the seat may prove uncomfortable and difficult to maintain. Hansen (1984) suggests that some women and a few men have difficulty in cycling smoothly. In 1985 Cockcroft et al studied arterial desaturation in 9 patients with CAL during treadmill and bicycle exercise. A greater fall was identified during the self paced treadmill walk than the cycle test. The $\dot{V}O_{2\,peak}$ was in fact higher on the bicycle than the treadmill in contrast to studies on 'normals'(Hansen 1984). They remarked that care must be

taken when testing patients on a cycle and examining the arterial desaturation as it may underestimate the desaturation that occurs with walking.

2.3.6. Sub-maximal versus maximal exercise testing

In the use of both field and laboratory exercise tests opinion varies as to whether they should be maximal or sub-maximal. A test should be incremental as fixed level exercise protocols add little information to that gained from the resting measurements (Jones 1988). Wilmore (1984) proposes that sub-maximal (which may be single or multi-stage) testing with end points determined on predicted maximal heart rates is not considered desirable as the standard deviation of predicted maximal heart rate can be +/-10 beat.min^{-1}. Bruce (1984) supports this view and highlights that predetermined end points (HR, O_2 requirements or work load) are based upon average values for the 'normal' person. Lung disease can limit exercise at heart rates less than 130 beat.min^{-1} and therefore estimation of the $\dot{V}o_{2\,peak}$ at these low levels may not possible. Once one of these end points has been reached it then relies on the patient reporting whether the exercise represented a high, medium or low fraction of his capacity. Ideally the exercise protocol should therefore stress the patient's respiratory system progressively to a symptom limited maximum performance.

Maximal testing with self determined symptomatic end points allows individual patients to attain a maximal performance that is more reproducible than the response to sub-maximal work load and from these maximal values a comparison can be made to expected normal values to define the limitation to exercise and assess the patients 'true' functional capacity. Spiro (1977) identified that motivation is important and will vary considerably amongst patients. Furthermore, an incremental exercise protocol stresses the cardiovascular system gradually, unlike the

sub-maximal tests where the stress may be maximal from the start so an incremental test may be safer for the patient.

2.4 THE NORMAL VENTILATORY RESPONSE TO EXERCISE

It is appropriate to consider the determinants of the ventilatory response to muscular activity as this provides a reference point for considering the patterns of abnormal responses and to identify the site(s) of the system's limitations.

The performance of exercise requires a co-ordinated response from the respiratory and cardiovascular system to transport oxygen from the atmosphere to the contracting muscles and dispose of carbon dioxide. The normal response is precisely regulated in response to the metabolic requirements of the system. The ability to take in and utilize oxygen depends upon firstly the efficiency of the respiratory system, ie pulmonary ventilation, diffusion of the oxygen from the lung alveoli to the pulmonary capillaries. Secondly, cardiac performance ,ie redistribution of blood flow to the skeletal muscle and finally the extraction and utilisation of the oxygen by the contracting muscle (ACSM 1991). However this discussion will be confined to the response made by the respiratory system to exercise.

2.4.1 The ventilatory response to exercise

The normal response to exercise is an increase in ventilation ($\dot{V}E$) from the resting 6.0 $l.min^{-1}$ to 100-150 $l.min^{-1}$ (in extreme cases up to 200 $l.min^{-1}$). The increase is to maintain the physiochemical environment of the contracting muscle cells (Whipp & Ward 1991) ie, to transfer O_2 and clear CO_2 at rates appropriate to their consumption and production. This increase in $\dot{V}E$ with progressive exercise is achieved initially by an increase in the tidal volume (V_T) with a modest increase in the frequency (these changes occur before there has been any

alteration in the CO_2 production (Jones 1991)). The changes occur virtually simultaneously with the onset of exercise and it has been suggested that the increase in $\dot{V}E$ is associated with the increase in pulmonary blood flow (Whipp & Ward 1991), possibly activated by mechanisms originating in the right ventricle. The rapid changes in $\dot{V}E$ had traditionally been considered to be secondary to the activity of exercising limbs. Subsequent increases in $\dot{V}E$ (after 20s) are proposed to be a response to peripheral and central chemoreceptors by the altered blood gas composition. As the intensity of the exercise increases a maximum V_T is reached and any increase in $\dot{V}E$ is a result of an increase in the respiratory rate (at maximum exercise this may reach 50 breath.min^{-1} (Pardy 1984)). $\dot{V}E$ increases in a linear relationship with O_2 consumption and CO_2 output to approximately 50-60% of the maximal oxygen uptake ($\dot{V}O_{2\,max}$)(Jones 1988). The maximally attained tidal volume represents 50-60% of the vital capacity (Gibson 1990). It is thought that any further increase in the V_T is limited mechanically due to the decreased compliance of the lungs which in turn is thought to be reduced because of the increased volume of blood in the lungs causing the tissues to stiffen (Gibson 1990). With this increase in exercise intensity is a fall in the end expiratory volume to below the FRC, this force generated by the expiratory muscles considerably reduces the pressure generated by the inspiratory muscles for a given V_T (Jones 1991). The ratio of inspiration/expiratory time remains fairly constant from rest to exercise (Ti/Ttot 0.35-0.4) as does the ratio of inspiratory and expiratory flow (inspiration is approximately 1.5 times expiratory flow) (Grimby 1971).

Grimby et al (1976) indicated that during exercise the diaphragm generated most of the driving force of the inspiratory effort and remained within an acceptable range of the length-tension curve.

The physiological dead space (V_D) increases with exercise

although not as much as the increase in the V_T, consequently the V_D/V_T ratio which is normally 25-35% at rest falls to values between 5-20% (Jones 1988). The implications of these changes in absolute values and the ratio is unclear (Jones 1991). It is thought that the airways resistance is reduced with exercise allowing an increase in the tidal volume. The increase in the V_D potentially worsens gas exchange (V/Q ratio). Whipp and Ward (1991) suggest that the V_D/V_T ratio influences the effectiveness with which V_E can clear a given volume of CO_2 per minute, also taking into account the alveolar and arterial pCO_2. A decrease in the latter and a rise in the V_D/V_T ratio requires a greater ventilatory response per unit of CO_2 exchange and vice versa. In the ideal lung the mean alveolar and arterial pCO_2 is equal and both are determined by the appropriateness of the alveolar response to the CO_2 output of the lungs (Whipp & Pardy 1986). This alveolar ventilation is influenced by both the level of CO_2 output and the $PaCO_2$, for example a high $\dot{V}CO_2$ during exercise requires a large ventilatory response to regulate the $PaCO_2$. An increase in the alveolar ventilation - perfusion ratio further increases the need for the alveolar ventilation to increase. However the total ventilatory response is influenced by the $\dot{V}CO_2$, $PaCO_2$ and the V_D/V_T ratio.

In a steady state and non steady state phases of moderate exercise the increase in ventilation is closely matched to the increases in the $\dot{V}CO_2$. The coupling of the $\dot{V}CO_2$ to the V_E response allows regulation of the $PaCO_2$ and the H^+ in the steady state and results in only a small increase in the non-steady state. Consequently it is more appropriate to consider the relationship between $\dot{V}E$ and $\dot{V}CO_2$ rather that considering the effect of the $\dot{V}O_2$ upon $\dot{V}E$ (Whipp & Ward 1991). However, most types of exercise requiring dynamic work the increase in the $\dot{V}O_2$ is linearly related to the power output (Jones et al 1985). Wasserman (1967) demonstrated that changes in $\dot{V}E$ at steady state work rates

have a stronger relationship with alterations in $\dot{V}CO_2$ than $\dot{V}O_2$. Non steady state $\dot{V}_E$ responses are linear to the $\dot{V}CO_2$ but not the $\dot{V}O_2$. The linear $\dot{V}_E/\dot{V}CO_2$ relationship has a slope of approximately 25 $l.min^{-1}$ V_E per $l.min^{-1}$ CO_2 in healthy individuals (Wasserman & Whipp 1975). The linear relationship is preserved despite different test protocols until a point of sustained lactic acidosis is reached. This relationship between rising $\dot{V}CO_2$ and $\dot{V}_E$ during exercise is recognised but the linking mechanisms are unclear (Astrand & Rodahl 1986). It is proposed that the stimuli to increased ventilation is a combination of chemical (acidity and CO_2) and neurogenic signals (Gibson 1990).

CO_2 output at a given $\dot{V}O_2$ can be altered by a variety of metabolic factors. This ratio of CO_2 metabolically generated to O_2 consumption is labelled the respiratory quotient (RQ). The RQ value alters depending upon substrate utilisation, oxidative metabolism of free fatty acids is associated with a 30% reduction in $\dot{V}CO_2$ (RQ = 0.7) as compared to the $\dot{V}CO_2$ resulting from the aerobic metabolism of glucose or glycogen (RQ = 1.0) (Wasserman and Whipp 1975). The implication is that the rate of ventilation during exercise can be influenced quite markedly by the fuel source that is used. At rest the RQ value is approximately 0.8 this tend to rise with exercise to 1.0. This is however influenced by the duration and type of exercise performed. The mobilisation of fatty acid stores can take up to 20 minutes but after this point the longer exercise continues at low /moderate intensity the lower the CO_2 output will be.

At the lungs the ratio of CO_2/O_2 exchange is termed the respiratory exchange ratio (RER or R). R can differ from the RQ value particularly during exercise when CO_2 can be stored in the exercising muscle (Whipp & Ward 1991). Brown and Wasserman (1981) predicts that a substrate mixture dominated by fatty acid oxidation would be less stressful to the respiratory system during exercise as opposed to a

mixture dominated by carbohydrate oxidation. For prolonged exercise at a constant work rate the R value decreases. The result is a slightly increased cost for the work performed and a reduced CO_2 load to be cleared (Whipp & Wasserman 1988). The R value is also altered by the release of certain hormones that have their effect on fuel metabolism. The hormonal changes during exercise encourage lipolysis, there is a reduction in the level of insulin with elevation of catecholamines which favours the increased mobilisation of free fatty acids (Calles-Escandon 1984).

2.4.2 Maximal oxygen uptake

The ability to deliver O_2 to contracting skeletal muscle is vital to the performance of exercise. Maximal oxygen uptake ($\dot{V}O_{2\,max}$) is an important index of the capacity for sustained work performance (ACSM 1991). $\dot{V}O_{2\,max}$ has been described as a measure of the functional capacity of the body (Snell & Mitchell 1984), Astrand & Rodahl (1986) describe $\dot{V}O_{2\,max}$ more precisely as the 'highest oxygen uptake the individual can attain during exercise engaging large muscle groups while breathing air at sea level'. This gives an indication of the individual's aerobic power and can be identified by no further increase in the O_2 uptake despite an increased work load. One way in which this can be confirmed by a blood lactate concentration exceeding 8-9 $mmol.l^{-1}$ (Astrand & Rodahl 1986).

The determinants of $\dot{V}O_{2\,max}$ can be divided into four main categories; the respiratory system, the central and peripheral circulation and the muscle metabolism (Snell & Mitchell 1984). These factors in turn can be influenced by certain physical attributes to affect the overall performance in a healthy population. Stature affects the size of the heart, lungs and muscle. Age affects the maximal heart rate and the haemoglobin content of the blood. Exercise training can increase the effectiveness of the determinants of 'oxygen transport/delivery'. Endurance training improves the cardio-respiratory response to

exercise resulting in a higher $\dot{V}O_{2\,max}$, based upon a higher stroke volume and an increase in the arteriovenous O_2 difference. This type of training also evokes major changes in muscle oxidative capacity (Jones 1988) (beyond the scope of this review). Gender influences $\dot{V}O_{2\,max}$. Astrand & Rodahl (1986) suggest that the difference although at first appears to be significant in fact becomes insignificant when individual weight is expressed as kilo/fat-free body mass. The effects of inactivity are quite dramatic causing the $VO_{2\,max}$ to fall. The detrimental effects can be observed in the muscle and cardio-vascular system (Jones 1988).

2.4.3 Metabolic acidosis

Pyruvate is the end point of glycolysis and the subsequent fate of pyruvate depends on the conditions of the cell. The purpose of glycolysis is to produce ATP and substrates for the tricarboxylic (TCA) cycle for oxidation. Pyruvate formation is also associated with the reduction of nicotinamide adenine dinucleotide (NAD^+) to NADH. To maintain glycolysis, NADH must be reoxidised (to NAD^+). This can occur either through oxidation in the mitochondria or through the action of lactate dehydrogenase (LDH)(Katz and Sahlin 1990). At mild to moderate levels of exercise the increase in glycolysis is balanced by an increase in the oxidation of pyruvate with no increase in the production of lactate. Lactate accumulation becomes apparent when an increased proportion of pyruvate is reduced to lactate, and the latter released from the contracting skeletal muscle. This usually occurs at high exercise intensity and is indicative of accelerated glycolysis. This increase in the lactate production is observed at approximately 50-70% of $\dot{V}O_{2\,max}$, ie well before the aerobic capacity is fully utilised (Katz and Sahlin 1990).

The classic explanation is that the O_2 supply to the contracting muscles is inadequate and part of the energy requirements must be provided by increasing the amount of

ATP derived anaerobically (although the mechanism for the increased production is not fully understood). At this point predominately anaerobic metabolism occurs with the excessive production of lactic acid beyond its level of uptake with the consequent accumulation of lactic acid in the plasma. The work rate or $\dot{V}O_2$ at which this occurs is commonly named the anaerobic threshold (AT) (Stainsby and Brooks 1990, Jones 1991). Originally, the concept of an anaerobic threshold was introduced to identify the point at which the ventilatory changes associated with incremental exercise matched the metabolic acidosis (Wasserman et al 1973). It should be noted that the production of lactate and its entry into the blood continuously occurs even at low levels of exercise despite the muscle being well oxygenated, however it is simultaneously removed from the blood. The anaerobic threshold is identified by the increase in plasma levels of lactate and secondly as was suggested by Wasserman (1984), identified as the point where the linear relationship between $\dot{V}E$ and $\dot{V}CO_2$ deviates and there is an increase in the CO_2 production. The source of the increased $\dot{V}CO_2$ during heavy exercise is firstly metabolic, secondly as a result of the bicarbonate buffering and finally can be a result of hyperventilation (Wasserman 1984). This buffering of the H^+ accounts for the disproportionate increase of $\dot{V}CO_2$ compared to the $\dot{V}O_2$ when the blood lactate increases.

Whipp and Wasserman (1988) propose that an exercise test with one minute increments allows the identification of a period of 'isocapnic buffering', ie a change in $\dot{V}E$ proportional to the changes in the $\dot{V}CO_2$ in the same proportions as below the threshold despite two sources of $\dot{V}CO_2$. Once this has been identified it allows the investigator to exclude other causes of an increase in the ventilatory drive eg pain. This stage is transient and is followed by a respiratory compensation for this non respiratory acidosis. The rise in the $\dot{V}E/\dot{V}CO_2$ relationship as the work rate increases, and the pH and $PaCO_2$ drop is

initiated by the carotid bodies stimulating the increase in $\dot{V}_E$ beyond the increase in the $\dot{V}CO_2$.

The intensity of exercise at which lactate accumulation increases is 50-70% of the maximal oxygen uptake ($\dot{V}O_{2\,max}$) (Katz and Sahlin 1990, ACSM 1991). The measurement of the anaerobic threshold is unaffected by the protocol employed but like the measurement of $\dot{V}O_2$ it is affected by the mode of testing (Wasserman 1984). The threshold is however altered by factors such as good physical fitness and cardio-vascular performance (Kanarek et al 1979). The anaerobic threshold has often been documented using the alternative terminology 'onset of blood lactate accumulation'(OBLA). The terms are not synonymous, the latter refers to a reference value of blood lactate concentration, eg 2.5 or 4 mmol.l^{-1}. It is assumed that a threshold level of blood lactate concentration (corresponding to a predominately anaerobic metabolism) and the deviation of the linear $\dot{V}_E/\dot{V}CO_2$ relationship are highly correlated (Astrand & Rodahl 1986). However peak capillary blood lactate concentrations of 8 mmol.l^{-1} support the assumption that a healthy individual's aerobic power has been taxed to its maximum (Astrand & Rodahl 1986).

The description of an anaerobic threshold is not universally accepted. It is felt that the theory does not match the practical findings eg some muscle fibres employ anaerobic metabolism despite adequate O_2 delivery. Wasserman (1984, 1992) provides a list of evidence supporting the concept of the anaerobic/lactate threshold and its dependency upon the adequacy of O_2 delivery, defining the anaerobic threshold as the point below which work is performed totally oxidatively and above which the metabolism is at least partially anaerobic.

2.4.4 The limitation to exercise tolerance

The limit to exercise in healthy individuals is not the respiratory system. The work of the respiratory muscle is

to overcome the elastic resistance and flow resistance forces. The energy requirements of breathing are 0.5-1.0 ml $O_2.l^{-1}$ ventilation, obviously with increased work the cost increases up to 10% of the total O_2 uptake. Astrand & Rodahl (1986) dismiss this as not being a limiting factor to exercise because firstly after the $\dot{V}O_{2\,max}$ has been reached the exercise continues. Secondly, at maximal exercise it is possible to increase ventilation voluntarily, ie the respiratory muscles are not exhausted during spontaneous respiration. This is demonstrated by a comparison of maximum ventilation during exercise with the maximum voluntary ventilation (MVV) at rest, the former is between half and three-quarters of the maximum ventilatory capacity and therefore unlikely to be the initiating factor for the termination of exercise. Thirdly, with strenuous exercise $\dot{V}E$ depends on the volume of CO_2 produced. The measurement of the alveolar gas tensions indicate that gas exchange is effective.

The respiratory muscles may indirectly limit exercise by demanding a high percentage increase in their O_2 requirements and therefore deprive the exercising muscle of increased O_2 supply. It is not usual for this to occur in normal individuals and increase in ventilation beyond a critical point can be met by anaerobic metabolism. The identification of fatigue is more difficult in respiratory muscles than skeletal muscles (Jones 1991), making it difficult to identify fatigue and how it imposes limits to exercise. Electromyographic changes have been identified, as have alterations in breathing patterns (paradoxical movement of the abdomen and rib cage). Work has been completed to argue that these observations do not necessarily indicate respiratory muscle fatigue (Tobin et al 1987). Whipp and Ward (1991) suggest that in highly trained athletes who can exercise with their $\dot{V}E$ at 90% of their MVV respiratory muscle fatigue is likely to develop. Di Prampero (1992) reviews the current literature examining the limitations to $\dot{V}O_{2\,max}$ in healthy individuals at sea

level. The article identifies four resistances to maximal O_2 flow. Firstly the flow of O_2 from the atmosphere to the arterial blood, secondly transport by the circulation, thirdly the peripheral transfer of O_2 to the mitochondria and finally the efficacy of the mitochondria. He cites a number of authors considering this last factor in conjunction with the O_2 kinetics at the lung and tissue level as a limitation to exercise. However, the stroke volume attains its maximum volume at relatively low work rates. As a result of this any increase in cardiac output is manifested through an increase in the heart rate. At maximum exercise the normal individual is very close to the predicted maximal heart rate and tolerance to exercise is dictated by the maximum cardiac output that can be achieved (Gibson 1990).

2.5 RESPONSE TO EXERCISE IN PATIENTS WITH CAL

Exercise tolerance in patients with CAL is reduced. A number of reasons why patients experience this reduction have been reported (Brown and Wasserman 1981), ranging from compromised gas exchange to cardiac limitations. However the consensus of opinion suggests the major limitation is related to the abnormal mechanical characteristics of the respiratory system, ie an inability to increase ventilation (Jones 1966). The recognition of a ventilatory limit to exercise in patients with CAL was further supported by Jones and colleagues (1971) in work identifying that at maximal levels of exercise in patients with CAL the heart rate response is frequently below that predicted from the age (Jones et al 1971) and the patients complain of dyspnoea, reflecting a lack of stress on the cardio-vascular system. Further evidence of a ventilatory limit to exercise is revealed when ventilatory mechanisms are compared in the normal and in patients with CAL. A sedentary male may reach a maximum $\dot{V}_E$ of 140 litres in sharp contrast to a patients values. Values for patients maximum ventilation have been recorded as low as 26.9 $l.min^{-1}$

(Swinburn et al 1985) although other workers have reported higher values for $\dot{V}_E$ in groups of patients with differing FEV_1 values (Dillard et al 1985, Brown et al 1985, Kirsch et al 1989). Jones et al (1971) suggest that a relationship exists between the severity of the obstruction as measured by the FEV_1 and the maximum ventilation. A patient with an FEV_1 of 2 litres would have a maximum $\dot{V}_E$ of 60 litres. This value would fall to 45 litres with an FEV_1 of 1 litre. An alternative comparison with the norm can be made with regard to the MVV; in normal subjects the maximal exercise ventilation is usually around 70% of the MVV (Whipp and Pardy 1984) whilst in patients with CAL this value is commonly 100% (Jones et al 1971).

Blood lactate concentrations during exercise in patients are typically low, Wasserman and Whipp (1975) suggest that the values rarely rise above 3-4 $mmol.l^{-1}$ and in some cases may not rise above the resting levels (Jones et al 1985). If a metabolic acidosis does occur it is usually at a lower work rate than for normal subjects (Jones et al 1971). Jones et al (1985) propose that in pulmonary disorders associated with a serious decrease in ventilatory capacity, patients may be limited by this factor before lactate accumulation occurs. Lactic acid begins to accumulate in blood at about 55% of a healthy untrained aerobic metabolism (McArdle et al 1991). Exercise performance is frequently calibrated against HR therefore a patient exercising at a high percentage of his maximum predicted HR should be anticipated to produce a lactic acidosis.

It is now clear that patients with CAL can develop metabolic acidosis with exercise (Kanarek et al 1979, Severa et al 1983, Sue et al 1988). The presence or absence of a metabolic acidosis during exercise may have important implications for the choice of exercise levels within a training programme (Sue et al 1988). The identification of an anaerobic threshold in this group of patients can be

used as an aid to the diagnosis of exercise intolerance. Wasserman (1984) suggests that the AT is normal in patients with CAL whilst the $\dot{V}O_2$ is reduced. One explanation for the absence of an anaerobic threshold is the severe ventilatory limitation prevents the threshold from being recognised or alternatively the respiratory system imposes such a limitation that the threshold levels are not reached (Kanarek et al 1979). Wasserman and Whipp (1975) suggest that this may be due to arterial hypoxaemia or a detraining effect.

The maximal oxygen uptake measured at maximal exercise in these patients is lower than seen in a normal age matched population (Loke et al 1984, Mihn et al 1979). Because of this ventilatory limit to exercise the peak $\dot{V}O_2$ measured is often referred to as a symptom limited $\dot{V}O_{2\,max}$ (Belman 1986) or $\dot{V}O_{2\,peak}$. Gallagher (1990) questions the exact mechanisms of this reduced response to exercise and proposes an alteration in the pulmonary mechanics, an increase in the oxygen cost of breathing and poor exercise technique a possible reasons (ie poor treadmill technique). Astrand and Rodahl (1986) quote 2.55 $l.min^{-1}$ as a typical $\dot{V}O_{2\,peak}$ in a 55-59 year population. On the other hand Swinburn et al (1985) document a $\dot{V}O_{2\,peak}$ of just 0.8 $l.min^{-1}$ in a group of patients with severe CAL. The value of $\dot{V}O_{2\,peak}$ is occasionally reported as an oxygen pulse, ie the $\dot{V}O_{2\,peak}$ is divided by the heart rate, and is a product of stroke volume and the arterio-venous O_2 difference. The oxygen pulse is reduced at maximal exercise in patients with CAL (Kanarek et al 1979). Some authors have found that the ratio of heart rate to the $\dot{V}O_2$ is normal. An alternative finding is for the heart rate to be higher in patients at a set work rate when compared to normals and the $\dot{V}O_2$ to be reduced giving a reduced heart rate/$\dot{V}O_2$ slope. The interpretation of the oxygen pulse in this group of patients is not unanimous. Some authors (Mihn et al 1979) believe that it is an indication of a reduced stroke volume and therefore concurrent cardiac

abnormalities. Other workers (Nery et al 1983) suggest that the low values are consistent with a ventilatory limit to exercise reflecting that the cardio-vascular system has not been stressed.

Recently attention has been directed towards studying latent cardiac abnormalities affecting exercise performance in patients with CAL. Wagner (1992) proposes that mixed venous pO_2 is reduced at rest in these patients and could fall even with gentle exercise. The reason suggested for this is the relative increase in $\dot{V}O_2$ requirements to the cardiac output. Factors identified as limiting the cardiac output were co-existing ischaemic heart disease (most CAL patients are old and have smoked) and pulmonary hypertension (associated with structural abnormalities of the lung compounded by hypoxic vasoconstriction). It has also been documented that right ventricular function is decreased in this group of patients (Matthay et al 1992). Right ventricular afterload is increased for the reasons described above, the response of the right ventricle is to dilate and hypertrophy to maintain cardiac output, however the increased pulmonary vasculature reduces the right ventricular ejection fraction and there is a resulting tachycardia to maintain cardiac output (Rogers & Howard 1992).

It can be concluded that the mechanisms limiting exercise performance in patients with CAL is not fully understood. Although the main rate limiting factors may include ventilation, circulation, V/Q inequality, muscular and psychological, a consensus of opinion exists believing that most patients have a ventilatory limit to exercise.

2.5.1 The ventilatory response to exercise

If a patient with CAL is required to perform an incremental exercise test a point is rapidly reached when

the spontaneously generated expiratory airflow reaches the maximum values attainable by forced volitional effort (Whipp and Pardy 1984). This was demonstrated by Stubbing et al (1980). In a study of 6 patients with CAL it was identified by using body plethysmography that at rest all but 1 patient reached their maximum expiratory flow volume curve (MEFV), but no patient exceeded it. On exercising all the patients reached their MEFV curve, indicating that this inability to increase flow rates is a major constraint on maximum $\dot{V}_E$. In the same piece of work it was identified that these patients exhibit significant increases in their FRC and RV. In contrast to normal subjects (Dodds et al 1984), the FRC is increased with exercise particularly those with severe CAL (Younes 1991). The reasons for this are thought to be as a result of the breathing pattern adopted by the subject (due to the reduced expiratory flow rates) and secondly it is actively elevated by activity of the inspiratory muscles to allow a greater expiratory flow at higher lung volumes (Younes 1991). This increase in the FRC allows higher expiratory flow rates to be reached for the same driving pressure (due to the shift of the exercising flow/volume curve within the MEFV curve). The result is a delay in the onset of mechanical limitation to exercise. However this is complicated by the exacerbation of dynamic airways compression associated with the increased driving pressures required to generate the maximum expiratory flow. The generation of pressures in excess of a critical point would result in increased respiratory work but not in expiratory flow. Leaver and Pride (1971) suggest that this point is not exceeded in patients with CAL and adequate pressures are generated to induce maximum expiratory airflow but not to cause unnecessary airway and alveolar compression.

A second detrimental effect of increasing the FRC is to mechanically disadvantage the inspiratory muscles as they are placed at an inefficient part of their force length

relationship and to produce a given force at this position requires an increase of muscle excitation. Consequently, it would be anticipated that the inspiratory muscles would fatigue more rapidly (Rochester et al 1979). This volume increase associated with an increase in the volume of the thorax if too large can lead to a further decline in the efficiency of the inspiratory muscles. Consequently the changes in the FRC become self limiting, requiring higher and higher pressures to be generated in the inspiratory muscles resulting in fatigue. The dynamic hyperinflation is also likely to account for the rapid increases in O_2 consumption when $\dot{V}E$ rises. Dodds et al (1984) suggests that the hyperinflated lung with a flattened diaphragm requires greater activity of the inspiratory inter-costal muscles and again predisposes to fatigue and this combined with respiratory muscle dysfunction leads towards limitation of exercise performance. Sharp et al (1968) demonstrated that the maximal inspiratory muscle pressure measured at FRC was significantly lower in patients with CAL than in normal subjects (31 vs 78 cm H_2O) and this weakness contributes to exercise limitation. With these limitations the patient with CAL must increase his $\dot{V}E$ in response to exercise by using the following strategy. The FRC would increase, V_T must decrease and the respiratory rate must increase. This approach overcomes the problems imposed by the MEFV curve. To increase V_T the FRC would need to decrease which in turn would decrease the maximal flow on expiration and therefore decrease $\dot{V}E$. Consequently the above approach is adopted to support moderate exercise (Beck et al 1991).

During an incremental exercise test patients exhibit a higher ventilation than normal at a prescribed metabolic rate/power output/$\dot{V}O_2$ (Jones et al 1985) and usually although not always, an increase in the slope of the $\dot{V}E/\dot{V}CO_2$ relationship, which increases with the intensity of the exercise (Whipp et al 1984). This rise is thought to be mainly due to the large increase in dead space ventilation

which occurs as a result of the high frequency of breathing as the work rate increases (Wasserman and Whipp 1975). Total ventilation is conventionally divided into alveolar and dead space components. The former is usually defined in terms of the arterial pCO_2. Alveolar under-ventilation frequently occurs in patients with CAL but it is seldom to such a degree as to reduce the total $\dot{V}E$ response to exercise. Jones, Killian and Stubbing (1985) propose that these patients usually have an increased $PaCO_2$ during exercise, unlike normal subjects. Dead space ventilation is expressed as the proportional difference between $PaCO_2$ and $PECO_2$.

The V_D/V_T ratio is defined using the Bohr-Enghoff equation as,

$$V_D/V_T = PaCO_2 - PECO_2 \;/\; PaCO_2$$

(Jones et al 1985) and is regarded as an index of the efficiency with which $\dot{V}E$ clears CO_2 from the alveoli. In CAL patients the V_D/V_T ratio is often high in exercise due to a limitation upon the increase of V_T and poor gas exchange efficiency. A high V_D/V_T ratio leads to a high ventilation for a given CO_2 and therefore predisposes to dyspnoea. In some patients alveolar under ventilation lessens this effect but are consequently exposed to the effect of an increased $PaCO_2$. A patient's ratio during exercise may reach 0.5, the normal exercising value is 0.05 - 0.2 and is lowest in those individuals with a high V_T and low breathing frequency.

For patients to maintain a $PaCO_2$ within the normal range, $\dot{V}E$ at a given $\dot{V}CO_2$ must increase. This need to increase the $\dot{V}E$ will ultimately encroach upon the ventilatory capacity and contribute to the dyspnoea and the termination of exercise. Younes (1991) suggests that this ability to increase the frequency of breathing is limited to 20/min in moderate disease and even lower in more severe disease, at these critical values there is no increase in the $\dot{V}E$ and the

V_T falls. There appears to be no consensus as to how patients with CAL increase their V_T. Dodd et al (1984) in his study of patients with severe CAL (and marked hyperinflation) revealed that the driving force for the increase in volume arose from the intercostal and accessory muscles for inspiration and the abdominal muscles increased expiration. Conversely, Pardy et al (1981) studying the effect of physiotherapy versus the effect of inspiratory muscle training in patients with CAL identified that the primary increase in $\dot{V}E$ was due to the diaphragm.

An alternative strategy used in patients with CAL to increase ventilation besides the disproportionate increase in frequency (Younes 1991), is to increase the time allowed for the expiratory phase of the breathing cycle. This requires the inspiratory flow to increase and a shortened Ti. In mild to moderate CAL the respiratory cycle (Ti/Ttot) is not reduced, but in more severe disease the value falls to 0.35 to 0.4 (Dodd et al 1984). It has been suggested that these values may fall as low as 0.3 (normal 0.4-0.5). Younes (1991) proposes that patients with severe CAL do vary in their Ti/Ttot and frequency in response to exercise.

The work of breathing has two main components, firstly the work against lung elasticity and secondly the work performed in generating airflow, both of which are disturbed in patients with CAL (Beck et al 1991). In CAL the lung elasticity is reduced and the airways resistance is increased which leads to increases in the work of breathing (at rest the power output of the respiratory muscles is 10-12 times that of normals (McGregor & Becklake 1961). The result of these demands is that the work rate and the O_2 consumption of the respiratory muscles is increased and it has been proposed that respiratory muscle fatigue may contribute to the termination of exercise. The magnitude of this increase is uncertain due to the

difficulties associated with measurements of respiratory muscle work, increases up to 35-40% of the total O_2 consumption have been quoted (Loke et al 1984) and this obviously leaves little O_2 for the exercising muscle. Dodd et al (1984) suggest that the expiratory muscles are also inefficient in their energy consumption, it is believed that these muscles generate high positive pleural pressures beyond which maximum flow is generated.

Jones (1966) examined pulmonary gas exchange in patients with CAL who were divided into two categories, emphysema and chronic bronchitis. The main differences revealed were that the chronic bronchitis patients were able to exercise to a significantly higher workload and had a significantly lower arterial PO_2 at rest that did not fall with exercise, unlike the patients with emphysema where a significant fall in their arterial saturation was observed. The cause of this difference is related to the poor V/Q ratio that is accentuated with exercise. Minh et al (1979) exercised 17 patients with CAL and divided them into two groups based upon whether desaturation occurred. The patients who desaturated appeared to have a higher FRC, RV and TLC but a lower FEV_1 and MVV compared to the group of patients with CAL who did not markedly desaturate with exercise and contributed this alteration of saturation levels to the V/Q mismatch. Dantzer (1986) also showed that in his group of 7 patients with severe CAL (mean FEV_1 0.56) the V/Q ratio did not alter significantly despite the sharp fall in the arterial blood gases. Loke et al (1984) proposes that emphysematous patients tend to desaturate on symptom limited exercise whilst in chronic bronchitic patients the response is influenced by the degree of obstruction. Saturation monitoring is useful in exercise testing to assess the severity of the gas exchange impairment associated with the loss of alveolar surface area and capillary beds (Jones 1988).

2.6 THE MEASUREMENT OF $\dot{V}_E$ AND $\dot{V}o_2$ IN PATIENTS WITH CAL

The measurements of $\dot{V}_E$ and $\dot{V}o_2$ at both rest and exercise in patients with CAL is relatively well documented. The measurement of $\dot{V}O_{2\,peak}$ in patients with CAL is synonymous with a symptom limited $\dot{V}o_2$. Jones (1988) suggests this value is a close approximation of a true $\dot{V}o_{2\,max}$, it is however a true $\dot{V}o_{2\,max}$ for these patients. The primary difference between a $\dot{V}o_{2\,peak}$ and a true $\dot{V}o_{2\,max}$ is the nature of the limitation. Assessment of the degree of exhaustion is difficult as patients often terminate the test before the maximal heart rate is attained, the basis of effort evaluation in normals. It is documented that the measurement of $\dot{V}o_{2\,peak}$ is reproducible in these patients (Severa et al 1983).

Brown et al (1985) examined the reproducibility of $\dot{V}o_{2\,peak}$ employing three different incremental cycle ergometer exercise protocols (not described). The group (n=11, mean FEV_1 1.5 l) had remarkably similar mean $\dot{V}o_{2\,peak}$ and $\dot{V}E_{\,max}$ for the 3 tests (1.31, 1.31 and 1.32 $l.min^{-1}$ $\dot{V}o_{2\,peak}$ and 52.8, 50.2 and 53.7 $l.min^{-1}$ $\dot{V}E_{\,max}$), despite the different modes of testing. Despite the mean values being similar these results do not indicate that there was good agreement between the tests. The authors however did indicate that a degree of variability may be anticipated in this category of patients due to firstly the problem that a true $\dot{V}o_{2\,peak}$ is hardly ever measured. Similarly the degree of patient effort is difficult to determine. The authors suggest that even stable patients vary in their lung mechanisms resulting in variability of their $\dot{V}o_{2\,peak}$.

Belman et al (1991) concurrently measured the reproducibility of exercising measurements whilst assessing the reproducibility of the Borg breathlessness scale. Eleven patients (mean FEV_1 1.18 l) performed one incremental test and four subsequent tests at 95% $\dot{V}o_{2\,peak}$. The $\dot{V}_E$, HR and $\dot{V}o_{2\,peak}$ stabilised after 1 or 2 attempts. The mean $\dot{V}o_{2\,peak}$ was 1.07 $l.min^{-1}$ ($\dot{V}_E$ and HR data not presented).

An early study (Jones et al 1971) divided 50 patients into various categories (FEV_1, diagnosis) for analysis. All subjects performed an incremental and steady state cycle test and a step test. The results identifying FEV_1 categories revealed decrease in $\dot{V}E_{max}$, from 56 $l.min^{-1}$ in the less affected group (FEV_1 > 1.6 l) to 38 $l.min^{-1}$ in the most disabled group (FEV_1 < 0.8 l). The mean maximal heart rate ranged from 132 - 151 $beat.min^{-1}$ in the 4 study groups. Spiro et al (1975), like Jones et al (1971) categorised the patients into 2 groups, depending on their FEV_1 value (mean values 1.45 l and 0.62 l), but also recruited a group of normal subjects. All individuals performed a maximal incremental cycle test. The values of $\dot{V}E_{max}$ and $\dot{V}O_{2\,peak}$ were lower than the normals in both clinical groups and lower for the patients with the lower FEV_1 ($\dot{V}E_{max}$ was 54.4, 48.6 and 30.0 $l.min^{-1}$, $\dot{V}O_{2\,peak}$ was 2.0, 1.5 and 1.0 $l.min^{-1}$ in the normal and patient groups, mean FEV_1 1.45 and 0.62 l respectively). The $\dot{V}E_{peak}$ of patients exceeded their predicted $\dot{V}E_{max}$ (FEV_1 x 35). For the more severely affected patient this represented 146% of their predicted $\dot{V}E_{max}$ and for the less affected patient 99%.

Following on from the work of Spiro et al (1975), Matthews et al (1989) and Nery et al (1983) directly compared the performance of patients and age matched controls. Patient groups were not divided into clinical categories. Matthews et al (1989) evaluated the response to a series of cycle ergometer exercise protocols (incremental and individually prescribed steady state) for both normals and patients (FVC 4.49 & 3.40 l and FEV_1 3.34 & 1.68 l respectively). He found that the resting $\dot{V}O_2$ was similar (0.33 and 0.34 $l.min^{-1}$ respectively), unlike the resting $\dot{V}E$ which was significantly higher in the patients, 11.3 $l.min^{-1}$ vs 13.6 $l.min^{-1}$, as was the resting HR (78 vs 85 $beat.min^{-1}$ in the control and patient group respectively). Results of the symptom limited test reveal a significant lower $\dot{V}E_{peak}$ (79

$l.min^{-1}$ vs 58 $l.min^{-1}$) (but a higher level of V_E at comparable work rates) and $\dot{V}O_2$ (2.08 vs 1.61 $l.min^{-1}$). The maximal values for the patients were recorded at a significantly lower work rate. In contrast to other studies (Nery et al 1983, Belman 1986) the maximal heart rate was not significantly different for the two groups, (156 normals vs 148). However in agreement with Spiro et al (1975) and Jones & Berman (1984) the heart rate values represented a higher heart rate than the normals for a prescribed $\dot{V}O_2$.

Nery et al (1983) studied the different exercise responses between normals, cardiac and respiratory patients (CAL n=6 mean FEV_1 1.1 l), employing an incremental cycle test. The resting $\dot{V}O_2$ was similar for the 3 groups (CAL patients 4.7 $ml.min^{-1}.kg^{-1}$) while the $\dot{V}O_{2\,peak}$ was 18.3 $ml.min^{-1}.kg^{-1}$ for the CAL patients and 30.7 $ml.min^{-1}.kg^{-1}$ for the control group. $\dot{V}E_{max}$ was again lower than normals 44.5 vs 80.9 $l.min^{-1}$, however at an equivalent metabolic rate the CAL patients had a significantly higher $\dot{V}E$, supporting the reports by Spiro et al (1975) and Matthews et al (1989) that a higher $\dot{V}E$ is required to complete the same work level as normals. The maximal heart rate was 141 $beat.min^{-1}$ (normals 154 $beat.min^{-1}$ $p<0.05$). The mean maximal oxygen pulse ($ml.beat^{-1}$) was significantly lower than the normal (8.3 vs 13.5 $ml.beat^{-1}$). The authors concluded that these patients were not experiencing a cardio-vascular limitation to exercise proposing that the low O_2 pulse, indicated a low stroke volume and lower heart rate, reflects the termination of exercise before the cardio-vascular system is stressed.

In opposition to this opinion is the work of Minh et al (1979). In study of 18 patients with CAL (mean FEV_1 1.85 l) they measured a max $\dot{V}E$ of 49 $l.min^{-1}$, a $\dot{V}O_{2\,peak}$ 1.18 $l.min^{-1}$ and a maximal heart rate of 137 $beat.min^{-1}$. This was assessed by an individually prescribed incremental treadmill test. However, unlike the cycle tests this test lasted for 16-20

minutes, and the authors document that 3 patients complained of leg pain at the end of exercise and 8 of general fatigue. The $\dot{V}O_2$ is not very different from the values reported above despite the different modes of testing [it is acknowledged (Hansen 1984) that treadmill testing provokes a higher $\dot{V}O_{2\,max}$ than cycle ergometry]. The values translate into an O_2 pulse of 8.56 ml.beat^{-1}. Although this value is comparable to that of Nery et al (1983), Minh et al (1979) interprets the low value as an indicator of a low stroke volume (SV) which occurs secondary to the loss of the pulmonary capillary bed. Matthews et al (1989) support the theory of Mihn et al (1979) but propose alternative cardiac abnormalities that may contribute to the higher HR at a given level of exercise when compared to normals.

Kirsch et al (1989) employed a universal cycle ergometer protocol to assess 6 patients. The mean FEV_1 was 1.28 l, the mean resting $\dot{V}O_2$ 0.28 l.min^{-1} and mean $\dot{V}E$ at rest was 15.8 l.min^{-1}. These values represent a slight increase from the normal values at rest ($\dot{V}O_2$ 2-300 ml.min^{-1} and $\dot{V}E$ 10-12 l.min^{-1}). This group of patients had a mean $\dot{V}E_{max}$ of 43 l.min^{-1} the mean $\dot{V}O_{2\,peak}$ was 1.04 l.min^{-1}. The significantly different result of this trial compared to those quoted above is the heart rate data. The mean maximal heart rate was just 101 beat.min^{-1} despite the age and FEV_1 values being similar.

In a group of more severely affected patients (n= 50 mean FEV_1 1.02 l) ZuWallack et al (1991) measured the mean $\dot{V}E_{max}$ to be 26.8 l.min^{-1} and the mean $\dot{V}O_{2\,peak}$ 890 ml.min^{-1}, equivalent to 13.7 ml.min^{-1}.kg^{-1}. These patients performed an incremental treadmill test that was set on estimated physical impairment. The low $\dot{V}E_{max}$ is consistent with the severe airflow obstruction indicated in the FEV_1 value.

Similarly low values were quoted by Swinburn et al (1985)

who examined the effect of 3 different types of exercise on $\dot{V}O_2$ and $\dot{V}E$. The patients (n=17) with severe CAL (mean FEV_1 0.8 l) performed an incremental cycle test, a paced step test and a self paced corridor walk test. The mean $\dot{V}O_{2\,peak}$ values were 0.8, 1.0 and 0.85 $l.min^{-1}$ respectively (significantly greater for the step test). The corresponding values for the $\dot{V}E_{max}$ were 26.9, 31.3 and 27.4 $l.min^{-1}$. The values for the self paced test indicate that these patient did not volitionally reach a $\dot{V}O_{2\,peak}$.

Lanigan (1990) studied the resting $\dot{V}O_2$ of normals and patients and standardised the results for body surface area. The mean $\dot{V}O_2$ was 0.18 $l.min^{-1}$ higher in patients which when standardised for body surface area represents a 10.9% increase in patients. This was significantly higher, however these patients did have severe airways disease (mean FEV_1 of 0.78 l). A fundamental difference in this trial compared to other trials is the method of gas analysis. The patients were assessed with an open canopy technique. The patient's head and chest is enclosed in a clear chamber that has a fresh gas flow and an exhaust system. This form of measurement was an attempt to overcome the problems identified by Askanazi et al (1980). These authors observed a 30% increase in the minute volume if a face mask was worn and a 14% increase if a nose-clip and mouthpiece used. The effect of apparatus on clinical measurement was documented by Beaumont and Cockcroft (1985). Whilst developing a self-paced 12-minute treadmill walking test they found that patients' performance (distance walked) was significantly reduced when using a mouthpiece.

Despite this apparent lack of agreement when directly measuring $\dot{V}O_{2\,peak}$ and $\dot{V}E_{max}$ in these patients there have been many attempts to develop predictive formulae of patients' maximal exercise capacity. If reliable these equations could replace expensive and invasive exercise tolerance

tests in some individuals (Carlson et al 1991).

Dillard et al (1985) proposed a two variable formula incorporating the peak inspiratory flow rate (PIFR) and the FEV_1 to estimate maximum $\dot{V}E$, which in turn is used as a predictor of the severity of the disease. The mean $\dot{V}E_{max}$, measured on an incremental cycle ergometer test (n=30, mean FEV_1 1.75 l) was 67.2(29)$l.min^{-1}$. Dillard presented the formula $\dot{V}E_{max} = 21.34\ FEV_1 + 6.28\ PIFR + 3.94$ (r= 0.967 for the predicted vs measured $\dot{V}E$ relationship).

In a subsequent piece of work again considering the importance of the inspiratory muscles contribution to $\dot{V}E_{max}$, Dillard et al (1989) proposed that $\dot{V}O_{2\,peak}$ could be predicted from an equation including static lung function values. The patients (n=20 mean FEV_1 1.72 l) had a mean $\dot{V}E$ max of 67 $l.min^{-1}$ and a mean $\dot{V}O_{2\,peak}$ of 1.8 $l.min^{-1}$. The FEV_1 had a moderate relationship with the $\dot{V}O_{2\,peak}$ (r=0.76). The peak inspiratory pressure (PIP), unlike the peak expiratory pressure (PEP) correlated well with $\dot{V}O_{2\,peak}$ (r=0.82 and 0.14 respectively). The $\dot{V}E_{max}$ in both studies by Dillard and colleagues is considerably higher than has been previously reported for this category of patients but the lung function values were also greater for this group.

In a recent study Carlson et al (1991) assessed the usefulness of predictive equations of $\dot{V}O_{2\,peak}$ in 2 groups of patients. The 2 groups had mean FEV_1 values of 1.44 and 1.40 l. The directly measured $\dot{V}O_{2\,peak}$ values were 1.25 and 1.23 $l.min^{-1}$. The authors concluded that they were able to predict exercise $\dot{V}O_{2\,peak}$ using measurements of the diffusing capacity of carbon monoxide, maximum voluntary ventilation, peak exercise V_D/V_T and resting $\dot{V}E$ (r=0.90).

Carter et al (1987) examined the usefulness of a number of these equations to predict $\dot{V}E$ max as a function of FEV_1 in 53 patients with CAL (mean FEV_1 1.0 l). Exercise testing (incremental cycle ergometry) revealed a peak $\dot{V}E$ of

37.7(13.6) $l.min^{-1}$ and a $\dot{V}O_{2\,peak}$ of 1.05 $l.min^{-1}$. The $\dot{V}E_{max}$ exceeded the mean MVV (32.9 l) perhaps indicating dynamic compression of the airways whist performing this manoeuvre. The group concluded that the most robust equation used to predict $\dot{V}E_{max}$ was FEV_1 x 37.5. This group of patients had a strong relationship between FEV_1 and $\dot{V}E_{max}$.

In summary, $\dot{V}O_2$ and $\dot{V}E$ are consistently increased at rest and limited at maximal exercise in patients when compared to normal. The degree to which they are limited appears, very broadly to relate, to the severity of the disease. It has been suggested that lung function tests explain only 50% of the variance of measured exercise tolerance (Carlson et al 1991). There appears to be a general trend that the more able patients (assessed by FEV_1 values) attain both a higher $\dot{V}E_{max}$ and a higher $\dot{V}O_{2\,peak}$ (Spiro et al 1975). Whilst the severely affected patient had a reduced ventilatory and cardio-vascular response to exercise, consistent with a ventilatory limit to exercise. The documented heart rate response at a given $\dot{V}O_2$ is not unanimous. Matthews et al (1989), Spiro et al (1975) and Nery et al (1983) quote higher than normal values at a given $\dot{V}O_2$, while Wasserman and Whipp (1975) did not see this raised heart rate response. Similarly Jones and co-workers (1971) proposed that this relationship was normal. Some of the increase in heart rate may be accounted for by the requirements of the respiratory muscles, but Matthews et al (1989) indicates that the low $\dot{V}O_{2\,peak}$ may indicate co-existing cardiovascular pathologies.

The variety of test methods may contribute to the lack of agreement, added to which a number of test procedures were adopted with incremental increases varying in both the timing and intensity of the increase. Where large resistance is applied maximal data may not have been measured because of the influence of skeletal muscle fatigue which may account for the results reported by Mihn

et al (1979). The results of Jones et al (1971) and Spiro et al (1975) are attractive when examining the patients' response to exercise as they allow the examination of the response to exercise at different stages of the disease as defined by spirometry.

2.7 THE MEASUREMENT OF BLOOD LACTATE CONCENTRATIONS AND METABOLIC ACIDOSIS IN PATIENTS WITH CAL

The frequency and degree of metabolic acidosis and the identification of an anaerobic threshold during exercise in patients with CAL is unclear. The confusion is compounded by the choice of measurement of the anaerobic threshold. Shah (1992) examined five methods of assessing this threshold that are commonly applied to normal subjects. He found little agreement between them with the results varying from 43% to 84% $\dot{V}O_{2\,max}$, these values also had a random relationship with the ventilatory threshold. This doesn't give any confidence in the validity of this approach.

Spiro et al (1975) investigated the effect of exercise on a group of normal subjects and a group of patients divided into two groups according to their FEV_1. All the subjects performed an incremental cycle exercise test. The peak rise in blood lactate (measured from ear lobe sampling) was smaller for the patient groups than the normals but there was a difference between the two patient groups. The patients with the greater FEV_1 (mean 1.45 l) had a peak blood lactate concentration of 3.6 $mmol.l^{-1}$ compared to 2.5 $mmol.l^{-1}$ in the more severely affected group (mean FEV_1 0.62 l). Neither of the patient groups exhibited a disproportionate rise in $\dot{V}E$ at maximum exercise intensity associated with a rise in blood lactate concentration. The mean maximum heart rate attained by the 2 groups represented 82% (less affected group) and 71% of predicted maximum.

Jones et al (1971) studied the exercise response of 50 patients divided into 2 clinical groups, emphysematous and chronic bronchitic. The blood lactate concentrations were calculated using a CO_2 balance technique at 60% of maximal work rate. The change in levels was greatest in the least affected group (FEV_1 > 1.6 l), 2.4 mmol.l^{-1} in comparison to a mean change of 1.36 mmol l^{-1} in the most affected group (FEV_1 < 0.8 l). The total patient group, unlike the study above (Spiro et al 1975) demonstrated a relationship between $\dot{V}o_2$ and HR that did not differ significantly from normal. However the exercise protocol varied the study from the Spiro et al (1975) who employed a maximal test. However the trend in both studies is similar, ie the patients with the more severe disease process (assessed upon FEV_1) are less likely to develop a pronounced metabolic acidosis.

Jakobsson et al (1990) studied 18 patients divided into 2 groups [8 with chronic respiratory failure (CRF), 10 without (NCRF)]. Both groups had severe CAL (mean FEV_1 0.69 and 0.99 l). Blood lactate concentrations was measured at 30 W (the mean maximal work rate for the CRF group which was sub-maximal for the NCRF group). Blood lactate concentration was significantly higher at a standard 30w work rate in the CRF group (3.3 vs 1.9 mmol.l^{-1}), although the maximal blood lactate concentrations were not significantly different. The mean maximal HR was almost the same for both groups (131 vs 129 beat.min^{-1}).

Sauntier et al (1979) studied glycolysis in a group of 11 patients with CAL and hypoxaemia (the mean maximal $\dot{V}_E$ was 37.27 l.min^{-1} and the $\dot{V}o_{2\,peak}$ was 1.19 l.min^{-1}). The blood lactate concentration rose to 4.6 mmol.l^{-1} after a maximal cycle test. The authors recognised that the lactate levels are considerably higher than those measured in young sportsmen during similar exercise but the $\dot{V}o_2$ vs blood lactate relationship paralleled the values obtained from normal subjects between 50 - 60 years.

The studies described above do not attempt to identify an anaerobic threshold in patients with CAL. However this is becoming increasingly important as a physiological indicator of the potential efficacy of a rehabilitation programme. The achievement of an anaerobic threshold is considered by some to be of primary importance when selecting patients for exercise training. Casaburi et al (1991) proposes that a reduction in blood lactate is a primary physiological effect of a training programme.

Sue et al (1988) studied the usefulness of the V-slope method proposed by Beaver et al (1986) to identify an anaerobic threshold in patients with CAL (briefly, this involves identifying the point at which the $\dot{V}CO_2$ vs $\dot{V}O_2$ plot deviates from its linear relationship due to the increased CO_2 production, indicating the buffering of lactic acid). Comparing those results with the change in blood bicarbonate. The study identified 14 patients who developed a metabolic acidosis and 8 patients who had no significant metabolic acidosis. The metabolic acidosis appeared to be greater in patients who have the least restriction upon their functional capacity indicated by their FEV_1/FEV ratio and VC. They could not be separated by their FEV_1 (1.16 l for the group that did not and 1.23 l for the group that did develop a metabolic acidosis) or FVC alone. The maximal heart rate for the 2 groups was slightly but not significantly different, but when the values were expressed as a percentage of predicted maximum it became apparent that those patients able to exercise nearer to their maximum heart rate were more likely to develop a metabolic acidosis. Furthermore the patients who were able to attain a $\dot{V}E_{max}$ near to their MVV, (83% and 96%) were also more likely to reach an anaerobic threshold. The $\dot{V}O_{2peak}$ of the two groups was 1.01 $l.min^{-1}$ (n=8) and 1.28 $l.min^{-1}$ (n=14). An anaerobic threshold was identified at 0.97 and 0.89 $l.min^{-1}$ using the two methods (significantly lower than that identified in a normal group, 1.5 and 1.4 $l.min^{-1}$). Although

these two methods employed by Sue et al (1988) had a strong relationship they were significantly different. Despite this the authors proposed that the V-slope method is a non-invasive satisfactory method of anaerobic threshold detection.

Nery et al (1983) in the study described above (n=6 FEV_1 1.1 l) identified the AT as the $\dot{V}O_2$ at which various alterations in the gas relationships occurred, primarily the $\dot{V}O_2$ at which the gas exchange ratio increases abruptly without hyperinflation. Interestingly the CAL patients had a similar $\dot{V}O_2$ at their anaerobic threshold compared to the normals (15.7 and 16.6 $ml.min^{-1}.kg^{-1}$ respectively), consistent with the proposals of Wasserman (1984), indicating that CAL patients exhibit a similar threshold but a decreased $\dot{V}O_2$ max. However, the heart rate was significantly higher at this point (138 vs 107 $beat.min^{-1}$) and the work rate was considerably lower. The $\dot{V}O_2$ values at the anaerobic threshold represent 85% and 54% respectively of the patients and normals $\dot{V}O_{2peak/max}$.

Kanarek et al (1979) discussed why there seemed to be some discrepancies regarding the measurement of an anaerobic threshold in these patients. His trial retrospectively divided a group of 12 subjects into two separate groups, that were based upon the detection of an anaerobic threshold by gas exchange alone, although blood gas and pH measurements were obtained. The subjects (mean FEV_1 1.03 l for the group that reached an anaerobic threshold and 1.04 l for the group that did not) performed an incremental cycle test to exhaustion. Despite the two groups being clinically similar at rest there were fundamental differences in their response to exercise. The group that developed an anaerobic threshold had a significantly higher $\dot{V}E$ (37.8 vs 28.7 $l.min^{-1}$) and consequently attained a higher percentage of their predicted $\dot{V}E$, and also reached a much higher heart rate

(159 vs 136 beat.min^{-1}). There was no significant difference between the $\dot{V}O_{2\,peak}$ (1.05 l.min^{-1} for both groups), the $\dot{V}CO_2$, R value or the oxygen pulse. The arterial blood gas results support the ventilatory measurements of the threshold, both the pH and the bicarbonate dropped significantly in the anaerobic threshold group.

From the data Kanarek and colleagues (1979) develop a new perspective when considering the development of an anaerobic threshold. The patients who demonstrate an anaerobic threshold utilised 100% of their breathing capacity, whilst the group that did not utilised just 74% indicating that it was unlikely to be a ventilatory limit to reaching an anaerobic threshold. Kanarek and colleagues (1979) postulated that the group that reached a threshold level were stimulated to increase ventilation and had a higher cardiac reserve, but an anaerobic threshold is not reached within the limits of exercise in many patients. The authors continued to suggest that the group developing the anaerobic threshold in fact have cardiac dysfunction. This assumption is based upon the $\dot{V}O_2$ at the threshold level (comparable to that detected in heart disease ,ie O_2 flow to the muscles is reduced) and the high heart rate at the end of exercise. The group that did not reach this threshold level, despite reaching a similar workload do not appear to fall into a distinct category of patients limited solely by their respiratory or cardio-vascular system. It is suggested that these patients are limited in their response to exercise by a combination of factors including muscle fatigue and weakness.

Elliott et al (1987) compared a direct (arterial lactate sampling) and indirect method (ventilatory response) to the determination of AT in a group of 6 patients (mean FEV_1 1.25 l) performing maximal cycle ergometry tests. The mean $\dot{V}E_{max}$ and $\dot{V}O_{2\,peak}$ and HR were 50.8 l.min^{-1}, 1.31 l.min^{-1} and 143 beat.min^{-1} respectively. The mean maximal blood lactate was

6.3 mmol.l^{-1}. In line with the study of Sue et al (1988) the patients that developed the greatest increase in blood lactate also developed the greater $\dot{V}E_{max}$, maximal HR (and % predicted), and $\dot{V}O_{2peak}$. These values did not appear to relate to the patients' spirometry. Elliott et al (1978) identified a strong relationship between the two methods, the most resilient ventilatory measurement that identified an AT in all six patients was the R value and the end tidal CO_2 ($F_{ET}CO_2$). A mean anaerobic threshold was identified in these patients at a $\dot{V}O_2$ of 10.3 ml.min^{-1}.kg^{-1} at a low work rate exercise.

In conclusion it appears that a rise in blood lactate concentrations can be detected with an incremental exercise test in some patients with CAL. However the degree of this lactic acidosis appears to depend upon how severely the patient is affected, reflected in his resting spirometry and how well the patient is able to utilise his exercise capacity. This is commonly assessed by measuring the heart rate and max $\dot{V}E$. There appears to be a diversity of opinion on the measurement of an anaerobic threshold relating to both the heart rate and work rate at which it occurs, if indeed it does. The apparently logical conclusions drawn from the work of Spiro et al (1975) and Jones et al (1971) relating to the severity of the lung disease are questioned by the work of Kanarek et al (1979), who identified an anaerobic threshold in a group of severely affected patients and proposed cardiac abnormalities in the group of severely affected patients that attained an anaerobic threshold.

3. GENERAL METHODS

3.1 EQUIPMENT

3.1.1 Lung function testing

The lung volumes, FEV_1 and the FVC were measured on a vitalograph wedge bellows spirometer. The same type of instrument was used at both Loughborough and Glenfield Hospital. The tests were performed at all times in standing. The correct procedure was explained to the patients. Expectoration of sputum was encouraged prior to testing. Subjects were required to perform three acceptable manoeuvres, that were at least 60 seconds apart. Acceptability was defined as a forced expiration time of at least 6 seconds, no detectable volume changes over the last 2 seconds, no coughing and no obvious leak. The best two results were required to fulfil the reproducibility criteria; the two FEV_1 and FVC values were recorded as being less than 5% different. The spirometry was recorded for every patient on each visit as for the study employing 'normal' volunteers. Predicted values of the FVC and FEV_1 were taken from those recommended by the European Community for Coal and Steel (Quanjer 1983) and are specific to an individuals age, height and sex. All values are expressed at B.T.P.S. (body temperature, ambient pressure and saturated with water vapour) FEV_1 and FVC measurements are taken to the nearest 0.05 l.

3.1.2 Height

Subjects' height was recorded for all of the trials. At Loughborough this was assessed using a Holtain Stadiometer, whilst at Glenfield a stadiometer attached to the balance scales was used. All subjects were bare footed and the measurement was taken to the nearest 1.0 cm.

3.1.3 Weight

Subjects were weighed at both Loughborough and Glenfield with a beam balance (Loughborough - Avery Ltd., Model 3306 ABV. Glenfield - Marsden Ltd., Model 150). All subjects

were weighed in bare feet wearing the items of clothing that they would exercise in and any extra items/articles were discarded. Measurements were made to the nearest 0.05 kg.

3.1.4 Blood pressure

The patients and healthy volunteers had their blood pressure measured for each visit as a safety precaution. The measurements were made with a sphygmomanometer. The cuff was wound closely around the upper arm and the site of the brachial artery was identified by palpation. The cuff was inflated to approximately 180 mmHg and slowly deflated and the systolic and diastolic points were detected by auscultation.

3.1.5 Heart rate

Heart rate was monitored using two different methods. For the shuttle walking test and the six minute test the Sports Tester PE3000 (Cranlea & Co) was used. This is a short range telemetry device that can monitor and record ambulatory heart rate. The patient was required to wear a transmitter that was fastened to an elasticated strap around the chest. The transmitter was positioned on the left hand side of the thorax approximately over the heart. To aid transmission it was necessary to dampen the two electrodes before positioning the strap. A 'watch like' receiver was worn on the patient's wrist. It was possible to define the upper and lower limits of a patients heart rate and programme the Sports Tester to alarm if either of these limits were violated. The upper limit used was 85% of the predicted maximal heart rate using the formula 210 - (0.65 x age). In addition, the Sports tester had a memory that when activated stores a particular set of values until the device is used again. The monitor also had a stopwatch facility that allowed the synchronisation of the heart rate response with the start of the exercise test. Reading were taken every 15 seconds.

Alternatively, for the trials employing the treadmill, the heart rate was monitored during each test using a Rigel oscilloscope (model 302) from three chest electrodes at Loughborough and a Graseby Medical heart rate monitor at Glenfield General Hospital. Two electrodes were placed on either side of the chest, the third was placed proximal to the right shoulder. Before the electrodes were applied the skin was cleaned with a Steret and abraded slightly to ensure a satisfactory contact was made. In addition some contact jelly was applied to improve the contact further. During the incremental treadmill test the heart rate was recorded every 15 seconds.

3.1.6 Borg breathlessness score

Patients were requested to report their perceived breathlessness at rest and post exercise for all the shuttle walks and the six minute walking test. Patients were advised to indicate the severity of their breathlessness on the scale ranging from 0 to 10, where 0 represents nothing at all or no discomfort with your breathing and 10 indicates that the intensity of the breathlessness is maximal. During the treadmill exercise tests patients were asked to indicate their breathlessness in the final minute of each stage of walking (Appendix B).

3.1.7 Borg exertion score

Normal subjects were required to report their perceived exertion on a Borg exertion scale with values ranging from 6 - 20. This was performed at the same times as described above during treadmill tests (Appendix B).

3.1.8 The Chronic Respiratory Disease Questionnaire (CRDQ)

The CRDQ (appendix C) requires an operator to administer the questionnaire to the guidelines provided (Guyatt et al 1987) and takes about 20 minutes for the first administration and 10-15 minutes for subsequent visits. The initial test requires the patient to identify 5 activities

that make him feel short of breath. These can be from the provided list or patients can volunteer activities specific to them. The activities that the patient selected form the dyspnoea component of the questionnaire and are the activities repeated in follow-ups use for the dyspnoea component. The questionnaire has a total of 19 questions that when analysed are divided into four component parts, dyspnoea as described above, fatigue, mastery, ie does the patient feel in control of their chest disease and emotional function. After each question the patient is presented with a colour coded card upon which are seven numbered responses and the patient selects the number that best corresponds with their perceived breathlessness/ fatigue etc. For follow-up questionnaires the patient is informed of the answer he gave last time. The 19 questions have a potential total score of 140, although the four components do not have an equivalent potential score. Significant change is documented if the score for each block has increased on average of 0.5 per question (dyspnoea 2.5, fatigue 2.0, emotion 3.5 and mastery 2.0).

3.2 EXPIRED AIR COLLECTION (Douglas bag collections)

Expired air was collected via a rubber mouthpiece (Harvard Equipment). A nose clip was worn (Harvard Equipment) during collection of expired gases. The mouthpiece was connected to a light weight two-way valve. Wide bore (30 mm) tubing (Falconia) connected the valve to a two way tap which was opened and closed manually at the appropriate time to allow the collection of the expired air in the 150 litre Douglas Bags (Harvard equipment).

3.3 EXPIRED GAS ANALYSIS

i. Oxygen analyser The oxygen content of the expired air was measured using a paramagnetic oxygen analyser (Sybron; Taylor Servomex, model 570A), with a digital display accurate to 0.1%. The calibration and gas analysis

procedure are described more fully in Appendices D and E.

ii. Carbon dioxide analyser An infrared carbon dioxide analyser (Mines Safety Appliances Ltd.; Lira Model 303) was used to measure the carbon dioxide content of the expired air. The percentage of carbon dioxide was expressed on a meter in an analogue form that was converted to a percentage of carbon dioxide with a dedicated calibration curve. The calibration and analysing procedures can be found in Appendices D and E.

iii. Gas meter The expired air was evacuated from the Douglas bags using a Moulinex vacuum pump. The volume of expired air was determined using a dry gas meter (Harvard Instruments). A thermistor linked to a thermometer (Edale type 2948, Model C), was sited inside the air inlet pipe allowing measurement of the temperature of the expired air.

3.4 SUBJECT RECRUITMENT AND CONSENT

Patients were contacted either by letter or informally at the medical out-patients clinics. Regardless of the method of contact the patients received a document outlining the aims of the study and their involvement if they consented to participate. This initial communication briefly outlined both the potential risk and the benefits from taking part in the study. At this stage patients were requested to complete a form indicating interest in taking part in the study. Further contact (telephone) confirmed the patients interest, resolved any queries and arranged the first appointment. At this first appointment written consent was sought and patients were informed that they could drop out from the study at any stage without having to give a reason.

3.6 STATISTICAL METHODS

Standard parametric statistical techniques were used

throughout (Cohen and Holliday 1979, Hicks 1988) for the data that was interval and/or ratio. Relationships between two or more variables was examined using the Pearson Product Moment correlation coefficient. To examine the test retest reliability of the shuttle walking test and the six minute walking test an intraclass correlation coefficient (R) was employed as recommended by Baumgartner and Jackson (1987). Students t-test was used for testing the significance between two correlated means. Differences and relationships were considered significant at the 0.05 level. According to the recommendations of Bland and Altman (1986) the level of agreement was analysed and expressed as the mean difference between two variables and their 95% confidence interval.

Non-parametric statistical analysis was employed for sample sizes of $n<10$, according to the recommendations of Siegel (1956). Spearman Rank order correlations are used to compare two sets of results and the Wilcoxon matched pairs signed ranks test is used to examine the difference between two related samples. In addition the results of the CRDQ and reported Borg scale data (both ordinal scales) for the study were analysed using non-parametric tests (Friedman two-way analysis of variance by ranks for repeat visits and the Wilcoxon matched pair signed ranks test for the comparison of two visits). However it is not uncommon in medical and related journals to analyse this data using parametric statistical analysis. For this reason the results relating to these two areas do express both the Pearson Product and the Spearman rank order correlation coefficients enabling a comparison to be made from data relating to similar patient groups.

Unless otherwise stated the values expressed in the text and the tables refers to the group means (x) and the standard deviation (S.D).

4. DEVELOPMENT OF A 10 METRE SHUTTLE WALKING TEST OF FUNCTIONAL CAPACITY IN PATIENTS WITH CHRONIC AIRWAYS LIMITATION.

4.1 INTRODUCTION

It is well documented that a patient's responses to static lung function tests are poorly related to their ability to perform exercise and cope with the activities of daily living (Swinburn et al 1985). Exercise testing is therefore employed to provide objective measures of functional capacity and quantify disability. Laboratory assessment, using a treadmill or cycle ergometer test is both expensive and time consuming. Consequently, attention has focused upon the development of reliable field exercise tests. These are predominately walking tests, although step tests which have their origins in the assessment of cardiac patients are also employed (Johnson et al 1977).

The most commonly used field tests are the 6 and 12 minute walking test (6 and 12 MWT). These tests are self paced and rely upon the individual to gauge an appropriate walking speed aiming to cover as much ground as is possible in the time allowed. It is assumed that the distance completed allows the operator to estimate an individual's functional capacity. Many authors have questioned the validity of these self paced walking tests as a means of assessing patients effectively and monitoring change in the patient's condition (Morgan 1989).

The purpose of this study was to develop and examine the reproducibility of an incremental, externally paced field exercise test that stresses patients with CAL to a symptom limited maximum performance. The principle was that employed in the 20 metre shuttle running test proposed by Léger and Lambert (1982) and is now widely used to assess functional capacity in sports men and women. Performance on

the 20m shuttle running test has a strong relationship (r=0.92) with directly measured $\dot{V}O_{2\,peak}$ (Ramsbottom et al 1988). A modification of this shuttle running test was first employed for patients with CAL by Scott (1989). The speeds of walking were directly proportional to the speeds of the running test. A 10m course was used and Scott (1989) reported adequate test/retest reproducibility. Problems were identified with the range of walking speeds selected and with the timing of the increments. The present study develops a more appropriate protocol with differing walking speeds and increments.

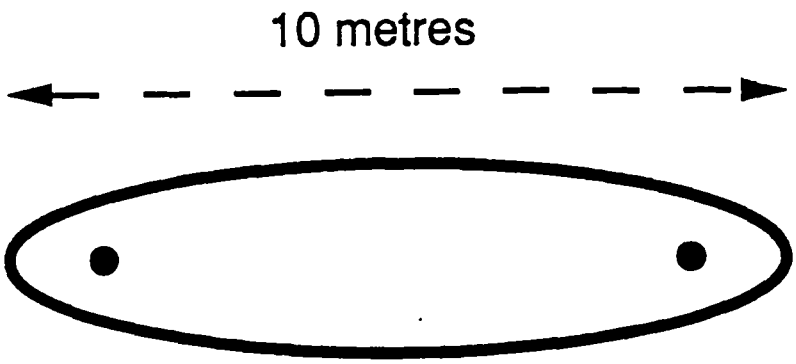
4.2 METHOD

In developing the new protocol some problems identified by Scott (1989) had to be addressed. A slower start was required that would allow the assessment of the more severely affected patient. For the less disabled patients an increased number of increments was needed (10 walking speeds were originally employed) and a faster final speed than the initial 10-level shuttle walk protocol. These modifications were based upon two observations; firstly in the group studied by Scott (1989) one patient completed the 10-level course, and secondly, as the mean FEV_1 was just 0.5 l, it was proposed to develop a more demanding test for the less disabled patients. The final proposal was to standardise the length of each increments to one minute, comparable to many incremental laboratory based tests.

4.2.1. TEST PROCEDURE

The test required the patients to walk up and down a 10 metre course (Fig 4.1). The course was identified by two cones inset 0.5m from either end to avoid the need for abrupt changes in direction. The speed at which the patient walked was dictated by audio-signals played from a tape recorder, originally generated from a BBC micro-computer. The accuracy of the timed signal was ensured by the inclusion on the tape of a calibration period of one minute

FIGURE 4.1 The shuttle walking test.



1 shuttle = 10 m

1 level = n shuttles

where n depends on walking speed

which could be checked against a stopwatch.

The explanation to the patient was standardised and recorded on the tape before the start of the test (Appendix A), advising the patient to "walk at a steady pace, aiming to turn around when you hear the signal. You should continue to walk until you feel that you are unable to maintain the required speed without becoming unduly breathless."

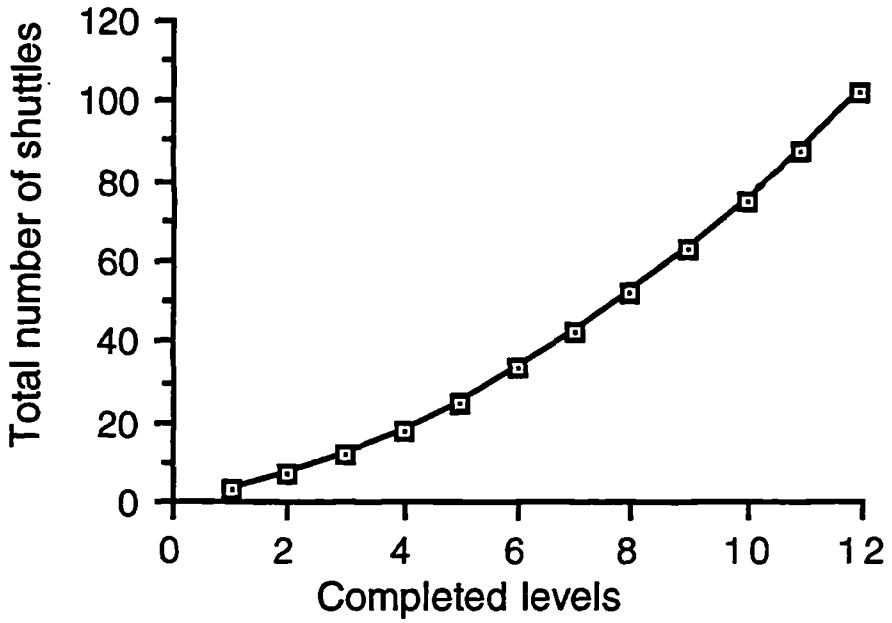
The start of the test was indicated by a triple bleep. Thereafter the tape emitted a single bleep at regular intervals at which points the subject attempted to be at the opposite end of the course, ie by the time the patient heard the signal he should be turning around the cone and proceeding back down the course. Each minute the speed of walking was increased by a small increment (0.17 $m.s^{-1}$), so the patient was required to walk progressively faster. A change of speed to a higher level was indicated by a triple bleep.

The first speed of walking was referred to as level 1, the second as level 2 and so on. Each level lasted for one minute and the tape continued for twelve minutes. The number of shuttles (10m lengths) in each level depended on the walking speed at that level (Table 4.1). For example, the patient is required to complete three shuttles in the first level. The number of shuttles the patient completes within consecutive levels increases by one, ie, for level 2, three shuttles, for level 3, four shuttles and so on. Figure 4.2 shows the total number of shuttles completed at the end of each level. To help the patient establish the routine of the test and the first, very slow speed of walking the operator walked alongside for the first minute. The patient has 20 seconds to complete each of the 3 shuttles in the first minute.

TABLE 4.1 The shuttle walking test protocol.

	SPEED				
Level	$m.s^{-1}$	$km.h^{-1}$	mile. h^{-1}	shuttle time (s)	No. of shuttles in level
1	0.50	1.80	1.12	20.00	3
2	0.67	2.41	1.50	15.00	4
3	0.84	3.03	1.88	12.00	5
4	1.01	3.36	2.26	10.00	6
5	1.18	4.25	2.64	8.57	7
6	1.35	4.86	3.02	7.50	8
7	1.52	5.47	3.40	6.67	9
8	1.69	6.08	3.78	6.00	10
9	1.86	6.69	4.16	5.46	11
10	2.03	7.31	4.54	5.00	12
11	2.20	7.92	4.92	4.62	13
12	2.37	8.53	5.30	4.29	14

FIGURE 4.2 The cumulative number of shuttles completed at the end of each level.



After this first minute the patients paced themselves to co-ordinate their walking speed with the timed signals. If the patient reached the cone before the signal they were instructed to remain at the end of the course until the signal indicated they could proceed with the test.

The operator sat along the 10m course and no encouragement was given. The only verbal contact was the advice given each minute to increase the walking speed slightly. In practice, all patients found it easy to pace themselves using the cues from the tape recorder.

The end of the test was determined by either (a) The patient; when he was too breathless to maintain the required speed or, (b) The operator; if the patient failed to complete the a shuttle in the time allowed, ie if the patient being more than 0.5m away from the cone when the bleep sounded or (c) Attainment of 85% of the predicted maximal heart rate. Maximal heart rate ($beat.min^{-1}$) was predicted by the formula [210 - (0.65 x age)].

The number of completed levels and shuttles was recorded and was converted from a total number of shuttles to a distance in metres.

4.2.2 PATIENT GROUP

The entire study was approved by the Leicestershire Health Authority ethical committee. Ten patients were recruited from medical clinics at Glenfield General Hospital and given a full explanation before informed, written consent was obtained. All patients were clinically stable throughout the trial, requiring no hospital admissions or alteration to their drug therapy.
Patients were excluded from the trial if they had documented:

(i) A diagnosis of hypoxia (arterial blood PO_2 less than 8 kPa).

(ii) Cor pulmonale or ischaemic heart disease.
(iii) Neurological or locomotor disorders.

The exclusion criteria represent an attempt to identify all patients whose limitation to exercise might not be due exclusively to the failure of the respiratory system to meet the demands of the test.

The patients made three visits to the hospital at intervals of one week, at the same time of day to preclude any diurnal variation in the disease. They administered no bronchodilator therapy for three hours prior to testing but continued to take all other medication as normal. The baseline measurements for each visit were:

(i) Spirometry (FEV_1 and FVC) (3.1.1)
(ii) Borg Breathlessness scale (Borg 1982) at rest (Appendix B).
(iii) Resting heart rate [measured with short range telemetry device(3.1.5)].
(iv) The Chronic Respiratory Disease Questionnaire (Appendix C)

The patient was always asked to report on their perceived breathlessness prior to the spirometry. The resting heart rate value was taken after 2-3 minutes of sitting after the telemetry device had been positioned.

Throughout the test heart rate was monitored and at the end of the test the patients rated their perception of breathlessness.

4.3 RESULTS

No patient was excluded or withdrew from the study (Table 4.2 shows the physical characteristics of the group) and no problems were experienced with patients finding it difficult to pace themselves. No patient was 'disqualified' because the speed of walking was misjudged.

The distances walked ranged from 90 m to 520 m ie, from

TABLE 4.2 Some physical characteristics [mean (SD)] of the patients, n=10.
(6 male, 4 female)

		Trial 1	Trial 2	Trial 3
Age (yr)	X	63.0	-	-
	SD	6.3	-	-
Height (m)	X	1.65	-	-
	SD	0.07	-	-
FEV_1 (l)	X	1.05	1.10	1.18
	SD	0.42	0.43	0.41
FEV_1 %predicted	X	41.4	44.1	47.6
	SD	16.9	19.4	18.4
FVC	X	2.22	2.40	2.52
	SD	0.63	0.53	0.59

level 2 plus 2 shuttles of level three to the end of level 8. No patient completed the 12-stage protocol. The mean distances walked for trials 1, 2 and 3 were 345, 376 and 378 m respectively (Table 4.3 and Fig.4.3). The agreement between the trials was examined in two different ways. The starting point was to examine the relationship between the distances walked on each trial (Table 4.4). Secondly the mean difference and 95% confidence interval of this difference were used to examine agreement.

The mean resting heart rate was 87, 84 and 85 beat.min^{-1} respectively. The results of the heart rate measurements are presented in Table 4.5 and Table 4.6 and Figure 4.4. This represented a mean increase from the resting level of 38, 44 and 42 beat.min^{-1}. The increase in the heart rate and the mean maximal heart rate values were not significantly different for the three trials. The horizontal line on Figure 4.4 represents the anticipated maximum heart rate for a 63 year old, the mean age of the group. The relationship between the distance walked and the percentage of maximal heart rate attained is shown in Table 4.7. Figure 4.5 represents the relationship from these values for trial 3. Figure 4.6 shows the heart rate values taken at the end of each minute for two representative patients.

There was a poor correlation between walking performance and patients' lung function values for all three trials (Table 4.8).

The Borg breathlessness ratings post-exercise are shown in Table 4.9 and 4.10. The mean increase from the resting values were 2.7, 2.5 and 2.6 for the 3 trials. There were no significant differences between trials for the reported ratings post- exercise test. There was no relationship between the Borg breathlessness rating and the spirometry results (FEV_1 and FVC).

TABLE 4.3 Mean, standard deviation and range of distances (m) completed on the 10m shuttle walking tests.

Trial	X	SD	Range
1	345	121	90 - 470
2	376	125	150 - 520
3	378	117	140 - 510

FIGURE 4.3 Mean (SEM) maximal distance (m) walked on trials 1, 2 and 3.

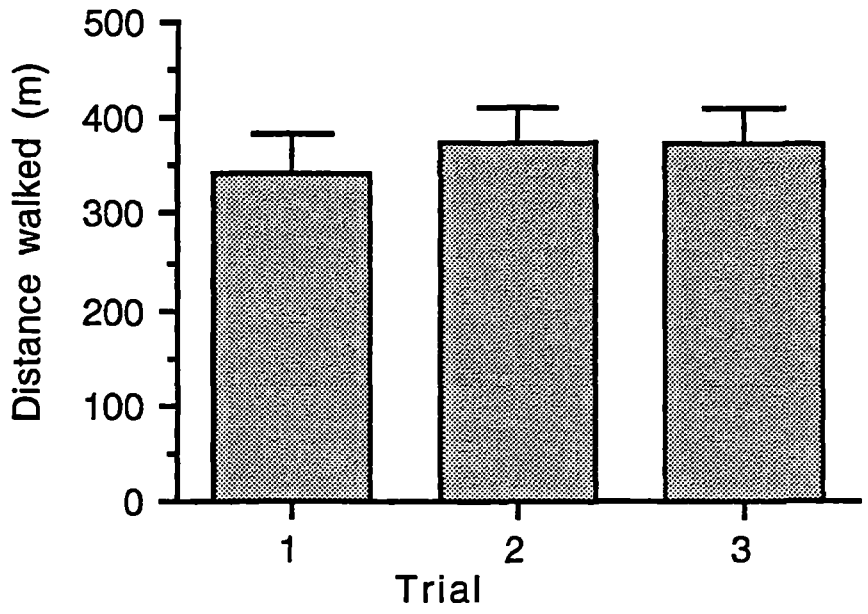


TABLE 4.4 Mean and standard deviation of between trial differences (m) together with 95% confidence intervals (m) and Intraclass Correlation coefficients (R) describing the relationship between distance walked on the 3 trials.

comparison	X	SD	95% CI	R
1 vs 2	-31.0*	25.1	-49.0 to 13.0	0.97
1 vs 3	-33.0*	21.1	-48.1 to 17.9	0.74
2 vs 3	-2.0	27.8	-21.9 to 17.9	0.87

* significantly different $p<0.05$

TABLE 4.5 Mean and standard deviation maximal heart rate ($beat.min^{-1}$) during the 10m shuttle walking test.

Trial	X	SD	range
1	125	17	97 - 145
2	128	17	97 - 151
3	127	17	95 - 150

TABLE 4.6 Mean and standard deviation for maximal heart rate (beat.min^{-1}) expressed as a percentage of predicted maximal heart rate [210 - (0.65 x age)].

Trial	X	SD	range
1	74	10	57 - 87
2	76	10	57 - 86
3	75	10	55 - 86

FIGURE 4.4 Mean (SEM) maximal heart rate (beat.min^{-1}) recorded for trials 1, 2 and 3.

TABLE 4.7 Pearson Product Moment correlation evaluating the relationship between the distance walked and percentage of predicted maximal heart rate attained.

Trial	r
1	-0.11
2	0.08
3	0.13

FIGURE 4.5 Mean maximal heart rate expressed as a percentage of predicted maximum plotted against the distance walked (m), trial 3.

FIGURE 4.6 The heart rate response (beat.min^{-1}) to the shuttle walking test for two representative patients.

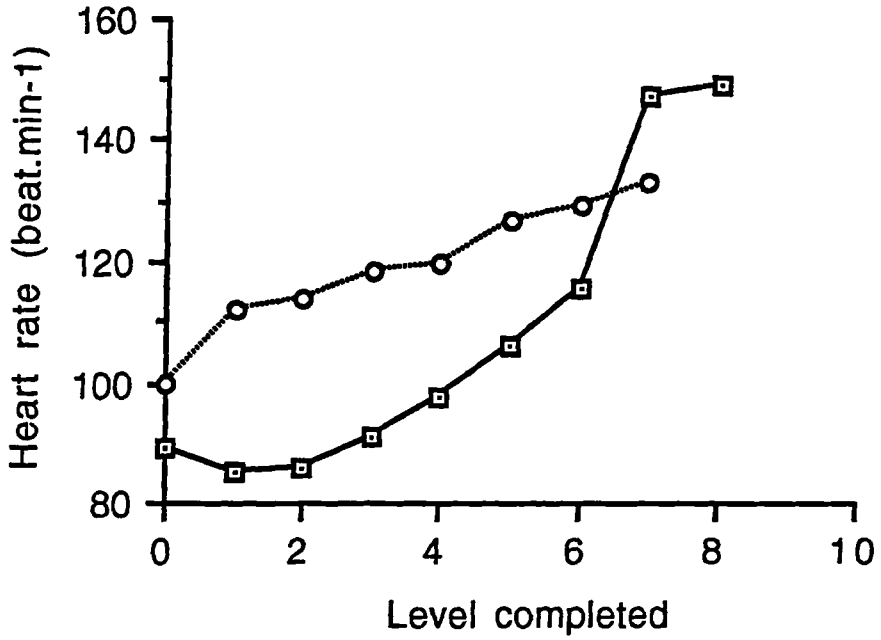


TABLE 4.8 The relationship between three lung function variables and patients' performance (Pearson Product Moment correlation) for three trials.

Trial	FEV_1	FVC	% FEV_1
1	0.58	0.28	0.25
2	0.53	0.37	0.46
3	0.24	- 0.04	- 0.09

TABLE 4.9 Post exercise Borg breathlessness scale scores for the three trials.

Trial	mean	SD	range
1	3.7	3.6	1 - 7
2	4.1	4.1	2 - 6
3	3.8	3.6	2 - 7

TABLE 4.10 Mean (SD) difference and the 95% confidence interval between the Borg rating for trials 1, 2 and 3 and the Spearman Rank Order Correlation coefficients, evaluating between trial relationships of these ratings.

Trial	d	SD	95% CI	rho
1 vs 2	-0.4	1.3	-1.3 to 0.5	0.49
1 vs 3	-0.1	1.6	-1.3 to 1.1	0.58
2 vs 3	0.3	1.9	-1.1 to 1.7	0.12

The results of the CRDQ, analysed according to the recommendations of Guyatt and colleagues (1987), identified a haphazard pattern of significant difference between visits for the four components of the questionnaire for the individual patients, the majority of the differences occurring between trials one and two. However using the Friedman two-way analysis of variance by ranks test there were no differences between the four components over the three trials. The patients were therefore assumed to be psychologically stable over the study period.

The relationship between the CRDQ response and the patients' spirometry measures for the 3 occasions is shown in Table 4.11. There was a moderate relationship between the dyspnoea and fatigue scores and the patients' FEV_1 and FVC, in particular the FEV_1 value for all three trials. The correlations between each individual component of the CRDQ and the distance walked are shown in Table 4.12. (r-values to allow comparison with other similar trials where this was the chosen test).

TABLE 4.11 Relationship between the CRDQ responses and the patients' spirometry results shown by the Spearman Rank Order Correlation coefficient (Pearson Product Moment Correlation).

Trial	Spiro-metry	Dysp-noea	Fatigue	Emotion	Mastery
1	FEV_1	0.44 (0.75)	0.42 (0.27)	0.17 (0.24)	0.52 (0.60)
	FVC	0.31 (0.48)	0.45 (0.49)	0.13 (0.06)	0.34 (0.36)
2	FEV_1	0.55 (0.83)	0.41 (0.48)	0.62 (0.63)	0.20 (0.37)
	FVC	0.47 (0.48)	0.77 (0.68)	0.42 (0.40)	0.23 (0.19)
3	FEV_1	0.42 (0.75)	0.56 (0.57)	0.46 (0.61)	0.45 (0.52)
	FVC	-0.27 (0.11)	0.57 (0.59)	0.29 (0.32)	0.23 (0.27)

TABLE 4.12 Spearman Rank order Correlation coefficients (Pearson Product Moment) between the four components of the chronic respiratory disease questionnaire and the distance walked on the three trials.

Trial	Dyspnoea	Fatigue	Emotion	Mastery
1	- 0.20 (0.33)	0.36 (0.42)	0.33 (0.18)	0.30 (0.39)
2	0.30 (0.36)	0.70 (0.61)	0.36 (0.24)	0.70 (0.64)
3	-0.39 (-0.02)	0.30 (0.38)	0.17 (0.18)	0.51 (0.43)

4.4 DISCUSSION

The performance of patients with CAL is limited by breathlessness due to a mixture of abnormalities of gas exchange, chest wall and pulmonary mechanics. However the limitation to individual performances cannot be predicted by the measurement of these factors alone (Lancet editorial 1987). It has been proposed that day to day activities are mostly of an irregular nature with a steady state rarely being achieved (Spiro 1977). Consequently, it is likely that the patients' symptoms are revealed or identified most clearly during an incremental exercise test.

The shuttle walking test fulfils the basic criteria for an exercise test in patients with CAL. It is based upon a familiar activity and, unlike cycle ergometry or treadmill walking, is simple for both the patient and operator and requires minimal equipment. The test is standardised, incremental and externally paced, diminishing the effect of the operator's influence. Although the operator walks alongside for the first minute this cannot constitute a positive effect on the speed of walking as this is externally paced and the operator invariably for the first minute is required to slow patients down. The operator then sat alongside the course and issued no encouragement. Obviously the presence of an operator can influence the patient's performance as is true for any other exercise test this influence is minimised because the external pacing does not allow the patient to walk faster. External pacing allows inter and intra-subject comparison. Patients who complete 500 m of an incremental exercise test have experienced a similar cardio-respiratory stress and therefore a comparison of individual performance is valid.

There was a significant difference between the distances walked in trial 1 and 2 but the difference between trials 2 and 3 was not significant, suggesting a small learning effect before the test is a reproducible measure of

disability (Fig.4.4 and Table 4.4). Therefore the shuttle walking test is a reproducible exercise test of disability after just one practice walk. The shuttle walking test appears to be an attractive alternative to existing field exercise tests on the strength of the test/retest results alone, because existing field tests require more than two practice walks before these test are considered reproducible. A training effect is an unlikely explanation for the increase in the distance walked between trials 1 and 2 as the trials were conducted at intervals of just one week, during which time the patients continued with their daily routine, participating in no extra strenuous activity. The possibility of a type II error (not rejecting the null hypothesis when it should be rejected) is possible because of the small group of patients. However the mean difference of -2m is equal to a difference of approximately 0.5% decreasing the possibility. Employing the nomogram proposed by Altman (1980) a vast number of subjects would need to perform the shuttle tests to be confident that there would be an 80% chance of detecting a significant difference at the 5% level if the mean difference was 2m.

The heart rate data (Fig.4.4, Table 4.5) supports this proposal of a learning effect; there is a strong correlation of the mean maximal heart rate between the three trials. There was a slightly greater difference between the maximal and resting heart rate values for trial 1 vs trial 2, but this was not a significant difference (Table 4.5). These data suggest that the difference in distance achieved between trials 1 and 2 was not due to patients utilising a higher percentage of their cardio-respiratory reserve during later trials. In fact the patients exercised to an equivalent level of cardio-respiratory stress in all three trials. The difference in distance between the two tests can therefore probably be assigned to patient familiarisation with the routine of the test. This study is consistent with the study of Brown et

al (1985) who confirmed the reproducibility of heart rate response during maximal exercise in patients with CAL.

No patient was stopped by the operator whilst performing the shuttle test because 85% of the mean maximal heart rate was attained. The mean maximal heart rate attained by these patients was well below 85% of the predicted maximal heart rate threshold, suggesting that the capacity of the cardio-vascular system was not the limiting factor in the termination of an incremental exercise test in this patient group. This assumption is supported by the data of Figure 4.4. The horizontal line drawn represents the mean maximal heart rate anticipated for a 63 year old, the mean age of the group. A ventilatory limit to functional capacity, although an attractive assumption in this group of respiratory patients, cannot be concluded from this data. This issue is addressed in Chapters 5 and 7 where the ventilatory response to exercise is measured directly.

There appears to be no relationship between the distance walked and the mean maximal heart rate expressed as an as a percentage of that predicted (Table 4.7). Therefore we are unable to suggest that a patient's performance and their ability to utilise their cardiac reserve is related. Figure 4.6 demonstrates that the test provokes a significant increases in heart rate and a graded cardio-vascular response. The incremental stress presented by the shuttle walking test shown is confirmed by the graded cardio-vascular response but could be examined more rigorously by measuring the $\dot{V}o_2$ requirements to the exercise test. Furthermore the heart rate date highlights the safety and the low risk of the shuttle walking test, the patient gradually responds to the controlled increase of walking speed to a point equivalent to a symptom limited maximum performance. The increase in the heart rate to this point indicates that the test presents a physiological challenge to the patients and stresses their cardio-vascular system

to a definite maximal end point unlike a sub-maximal unpaced test where the end point is not defined physiologically but usually by duration.

The lung function values, in agreement with other exercise studies (Knox at al 1988, Swinburn et al 1985), bore a poor relationship with the patients' performance (Table 4.7) and confirm the need to perform objective exercise tests to assess the true extent of a patient's disability. The ability to exercise is multi-factorial and is not reflected solely in an individual's ability to expire air forcefully. This finding is in agreement with of Dillard et al (1985 & 1989) who suggested that PIFR and peak inspiratory pressure measurements may aid the prediction and relationship between lung function values and exercise tolerance.

There was a small but significant difference between the resting Borg scale between trials one and two ($p<0.05$), otherwise the scores were not significantly different. This initial difference in the resting values could not be explained by the patients and no alteration in breathlessness (dyspnoea) was reported in the CRDQ for the week prior to the second trial. The initial higher score in the mean Borg rating may be related to an underlying anxiety during the first trial. The Borg data is in agreement with the work of Silverman et al (1988) and opposes the finding of the study of Belman et al (1991). That is, the Borg scale appears to be a reproducible measure of breathlessness in the present study group. The similarity between this study and that of Silverman and colleagues (1988) is that both employed maximal exercise tests. From these results it was concluded that the Borg scale, although a subjective measure, provided an easily applied, reproducible scoring of breathlessness that could be used in conjunction with the shuttle walking test on a day-to-day basis to assess patients' response to the

physiological stress of exercise.

No difficulties were experienced in administering the CRDQ except in one patient who failed to identify the required five activities that cause breathlessness. The CRDQ scores were highly reproducible. From the data obtained it was concluded that our patient group was psychologically/ emotionally stable throughout the period of observation and it was therefore unlikely that the distances walked on the three occasions were influenced by pronounced mood changes.

Like the report of Weir et al (1991), examining the relationship between the CRDQ response in patients with CAL and cystic fibrosis, our patients did not demonstrate a strong correlation between the CRDQ scores and their FEV_1 and $\%FEV_1$ values (Table 4.10). However the relationship that was identified was considerably stronger than that of Weir et al (1991). For example the correlation coefficient reported by Weir between FEV_1 and dyspnoea was 0.068, whereas the strongest relationship that was identified in the present study for the same variables was evaluated as 0.55 (rho). It should be noted that Weir and Colleagues (1991) do not describe their method of statistical analysis. In the development of the CRDQ Guyatt et al (1978) analysed the data using parametric tests to examine between test differences (t-test) and the relationship between exercise test performance and the results of the CRDQ (Pearson Product Moment Correlations). Although not strictly correct, using a Pearson Product Moment Correlation to examine the relationship between the CRDQ scores and patients lung function values a strong relationship was identified for this patient group.

The distance walked also had an inconsistent and generally poor relationship with the CRDQ scores (Table 4.11). These findings are consistent with the study of

Guyatt and colleagues (1987) validating the CRDQ. Using parametric analysis Guyatt et al (1987) identified a moderate correlation between the CRDQ scores and patients' performance on a six minute walking test ($r=0.46$, 0.35 and 0.19 for dyspnoea, fatigue and emotion respectively). This moderate link between performance on the shuttle walking test and the CRDQ scores indicates that exercise tolerance and the individual's subjective assessment of their quality of life may be linked. However a patient's perception of feelings such as breathlessness or fatigue does not quantify functional disability. Despite the continuing number of quality of life measures being published, they do not offer a replacement for exercise testing but are rather a useful adjunct in the overall assessment of the patient.

In conclusion, the results of this reproducibility study suggest that the modified 12-stage protocol is, after just one practice walk, a reliable indicator of exercise tolerance in patients with CAL. Moreover, the protocol is easy for both the operator and the patient to perform. The results confirm that this modified protocol suits a wider range of patients having a more appropriate range of walking speeds and increments than the original protocol employed by Scott (1989). The 12-stage protocol had a slower start and more increments than the 10-stage protocol and could therefore accommodate the assessment of the more severely affected patient and stress the more able patients to a symptom limited maximum performance. However, reproducible results are obtained regardless of whether the patient completes 1 or all 12 levels of the shuttle test, lending itself to the assessment of both in- and out-patients. An objective measure of change in a patient's functional capacity is allowed with greater objectivity with the shuttle walking test than with the currently available alternative field walking tests.

From the work presented so far it is possible to state

that the shuttle walking test is both standardised and incremental, facilitating a valid intra- and inter-subject comparison of exercise tolerance. A measure of functional capacity can therefore be obtained from those patients with severe CAL through to those with minimal restriction of their exercise capacity.

The shuttle walking test has the potential to be used as a cheap and effective research tool to monitor patients response to various therapeutic interventions. For the shuttle walking test to become a widely accepted method of assessment it is necessary to validate the test against a traditional measurement of functional capacity. In addition it would be prudent to compare a patients response to the shuttle walking test and the traditional field walking test, the six minute walking test. These issues are examined in the following chapters.

5. EXAMINATION OF THE VALIDITY OF THE SHUTTLE WALKING TEST AS A MEASURE OF FUNCTIONAL CAPACITY BY COMPARISON WITH SYMPTOM LIMITED OXYGEN UPTAKE

5.1 INTRODUCTION

The results reported in Chapter 4 indicate the reproducibility of the shuttle walking test as a method of measuring exercise tolerance in patients with CAL. However to become an accepted method of assessment the shuttle walking test has to be valid as well as reproducible.

The traditional indicator of cardio-vascular fitness is considered to be the $\dot{V}O_{2\,max}$ (Astrand & Rodahl 1986). Unfortunately there is a paucity of data validating field exercise tests against $\dot{V}O_{2\,max}$. The original paper proposing the 12 minute walking test (McGavin et al 1976) revealed a poor relationship with directly measured $\dot{V}O_{2\,peak}$ (r=0.52). Despite this, the test is commonly used as an indicator of exercise tolerance. Comparison of the 12 minute walking test against a treadmill test was performed in patients with pulmonary vascular disease (Cremona et al 1991). A moderate relationship was identified between $\dot{V}O_{2\,peak}$ and distance walked (r=0.60).

The aim of this study therefore was to examine the relationship between the shuttle walking test performance and the $\dot{V}O_{2\,peak}$ measured directly during a comparable activity, ie during a treadmill walking test.

5.2 METHOD

5.2.1 Patient group

Twenty-two patients were recruited for this study from medical out-patients clinics. Informed consent was obtained. The selection of patients conformed to the criteria described in Chapter 4 (4.2.2). None of the patients had performed a treadmill test prior to this study although a few of the volunteers had taken part in the

previous study. No allowances were made for this and all 22 patients followed the prescribed protocol. The patients were required to make three visits, two to Glenfield General and one to Loughborough University. These visits as far as possible were made at intervals of one week. The patients were instructed to withhold relevant medication (4.2.2) and the baseline measurements including the CRDQ were as described for the reproducibility study (4.2.2) for all three visits. All patients were clinically stable.

5.2.2 Familiarisation visit

This first visit was conducted at Glenfield General Hospital. Patients were required to perform one practice shuttle walk and a submaximal treadmill test. The shuttle walking test was conducted according to the protocol established in Chapter 4 (4.2.1). The initial treadmill test (Cambridge Medical Instruments 3060) was conducted in the Cardio-respiratory Department.

The treadmill protocol chosen was modified Balke protocol (Nagle et al 1965). This test requires the individual assessment of speed appropriate to each patient aiming to reach a maximal performance in 6 - 10 minutes. All the patients then follow the same protocol, the inclination of the treadmill was increased from 0% by 2.5% every 2 minutes to a symptom limited maximal performance.

The aim of this first visit was to familiarise the patient with treadmill walking and to establish an appropriate speed for that individual to evoke a symptom limited maximal performance either 1 or 2 weeks later at Loughborough University. The treadmill test at this stage was sub-maximal and a suitable speed to evoke a maximal performance was gauged by a patients' heart rate response (Sports Tester PE3000 3.1.5.) and their perceived rate of breathlessness (3.1.6). During the treadmill walk the

patients had the opportunity to breathe through a mouth-piece with nose-clips in place, in preparation for the expired air collection at Loughborough University. (The test was sub-maximal primarily because there was no medical cover). The patients were also requested not to hold on to the hand rail as far as was possible.

The second and third visit were a balanced design of a visit to Loughborough and a shuttle walk test at Glenfield Hospital or vice versa.

5.2.3 The shuttle walking test

The second shuttle walking test was conducted according to the protocol described in Chapter 4 (4.2.1). Heart rate was monitored using the Sports Tester PE3000 (3.1.5) during the walk and the Borg breathlessness scale (3.1.6) was recorded at the end of the exercise test.

5.2.4 The treadmill test

The visit to Loughborough required the patients to perform a symptom limited maximum treadmill walking test. The patient's height and weight was recorded (3.1.2) and three electrodes were attached to the chest to monitor heart rate (3.1.5). The patients performed the treadmill test at the predetermined speed. Expired air was collected into Douglas bags (3.2) for the second of each two minute increment. During this second minute patient's heart rate and the Borg breathlessness scale response was recorded. When the patient felt that he could continue for only one more minute he indicated this with a previously agreed signal. During this final minute of the test expired air was collected and recordings made as above. The visits to Loughborough had full medical cover.

5.3 RESULTS

Twenty-two patients completed the study, but three were excluded from the final analysis. The reasons for exclusion were, invalid Douglas bag measurement, patient discomfort during the shuttle walking test (foot soreness) and thirdly one patient developed a 'cold' affecting his shuttle performance. This patient made a repeat visit for the shuttle test but had not recovered and felt in view of the seasons changing he was unlikely to be completely well until the spring (in 6 months time). The results of the 22 patients will be reported initially with a subsequent report on the 19 patients for whom complete data sets are available.

The physical characteristics of the group are shown in Table 5.1. There was no significant difference in the spirometry values recorded for the patients between the three trials. The mean FEV_1/FVC ratio for the three trials was 52%, 52% and 54%, consistently demonstrating moderate impairment. The range of this value fell to below 30%, indicative of severe impairment, and in one individual rose to 78% indicating mild impairment. The group of patients therefore represented a wide range of disability.

As anticipated there was no strong relationship between the FEV_1 values and the shuttle performance (shuttle 2 vs FEV_1 r=0.36).

Throughout the trial period the patients were assessed by the CRDQ to be both psychologically and emotionally stable. Examination of the results for the four components of the questionnaire revealed an occasionally irregular distributed difference between trials for five of the patients. This difference proved not to be significantly different with test/retest.

No patient was excluded from the study because of non

TABLE 5.1 Some physical characteristics of the patients, Mean (SD). n=22 (17 male, 5 female)

	1	Shuttle	Treadmill
Age (yr)	61.5 (7.2)	- -	- -
Weight (kg)	72.49 (14.58)	- -	- -
Height (m)	1.70 (0.06)	- -	- -
FEV_1 (l)	1.39 (0.52)	1.38 (0.55)	1.45 (0.57)
FEV_1 % predicted	47.4 (16.8)	46.9 (17.6)	49.9 (18.7)
FVC (l)	2.69 (0.75)	2.63 (0.79)	2.67 (0.73)

compliance to the protocol of the shuttle walking test and all patients tolerated the treadmill test and mouthpieces well.

The distance the patients walked on the two shuttle walking tests is summarised in Table 5.2. There was a significant difference between the two shuttle test distances. The mean maximal heart rate attained at the end of each shuttle was not significantly different (mean difference -2.2 beat.min^{-1}). The mean maximal heart rate represents 67% and 68% of the predicted maximal heart rate for this group. The distance completed on the second shuttle walking test had a moderate relationship with the mean maximal heart rate (r=0.65).

The mean maximal Borg score reported post exercise was not significantly different for the two shuttle tests, ie 4.3 post shuttle 1 and 4.3 after the second shuttle walk ($p>0.05$). Both exhibited a very weak relationship with the distance walked (r=0.18, shuttle 2).

The result of the treadmill test are shown in Table 5.3. The mean speed the patients walked was 2.52 mph. The mean duration of the treadmill test was 7.1 (1.7) minutes (range 4-10). The ventilatory measurements for the 22 patients are also expressed in Table 5.3. The mean $\dot{V}O_{2\,peak}$ was measured to be 14.72 ml.min^{-1}.kg^{-1}. The individual percentage of predicted maximal $\dot{V}O_2$ is shown in Figure 5.1. The mean percentage of predicted $\dot{V}O_{2\,max}$ attained was 48.9% employing the calculations proposed by Bruce et al (1973). This method uses the patient's age, sex, weight and level of physical activity to estimate a $\dot{V}O_{2\,max}$. These values were based upon treadmill exercise testing of 295 healthy individuals, 170 of which were 45 years or over (100 males & 70 females).

The measurements of maximum $\dot{V}E$ were calculated initially to STPD (mean 37.44 l.min^{-1}), however the majority of

TABLE 5.2 Mean and standard deviation, distance (m) walked on the two shuttle walking tests and the mean difference (m) and 95% confidence interval.

	Mean	SD
1	379.5	137.3
2	412.7	142.3

	Mean	95% confidence interval
1 vs 2	-33.2*	-52.4 to -14.0

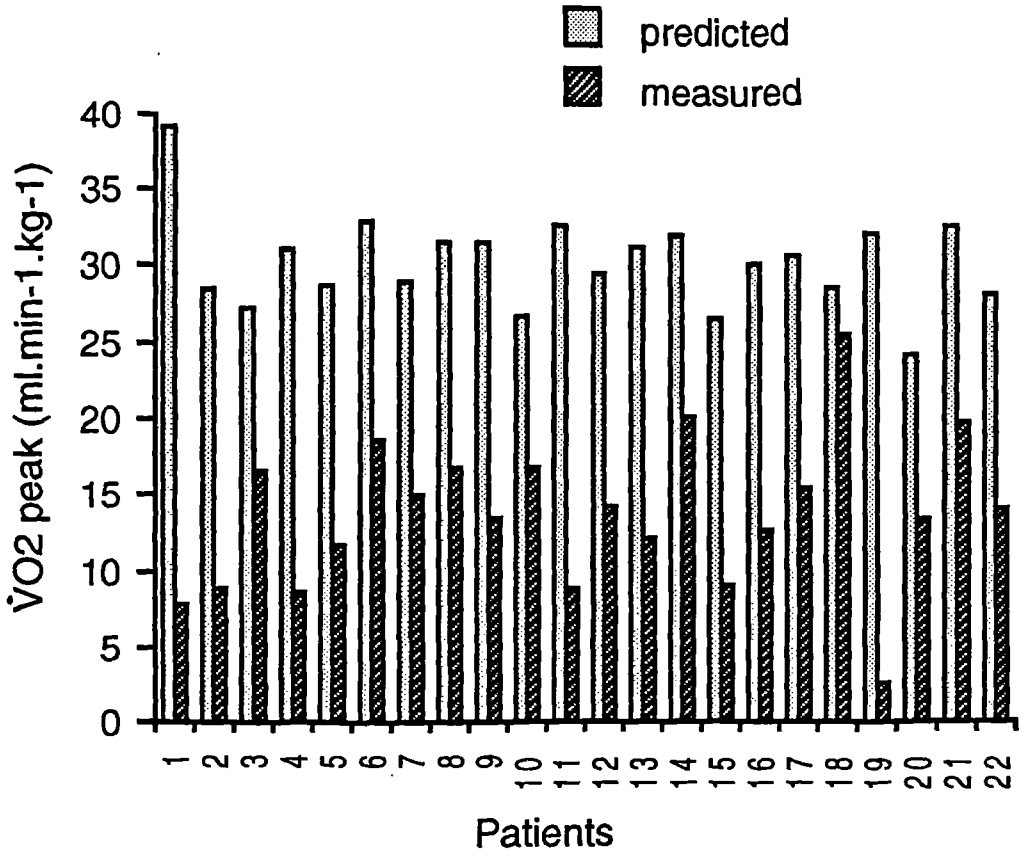
* $p<0.05$

TABLE 5.3 Mean (SD) treadmill performance and ventilatory results from the treadmill test, n=22.

Measurement	Mean (SD)
FEV_1 (l)	1.45 (0.57)
FEV_1/FVC	53.9 (11.5)
$\dot{V}O_{2\,peak}$ ($ml.min^{-1}.kg^{-1}$)	14.7 (4.8)
% predicted $\dot{V}O_{2\,max}$	48.9 (16.1)
$\dot{V}E_{\,max}$ ($l.min^{-1}$)	45.3 (15.1)
% predicted $\dot{V}E_{\,max}$	96.3 (25.8)
Heart rate max ($beat.min^{-1}$)	136 (21)
% predicted max HR	80 (13)
Oxygen pulse ($ml.beat^{-1}$)	7.8 (2.6)

NB.
$\dot{V}O_2$ expressed at STPD, Standard temperature (0°C) and pressure (760mmHg), dry.
$\dot{V}E$ expressed at BTPS, Body temperature (37°C) and ambient pressure saturated with water vapour.

FIGURE 5.1 Predicted $\dot{V}O_{2\,max}$ ($ml.min^{-1}.kg^{-1}$) plotted against the measured $\dot{V}O_2$ during the treadmill test (n= 22).



respiratory physicians present these values at BTPS. It was therefore necessary to apply a conversion factor (Cotes 1979) to express these values at BTPS (Throughout this chapter $\dot{V}_E$ from this point is expressed as BTPS). Consequently the mean maximal ventilation increased to 45.3 $l.min^{-1}$. Using the equation proposed by Spiro et al (1975) to predict maximal ventilation, $\dot{V}_E = (FEV_1 \times 18.9) + 19.7$, the mean value for the group reached 96.3% of predicted. The individual values of maximum $\dot{V}_E$(BTPS) plotted against predicted $\dot{V}_{E\ max}$ are shown in Figure 5.2 [$(FEV_1 \times 18.9) + 19.7$]. Eleven patients exceeded their predicted values indicating the difficulty in estimating patients exercise performance from resting spirometric measurements. The mean maximal R value was 1.06(0.12), indicating that these patients achieved level of exercise equivalent to their maximum aerobic capacity.

The heart rate data relating to the treadmill test (Table 5.3) revealed a mean maximal heart rate of 136 $beat.min^{-1}$, representing a mean value attained of 80% of patients' predicted maximal heart rate. This value is elevated in particular by four patients who exceeded 85% of their predicted maximal heart rate on the occasion of the treadmill test. The correlation coefficient for the treadmill performance and the maximal $\dot{V}O_2$ and the maximal heart rate was r=0.74, comparable to the values obtained from performance and heart rate response in the shuttle walking test. However the mean maximal heart rate for the treadmill test was significantly higher than at the end of the shuttle walking test. The elevated heart rate response demonstrated in the majority of patients can be observed in a comparison of equivalent work rates during the shuttle and treadmill test. Taking the speed of the treadmill and the heart rate at 0% inclination a comparable speed from the shuttle walking test was taken as a reference point to compare the heart rate, these results are expressed in Table 5.4. It can be seen that for the majority of

FIGURE 5.2 Predicted maximal $\dot{V}_E$ ($l.min^{-1}$) plotted against the measured $\dot{V}_E$ during the treadmill test (n=22).

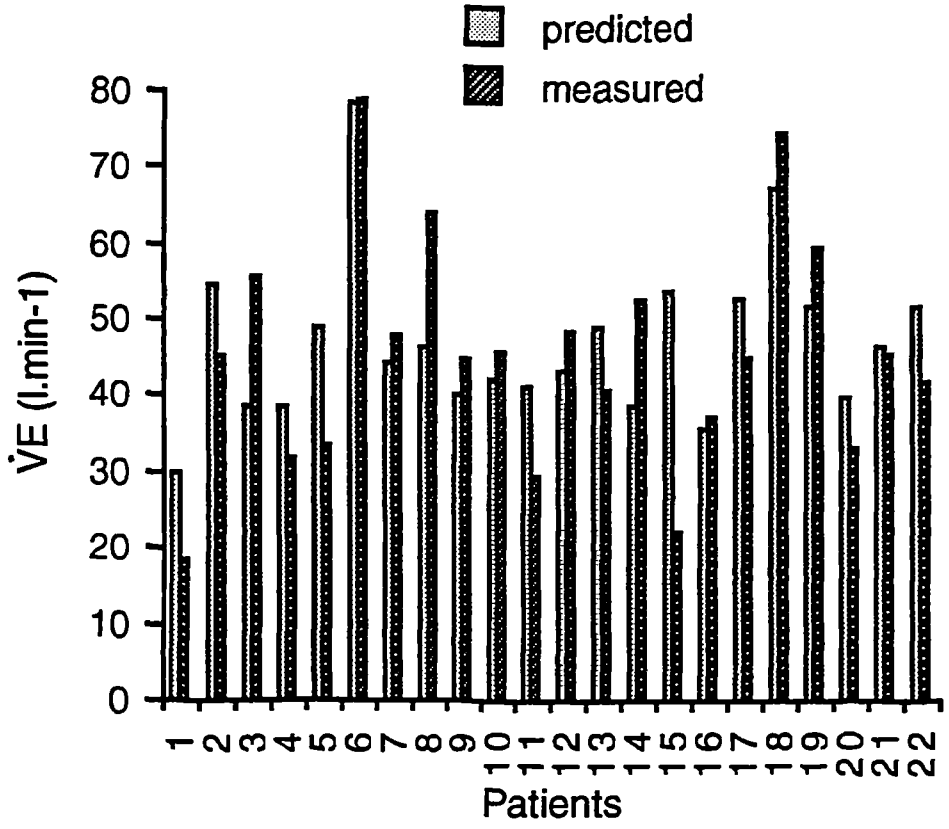


TABLE 5.4 Patients heart rate (beat.min^{-1}) at comparable speeds on the treadmill (0%) and on the shuttle walking test.

	Treadmill		shuttle test		
Pt	Speed mile.h^{-1}	HR	Level	HR	Δ treadmill-shuttle
1	1.5	106	2	98	8
2	1.5	92	2	77	15
3	3.0	115	6	106	9
4	1.8	113	3	111	2
5	2.0	106	3/4	89	17
6	3.5	116	7/8	106	10
7	3.0	107	6	100	7
8	2.5	107	4/5	89	18
9	2.8	93	5/6	92	-1
10	2.8	133	5/6	113	30
11	2.5	109	5/6	112	-3
12	2.5	94	5/6	99	-5
13	2.5	100	5/6	111	-1
14	1.75	138	2/3	120	18
15	2.0	107	3/4	91	16
16	1.5	120	2	99	21

TABLE 5.4 Cont'd

	Treadmill		shuttle test		
Pt	Speed mile.h^{-1}	HR	Level	HR	Δ treadmill-shuttle
17	3.25	122	6/7	111	11
18	3.5	137	7/8	122	15
19	3.5	117	7/8	122	-5
20	2.0	120	3/4	96	24
21	3.25	129	6/7	135	-6
22	2.8	118	5/6	105	13

N.B The speed of the treadmill is matched as far as possible to the speed of a level of the shuttle walking test. The values are taken at the end of the minute. The intermediate speeds that do not correspond directly to a shuttle speed an intermediate heart rate is taken.

patients there is a considerably elevated response to the treadmill test for an equivalent speed and grade.

The mean oxygen pulse at the final stage of exercise was measured to be 7.8(2.6) $ml.beat^{-1}$.

The heart rate data (Fig. 5.3) and ventilatory measurements (Fig. 5.4 & 5.5) demonstrate the anticipated increase in these measurements with an increasing workload for these three patients, a trend which was evident in all of the patients. This heart rate response has previously been demonstrated to occur in the shuttle walking test and was also apparent in the treadmill test.

The Borg breathlessness scale was found not to be significantly different at the end of the shuttle and treadmill test. Mean score post shuttle was 4.2 and post treadmill test was 5.0. Neither values had a strong relationship with performance indicators; distance on the shuttle test vs Borg was just rho=0.18 and the relationship between the Borg score and the $\dot{V}O_{2\,peak}$ was even weaker (r=-0.02).

In the comparison between the distance walked in the shuttle walking test and the directly measured $\dot{V}O_{2\,peak}$ revealed a correlation of 0.72.

Excluding the three patients who failed to complete the study protocol satisfactorily, the relationship between the distance walked on the shuttle walking test and the measured $\dot{V}O_{2\,peak}$ increased to r=0.88, Figure 5.6. The regression equation and 95% confidence interval for this relationship was $\dot{V}O_{2\,peak}$ = 4.19(1.12 to 7.17) + 0.025(0.018 to 0.031) distance (Fig.5.7). The FEV_1 values for the three excluded patients (No. 11, 14 & 18) were 2.55, 1.00 and 1.15 l altering the mean FEV_1 of the group (n=19) to 1.5(0.55)l. The mean values of $\dot{V}O_{2\,peak}$ drops slightly to

FIGURE 5.3 Heart rate response (beat.min^{-1}) during the treadmill test of three representative patients.

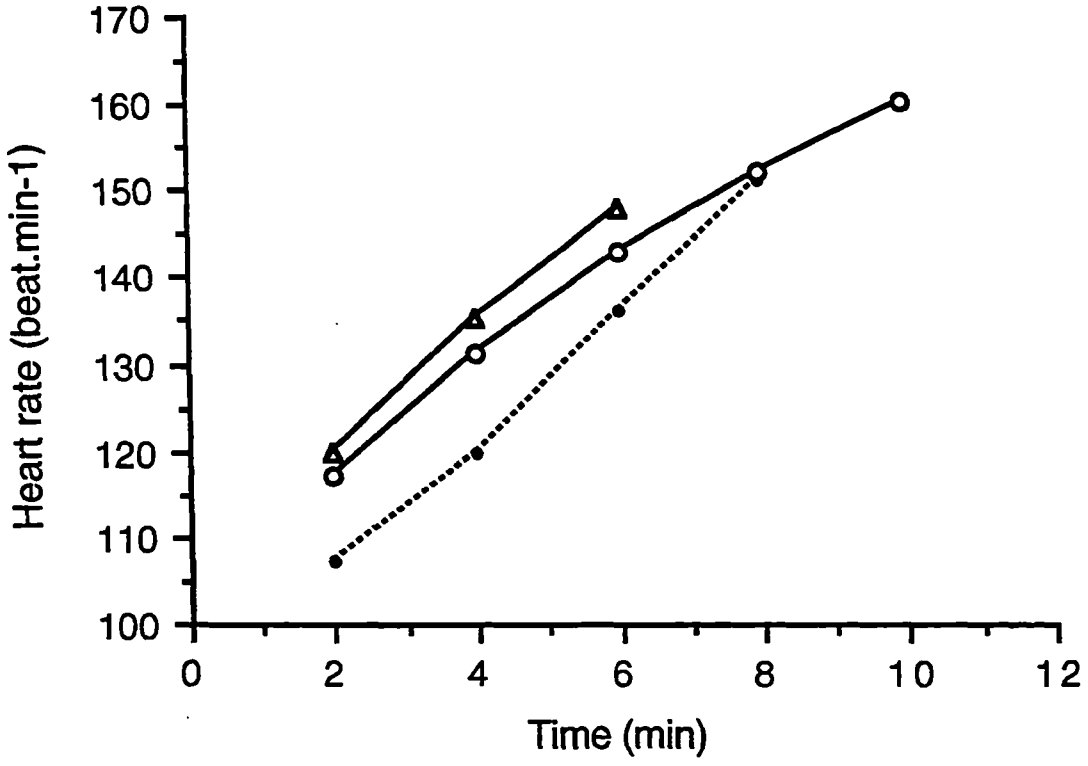


FIGURE 5.4 Ventilatory response ($l.min^{-1}$) during the treadmill test of three representative patients.

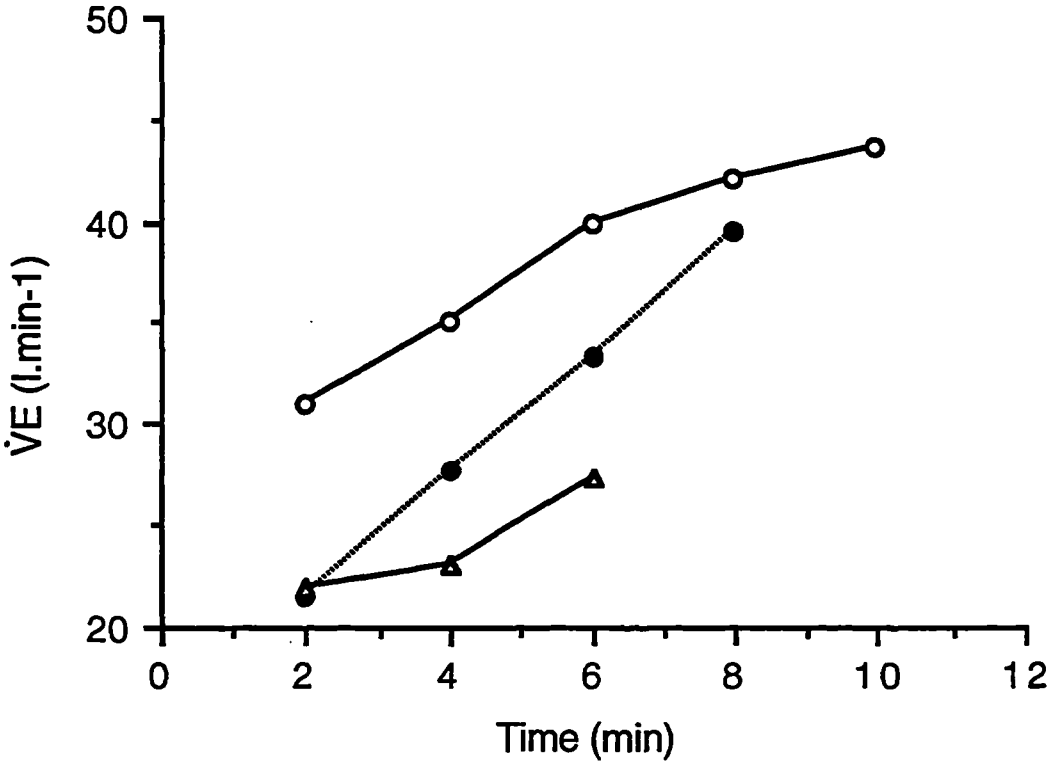


FIGURE 5.5 Oxygen uptake ($ml.min^{-1}.kg^{-1}$) response measured during the treadmill test of three representative patients.

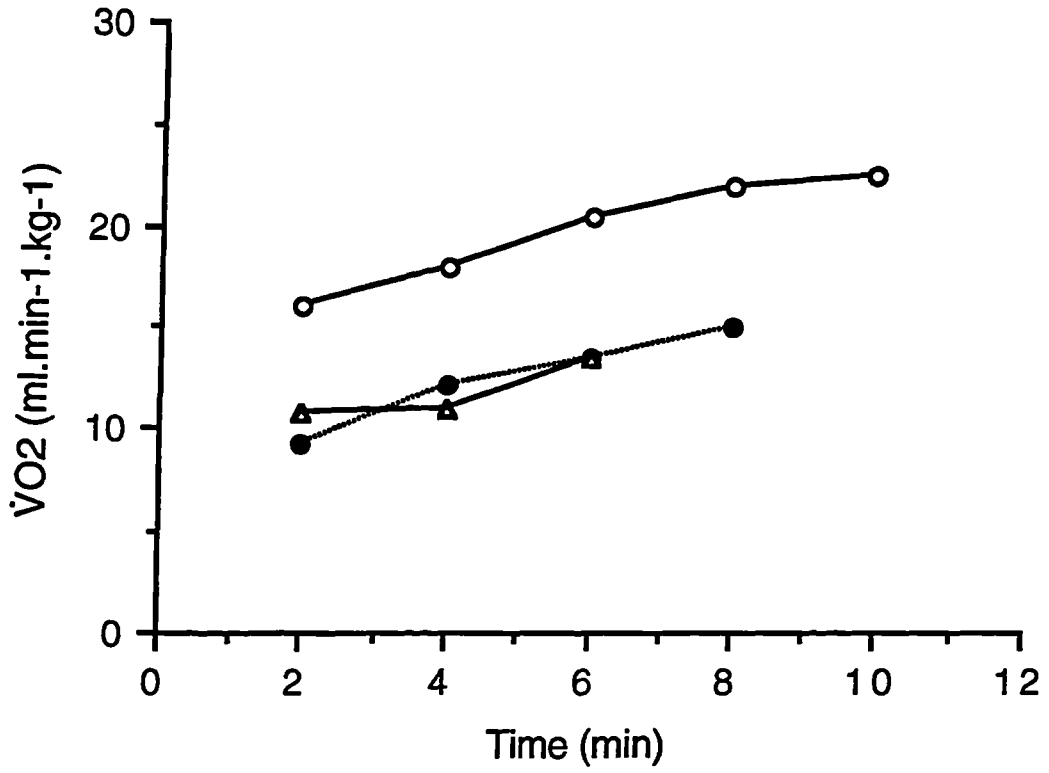


FIGURE 5.6 $\dot{V}O_{2\,peak}$ ($ml.min^{-1}.kg^{-1}$) measured on the treadmill test against performance [distance walked,(m)] on the shuttle walking test.(n=19)

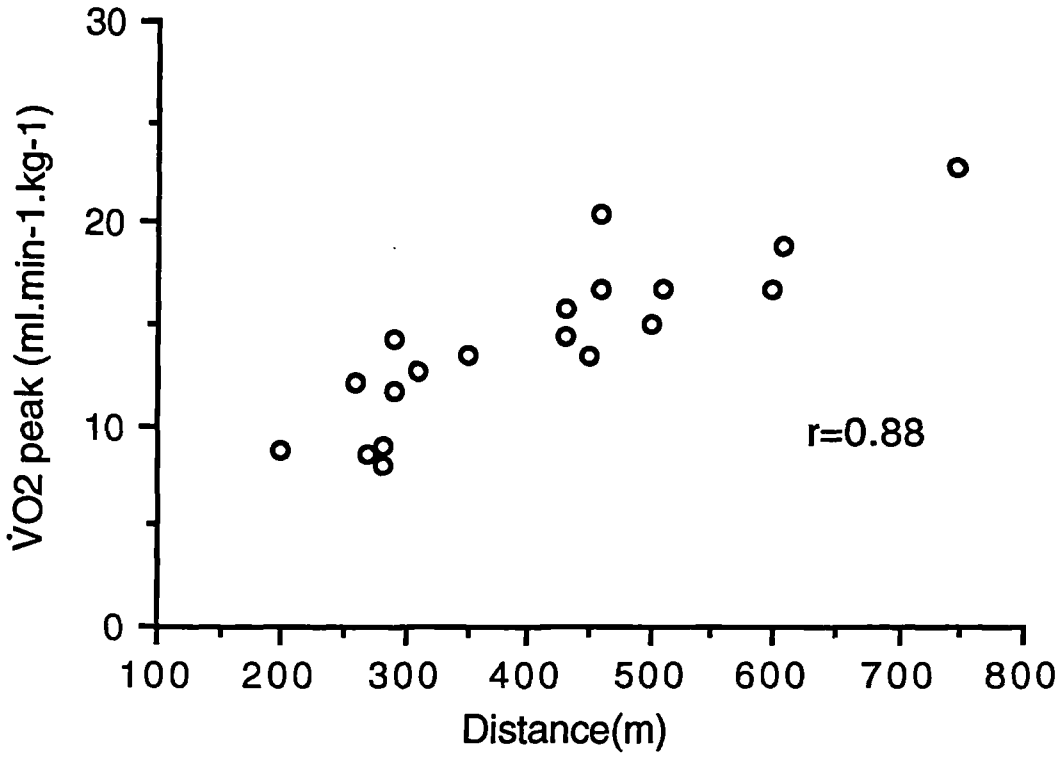
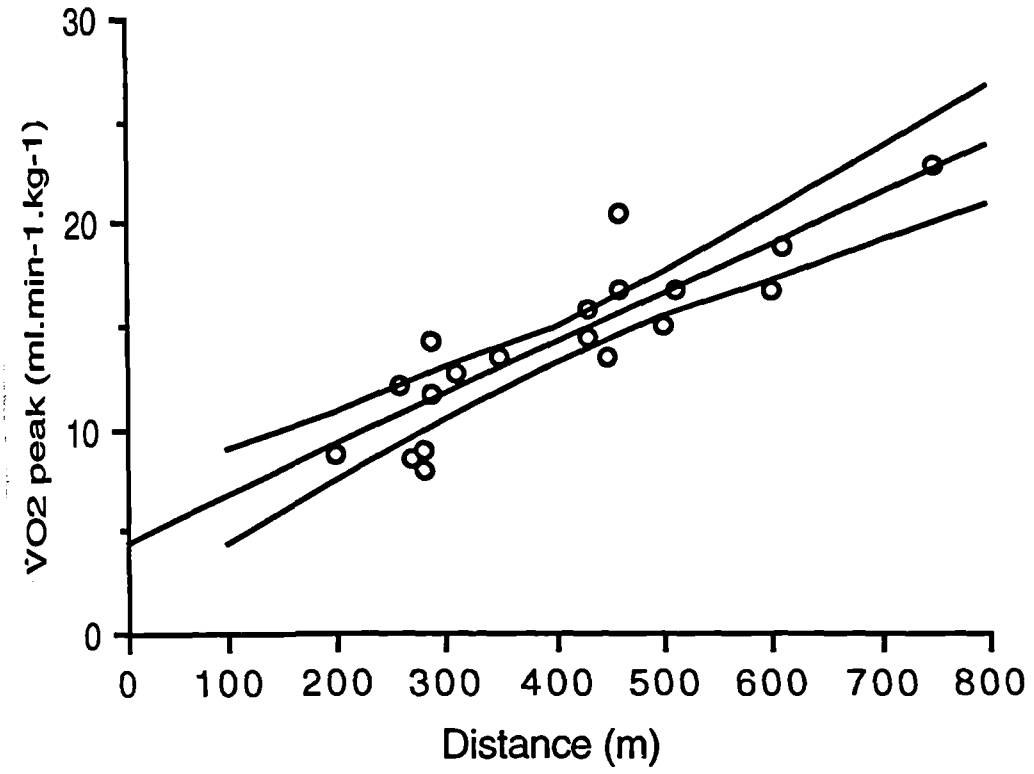


FIGURE 5.7 $\dot{V}O_{2\,peak}$ ($ml.min^{-1}.kg^{-1}$) measured on the treadmill test against performance [distance walked,(m)] on the shuttle walking test.(n=19) With the 95% confidence intervals for the relationship.



14.2(4.1) $ml.min^{-1}.kg^{-1}$ and the mean value of $\dot{V}E$ max decreases slightly to 44.2(14.1) $l.min^{-1}$. The latter translating into 47.2% of predicted $\dot{V}o_{2\,peak}$ and 94.8% of predicted maximal ventilation. The mean maximal heart rate data of the two shuttle tests and the treadmill test drops slightly to 67%, 68% and 76% of predicted, although the disparity between the two decreases the difference remains significant (mean difference 17(11) $beat.min^{-1}$).

The results can be alternatively examined by sub-dividing the group of 19 patients into two distinct clinical groups dictated by their lung function, creating two slightly more homogenous groups (Table 5.5). The group was arbitrarily divided into two, based upon their FEV_1 values, ie a group was formed with an FEV_1 below 1.4 l and a group above this value. This conveniently divided the group into two sub-groups of n=10 above and n=9 below. The mean FEV_1 values of the two groups were 1.8(0.48) l and 1.03(0.23) l, this second group contained one patient with an FEV_1 of 3.10 l, 1.25 l greater than the next highest.

Re-examining the mean $\dot{V}o_{2\,peak}$ and the mean $\dot{V}E_{\,max}$ data for these two groups revealed a $\dot{V}o_{2\,peak}$ and $\dot{V}E_{\,max}$ of 15.0 (4.72) $ml.min^{-1}.kg^{-1}$ and 47.7(15.2) $l.min^{-1}$ respectively for the group with an FEV_1 above 1.4 l and values of 13.2(3.17) $ml.min^{-1}.kg^{-1}$ and 40.3(11.3) $l.min^{-1}$ for the group with a mean value below 1.4 l. The former group were able to utilise 88.7(26.4)% of their predicted $\dot{V}E_{\,max}$ whilst the second group utilised 101.6(23.5)%. These results employ the equation [(FEV_1 x 18.7)+ 19.5] (Spiro et al 1975) to predict $\dot{V}E_{\,max}$. The corresponding values of predicted $\dot{V}o_2$ were 48.4(13.3)% and 46.0(13.7)% for the less and more severely affected group judged on FEV_1 alone. For ease of comparison with other documented values of $\dot{V}o_{2\,peak}$ the values of this study translate into 1.23 $l.min^{-1}$ and 0.92 $l.min^{-1}$.

The mean maximal heart rate after the treadmill test for

TABLE 5.5 Some physiological variables [mean (SD)] of the two sub-groups divided by their FEV_1 values.

Characteristic	FEV_1 < 1.4 l n=9	FEV_1 > 1.4 l n=10
FEV_1 (l)*	1.03(0.23)	1.80(0.48)
weight (kg)	69.2(16.2)	76.3(14.5)
maximum HR ($beat.min^{-1}$)	129(16)	133(18)
$\dot{V}O_{2\ peak}$ ($ml.min^{-1}.kg^{-1}$)	13.2(3.2)	15.0(4.7)
% predicted $\dot{V}O_{2\ max}$	46.0(13.7)	48.4(13.3)
$\dot{V}E_{\ max}$ ($L.min^{-1}$)	40.3(11.3)	47.7(16.0)
% predicted $\dot{V}E_{\ max}$	101.6(23.5)	88.7(24.4)
oxygen pulse ($ml.beat^{-1}$)	7.0(2.8)	8.5(2.4)

* Significant difference between the two groups $p<0.05$

the two groups was 133(18.6) and 129(16.3) beat.min^{-1} representing 76.6% and 76.4% of predicted for the less and more severely affected patient groups. The oxygen pulse for the two groups at the final stage of the treadmill exercise test was 7.3 ml.beat^{-1} and 8.5 ml.beat^{-1} for the groups with the lower and higher FEV_1 values. None of these physiological parameters represent a significant difference between the two groups.

5.4 DISCUSSION

The measurement of $\dot{V}O_{2\ peak}$ is considered to be the traditional measure of functional capacity. In order to ensure that the shuttle walking test accurately reflects a patients functional capacity it was necessary to examine the strength of the relationship between these two variables.

The group of patients that volunteered to participate in the study presented with a diverse spread of lung function values. This was important for this stage of the study to recruit a wide range of patients with CAL and not confine the study to a group falling predominately into the mild, moderate or severe category.

There appears to be no consensus of opinion regarding a universal treadmill test for patients with respiratory disease, unlike the assessment of cardiac patients were there is some measure of agreement. By adopting an individualised constant speed the protocol employed was therefore identical for each patient. This appeared to have several advantages for this patient group:-

- Each patient's exercise test could be individually tailored to his/her capacity, although patients would adhere to the same protocol.
- A fixed speed protocol would not have evoked a

symptom limited performance in all of the patients in 6 -10 minutes. In addition to this a universal speed would require some patients to walk at a steep incline where the limitation to exercise may in fact be peripheral. The treadmill protocol selected is in line with the views of Myers et al (1992) advocating the use of an individualised protocol to ascertain the $\dot{V}O_{2\,peak}$.

The primary aim of this study was to validate the shuttle walking test in this cohort of patients. In the group of patients who completed the study successfully (n=19) there was a strong relationship between the distance walked on the shuttle test and the $\dot{V}O_{2\,peak}$ measured with Douglas bag techniques whilst performing a treadmill exercise test (r=0.88). The strong relationship between the $\dot{V}O_{2\,peak}$ and the patients' shuttle performance allows the prediction with some accuracy of the patients' $\dot{V}O_{2\,peak}$. The coefficient of determination is 77.4%, indicating that 77.4% of the variance is common to both measures.

Although it is acknowledged that the accurate measurement of a 'true' symptom limited $\dot{V}O_{2\,peak}$ is multi-factorial a large majority of patients (35 of the 38 exercise tests) stopped exercising due to the limits reportedly imposed upon their exercise tolerance by their respiratory system. None of the present study group reported leg pain but a small section reported fatigue the following day which they attributed to the exercise although this tiredness did not appear relate to their spirometry and degree of respiratory impairment. Patients did not report their perceived level of exertion because it was felt that it would confuse some patients to report on exertion and breathlessness as separate entities. However this may have identified alternative reasons for the termination of exercise.

All of the patients reported breathlessness to be the limiting factor on the treadmill test and all but three

reported it as their reason for withdrawal from the shuttle walking test. The remaining three patients were withdrawn by the operator due to their inability to maintain the required speed, however two of the three patients reported moderate or severe breathlessness post-exercise. It was felt that with the third patients there was a considerable lack of effort during both the shuttle walking test and the treadmill test despite reporting a level of '8' on the Borg breathlessness scale at the end point of the treadmill test.

Overall, the patients' subjective opinion of the two exercise protocols was not significantly different judged by the Borg breathlessness scale. This study did not aim to make a comparison of the relative merits of the treadmill and shuttle test. The treadmill is a more comprehensive exercise test that allows detailed and sophisticated measurements to be made. However, one theoretical /practical advantage of the treadmill test over the shuttle test is the facility to increase inclination to further increase the intensity of the exercise. A point may be reached in the very minimally affected patient were they find it impossible to walk faster due to the biomechanical constraints of their limbs during the shuttle test. However this did not occur in the present study which consistently provoked a symptom limited maximal performance.

These results are consistent with the conclusion drawn from the reproducibility study (4.3); one practice walk is required to counteract any learning effect and the heart rate data indicates that it is unlikely to be the cardio-vascular system limiting exercise performance.

The heart rate responses for both exercise tests produced the same pattern of an incremental increase in rate with the increase in exercise intensity. There was some disparity in the heart rate recordings for the two tests.

The treadmill test evoked a significantly greater heart rate than the shuttle test (mean 18 beat.min^{-1} higher). This may have been due to one or a combination of four factors. Firstly the patients may have had a higher cardio-vascular response to exercise due to the anxiety associated with the unfamiliarity of the laboratory at Loughborough. This suggestion is supported by the data presented in Table 5.4 where it is apparent that at broadly comparable work levels the patients exhibit a higher heart rate on the treadmill. Nevertheless it is difficult to make any valid statistical comparison at comparable speeds. This effect may have been compounded by the breathing apparatus that the patient was required to wear. Secondly, the patients may have had an elevated resting heart rate. This was not measured but would consistent with the reasoning above, or it may be that the heart rate increased disproportionately at the start of exercise with the mouthpiece positioned and supported. Thirdly the patients were offered some verbal support to reach their $\dot{V}O_{2\,peak}$ unlike during the shuttle walking test.

It is generally accepted that a $\dot{V}O_{2\,peak}$ in normal healthy subjects cannot be increased with encouragement although performance can be ie, the individual would begin to rely increasingly on anaerobic glycolysis and the distance completed may increase although the $\dot{V}O_{2\,peak}$ is a definite point that cannot be influenced by encouragement. The level of encouragement offered to patients during a laboratory exercise test is not commonly documented and it is worth considering the potential effects of encouragement on a patient's performance. Unlike healthy individuals, patients with moderate/severe CAL do not consistently reach an anaerobic threshold and therefore often exercise within the limits of their aerobic capacity. The question that needs considering is whether patients tolerate the same degree of symptoms to produce a reproducible symptom limited maximum performance regardless of encouragement. Finally the

treadmill test may genuinely have been a more stressful exercise test, although this is not supported by the patients' subjective ratings of the two tests. Without the knowledge of the $\dot{V}O_{2\,peak}$ during the shuttle walking test this cannot be resolved. This issue is addressed in Chapter 7.

The strong relationship between the patients' performance on the shuttle walking test and $\dot{V}O_{2\,peak}$ allows the prediction of a patient's functional capacity, unlike self paced field exercise tests (McGavin et al 1976). In addition it potentially enables an objective training stimulus to be chosen for any individual patient based upon their performance on the shuttle walking test and matching this to the $\dot{V}O_2$ measurements. From this value a walking speed (that relates to the speed of any particular level in the shuttle test protocol) could be selected that relates to the prescribed percentage of the attained $\dot{V}O_{2\,peak}$. This level of training can be secured further by matching it to a perceived level of breathlessness or heart rate.

The use of a variety of testing methodologies may contribute towards the disparity of measurements within clinical exercise testing. Allowing for these differences, comparison of the ventilatory measurements from this study appear to be consistent with those previously reviewed (Belman et al 1991, Kirsch et al 1989, Mihn et al 1979). To make valid comparisons is further compounded by other between patient differences that may influence results including the patients nutritional status (Donahoe et al 1989) and drugs used. All the studies reported above seem to document a proportion of the physiological parameters that make only a partial comparison possible. It should be noted that, for many patients with CAL psycho-social characteristics may interact with physiological abnormalities to work limitation (Carlson et al 1991).

The group of patients in this present study revealed a

wide range of FEV_1 values (0.55 - 3.10 l), constituting a heterogenous cohort, with a mean $\dot{V}O_{2\,peak}$ of 14.2(range 7.9 to 22.7) $ml.min^{-1}.kg^{-1}$ (n=19). Kirsch et al (1989) reported in his small group a mean $\dot{V}O_{2\,peak}$ of 1.04 $l.min^{-1}$. This latter group, despite its relatively young age reached a mean maximal heart rate of just 101 $beat.min^{-1}$, considerably lower than the heart rate of the present study results. In a slightly larger group of patients with comparable airways disease to the present study Brown et al (1991) reported a $\dot{V}O_2$ of 1.3 $l.min^{-1}$ and a $\dot{V}E$ of 52 $l.min^{-1}$. These values appear to be slightly high compared to the present study and other reports (ZuWallack et al 1991, Mihn et al 1979).

By creating the two separate patient groups (judged by spirometry,ie FEV_1 above or below 1.4 l) the present results are in even closer agreement with previously documented studies that have recruited small patient groups. The present results parallel the trend documented by Spiro and colleagues (1975) and Jones et al (1971). Both of these studies divided the initially large study group into smaller groups based on the FEV_1 and reported higher $\dot{V}E$ and $\dot{V}O_{2\,peak}$ in the less severely affected patients.

However unlike the study of Spiro et al (1975) the present study demonstrated that the mean maximal heart rate was similar in both groups. Alternatively, Kanarek et al (1979) retrospectively identified a significantly different cardio-vascular response in a group of patients with a mean FEV_1 of just 1.04 l. This single group manifest two distinct responses.

The discrepancy between ventilatory values is similarly less pronounced in the present study than in the study of Spiro et al (1975). The more severely affected group in the present study reached a $\dot{V}O_{2\,peak}$ 46% of their predicted, corresponding to 13.2 $ml.min^{-1}.kg^{-1}$ whilst the less severely affected group attained a $\dot{V}O_{2\,peak}$ 48% of their predicted,

corresponding to 15.0 $ml.min^{-1}.kg^{-1}$. The values are not expressed as a percentage of predicted by Spiro et al (1975). Jones et al (1971) do not present data on $\dot{V}O_{2\,peak}$. The magnitude of $\dot{V}_E$ values for the two separate groups in the present study and that of Spiro et al (1975) are more closely related, with the less severely affected group able to consume a relatively larger volume than the more severely affected group. These values, again in agreement with Spiro et al (1975) (not expressed by Jones 1971) translate into a greater percentage of predicted maximal ventilation being achieved by the more severely affected group. Lockhard (1979) suggested that the limitation to ventilation is accompanied by an almost proportional reduction in $\dot{V}O_{2\,peak}$. The present data would go some way to supporting this proposal.

The prediction of maximum $\dot{V}_E$ is difficult especially in patients with a severe restriction. Belman (1986) comments that 'although the use of these equations has been suggested to be valuable it is difficult to see how they can be useful when the range of predicted values is so wide'. This comment is supported by the work of Spiro et al (1975). Formulae employing the FEV_1 alone have poor precision (Dillard et al 1985), although this can be reduced by incorporating more sophisticated measurements of peak inspiratory and expiratory pressures. The simple commonly employed equation, ie FEV_1 x 35 considerably underestimates $\dot{V}E_{max}$ in patients with an FEV_1 less than 1.0 l (Spiro et al 1975). However of the patients presenting for this study only two had an FEV_1 of less than 1.0 l. Spiro et al (1975) proposed the formula (FEV_1 x 18.9) + 19.7 to predict $\dot{V}E_{max}$ in a wide range of patients with CAL, which was the formula adopted for this particular study, unfortunately no 95% confidence interval is quoted for this equation.

Cotes et al (1982) suggests that if a patient with CAL

discontinues exercise at a maximal $\dot{V}_E$ below the lower limit of the 95% confidence interval then an alternative reason to breathlessness must be sought.

In the present study, nine (of the 19) individuals reached 100% or more of their predicted $\dot{V}_E$, consistent with the findings of Spiro et al (1975). Analysis revealed that the FEV_1 values of these patients were at the lower end of the range. Contrary to this one of the female patients (No.15) with FEV_1 greater than 1.4 l reached less than 60% of predicted $\dot{V}_E$. Despite the results portrayed in Figure 5.2 all of the patients reported breathlessness post-exercise and that this was the limiting factor to the continuation of the exercise test. Viewing Figure 5.2 it can be seen that 18/22 and 16/19 (excluding No. 11, 14 & 18) patients exceeded 75% of their predicted maximum $\dot{V}_E$. On the other hand it is reported that in healthy individuals approximately 60% of their ventilatory capacity is reached at the point of their $\dot{V}O_{2\,peak}$ (McArdle et al 1991, Beck et al 1991).

Maximal ventilatory values from this present study are in excess of these values and would support an overall trend towards a ventilatory limit to exercise. Perhaps the most curious result is that of the disparity between the percentage of predicted $\dot{V}_{E\,max}$ the two patient sub-groups are able to utilise. It is probable that the more severely affected patients were inhibited by a ventilatory limit to exercise, utilising 100% of their ventilatory capacity. Cardio-vascular factors appear to be relatively insignificant in limiting the exercise tolerance in this patient group, the maximal heart rate values falling well short of the predicted values anticipated for the patient's age. An alternative cause of limitation, ie peripheral muscle limitation was not monitored (blood lactate concentration) at this stage.

The sub-group with the greater FEV_1 values contained three patients exceeding their predicted $\dot{V}E_{max}$ and all but two patients exceeded 75% of predicted $\dot{V}E_{max}$. These female patients reached 42% (No. 15) and 69% (No.5) of predicted $\dot{V}E_{max}$; post exercise they both appeared moderately stressed and reported that dyspnoea was the limiting factor. As Belman (1986) hypothesised, these subjects may manifest a heightened perception of breathlessness limiting exercise tolerance rather than a true ventilatory limit.

By forming these two sub-groups there was no disparity in the level of breathlessness reported post exercise or the mean maximal heart rate. It should be noted, however, that two patients (FEV_1 >1.4 l) did exceed 85% of their predicted heart rate. One of these two patients also exceeded their prescribed ventilatory limit. The remaining five patients did not reach either a ventilatory or cardio-vascular limit and although these patients reported severe breathlessness the results of their tests do not allow us to draw any firm conclusions as to the limiting factors of exercise. Besides lack of motivation and probable deconditioning in this group, Matthews et al (1989) proposes three alternative mechanisms for the lack of definitive results. Firstly, the patient's lung function may be at a transient stage where it is becoming the limiting factor to exercise over and above the normal cardiac limit. Secondly, he suggests that the increased heart rate is a compensatory mechanism for the pulmonary dysfunction and finally he acknowledges that it is more likely to be a combination of factors including a mechanical limit to ventilatory capabilities, eg occult left ventricular failure, developing respiratory muscle weakness or deconditioning. A lack of effort was apparent in at least one of this group. It seems apparent that the cycle of dyspnoea, reduced activity, more dyspnoea and so on may in fact begin at the moderate stages of the disease as shown in this group of patients. Several recent reports have suggested that the strength of the respiratory muscles

and, consequently, the inability of the lungs to support the increased ventilatory demand may be an important determinant of exercise tolerance (Grassino 1979, Bye et al 1985).

In a recent publication, Rampulla et al (1992) identified that the most frequently reported factor limiting exercise (on the treadmill) was in fact fatigue and not dyspnoea in patients with CAL. Surprisingly, of those patients who were identified as stopping due to breathlessness only 10/28 rated the sensation near to maximal.

The sub group with the FEV_1 less than 1.4 l included just one patient who exercised within the theoretical constraints of his respiratory system. Surprisingly this patient with severe airways disease (No.1) exercised to only 62% of his predicted $\dot{V}E$. Clinically this patient was exhibiting respiratory embarrassment post exercise and undoubtedly reached a symptom limited maximum performance. This patient was extremely thin and the calculations of his $\dot{V}E_{max}$ may have over estimated his capacity. One patient exercised to 144% of her predicted $\dot{V}E$ demonstrating the unreliability of predictive resting measurements.

The oxygen pulse at maximal exercise was consistent with the measurements of Nery et al (1983). These authors suggest that the low value is not indicative of compromised O_2 transport as suggested by Mihn et al (1979) but is simply the result of the patient terminating exercise due to a ventilatory limit before the cardio-vascular system was maximally stressed.

The average speed of walking on the treadmill was 2.5 mph. This was a speed (with an increased gradient) at which a maximal performance would be provoked for this present group. Examining the data comparing the $\dot{V}O_{2\,peak}$ and the shuttle tests results a mean $\dot{V}O_{2\,peak}$ of 14.2 $ml.min^{-1}.kg^{-1}$ is in

indicative of a maximal walking speed of between 3.3 and 3.7 mph. From this value a speed relating to 60 -70% of the $\dot{V}O_{2\,peak}$ would equal approximately 2.2 to 2.6 mph corresponding to 8 - 10 $ml.min^{-1}.kg^{-1}$ (see Figure 5.7). Alternatively, for healthy middle aged adults, a comfortable walking speed (3 mph) would demand oxygen at a approximately similar rate (11 $ml.min^{-1}.kg^{-1}$). For patients with CAL the increased cost of breathing both at rest and with the increasing intensity of exercise diverts a significant fraction of the overall Vo_2 away from the peripheral muscles. For this reason it is difficult to apply 'healthy adult values' of $\dot{V}O_2$ to the patient population and draw comparisons between physiological responses at definite speeds in the patient group and normal healthy adults. The data presented in this study supports this point. The predictive values used are from a population performing a treadmill walking test. The treadmill protocol was not the same as that employed for this study which may in itself be unrepresentative of the values obtained from a modified Balke protocol used.

To summarise, the results from the treadmill test indicate that the patients had a compromised ventilatory response to exercise, exhibiting a maximal ventilatory response well in excess of predicted values for 'normal' exercise responses. As a consequence of this premature cessation of exercise there was a concomitant reduction in the maximal $\dot{V}O_2$ values compared to those predicted.

Overall the study substantiated the proposal that the shuttle walking test is a maximal field exercise test of disability in patients with CAL that would give an objective measure of a patient's cardio-respiratory status. The validation of the shuttle walking test provides the evidence that this exercise test provides a superior measure of functional capacity to the existing field tests in patients with CAL. Furthermore it allows the prediction with some confidence of a patients $\dot{V}O_{2\,peak}$ estimated from

his/her performance on the shuttle walking test alone.

6. EXAMINATION OF THE PORTABLE OXYGEN CONSUMPTION METER

6.1 INTRODUCTION

This chapter addresses the validity of using a portable device for the measurement of oxygen uptake ('Oxylog', PK Morgan). The analysis of this piece of equipment is vital to the experimental procedures adopted in Chapter 7, examining the ventilatory and metabolic response to the shuttle walking test. However, more importantly there seems to be very little substantial data on the validity of employing this piece of equipment for patients presenting with CAL. There are some validation studies (Harrison et al 1982, McNeill et al 1985) examining the performance of the Oxylog in normal individuals. The levels of ventilation recorded in these individuals is considerably higher that those anticipate in a group of patients with CAL. Therefore it was considered necessary to examine performance at lower levels of ventilation.

This section will be divided into three main parts. Firstly a brief description of the Oxylog. The second section will describe four experimental studies examining the validity of measurements of the Oxylog: This was done by comparison with measurements made using traditional Douglas bag techniques in healthy volunteers, and secondly, two separate groups of patients performing both sub-maximal and maximal tests. The final section investigates some of the properties of the Oxylog that may have contributed to the discrepancy of measurements identified in the previous sections.

6.2 DESCRIPTION

The Oxylog (PK Morgan) is a portable device to measure oxygen consumption and ventilation in man (Humphrey & Wolff 1977). The equipment weighs 2070 g without the leather casing and strap and 2610 g with the casing. The dimensions including the casing are 18.5 x 8.2 x 21.5 cm. The

manufacturers suggest that the Oxylog should be worn with the shoulder strap passing diagonally across the chest and over the shoulder with the Oxylog sited in close proximity to the opposing hip. The subject wears a face mask incorporating both inspiratory and expiratory valves. The subject breathes in atmospheric air through a small turbine flowmeter which also contains a thermistor. Inspiratory volume is measured in the range 6 - 80 $l.min^{-1}$ ventilation and displayed as either total ventilation (maximum reading 99999 litres) or as minute ventilation, (of the proceeding minute) with resolution to 1 $l.min^{-1}$. These values are expressed digitally. The expression of ventilation is not corrected to S.T.P.D but corrected to 0^0C dry at the pressure of the experiment. This is achieved by measuring the atmospheric temperature at the inspiratory flowhead and correcting the volume of air, assuming 50% relative humidity. Deviations in relative humidity from 50% produce less than a 1.5% error in estimation of gas volumes (PK Morgan) except in extreme humidity or dryness at temperatures above 26°C (McNeill et al 1987).

Expired air passes through a flexible wide bore tube to the body of the oxylog where 1.5 cm^3 /breath is pumped into a mixing chamber by an integral pump triggered by a decrease in the inspiratory flow rate at the end of each inspiration. Simultaneously a similar size sample of atmospheric air is drawn into a second mixing chamber. Both samples of air are dried by passing the samples prior to analysis through drying tubes containing 'Drierite' ($CaSO_4$) before analysis. Small samples of the contents of these mixing chambers are analysed with two compact polargraphic oxygen sensors (Beckman, USA) and the pO_2 difference between the two samples is used, in conjunction with the inspiratory flow rate to calculate the oxygen consumption. The analyser derives a total oxygen consumption up to 9999.9 litre (resolution 0.1 l) or the minute oxygen consumption (range 0.25 - 3.00 $l.min^{-1}$, resolution 0.1 l).

The $\dot{V}O_2$ is expressed as S.T.P.D. The calculation of the volume of oxygen consumed is based upon the formula,

$$\dot{V}O_2 = \frac{(pO_2 \text{ inspired air} - pO_2 \text{ expired air}) \times \text{volume inspired air}}{760}$$

This formula is only correct if the R value is equal to unity. In situations were the R value is less than 1 the use of the inspired volume to calculate $\dot{V}O_2$ will be incorrect. The manufacturers suggest error in calculations ranging from -5.3% if the R value was equal to 0.7 to +1.8% if the R value was equal to 1.1. Volume is expressed at A.T.P.S (ambient temperature & pressure, saturated with water vapour).

The Oxylog is powered by internal rechargeable batteries with an endurance of up to 24 hours. A recorder output is available with a 3V positive pulse 30 msec long for every 0.1 l of O_2 consumed and minute O_2 output was recorded as 1 volt.l^{-1}.min^{-1}. Ventilation was recorded as 3 v positive pulse 30 msec wide for every 1 l of $\dot{V}E$ and as 0.1 v for every 10 l.min^{-1}. This recorded output was utilised to transfer and recorded data in a solid state data logger, the Squirrel (see below), which was preferable to manual collection of values in the laboratory and essential when the Oxylog was used in the field.

6.3 THE SQUIRREL

The Squirrel 1200 (Grant Instruments) is a solid state data logger used to interface with the Oxylog. It weighs 500 g and measures 18 x 12.5 x 6 cm. The display and logging functions are controlled by three push-buttons. The squirrel requires 6 AA manganese-alkaline batteries and has 19 channels available for monitoring a variety of physical parameters. However for this study 5 channels were employed to recorded an output of minute oxygen voltage and pulse output for each 0.1 litre of total oxygen and each 1 litre of ventilation. The Oxylog and Squirrel were connected with

a dedicated plug from the Oxylog (Lemo PE 0304 NY U). The corresponding connections to the Squirrel (15 way D-socket) were delicate and required stabilising with external fixation which demanded repeated checking. To receive the signals from the Oxylog the channels of the Squirrel had to be adjusted to accept the appropriate voltage. The internal clock was also calibrated before each trial with an external stop watch. Signals were recorded once logging was initiated and a visual display was monitored for each channel for continuity of logging. This was however only practical during the laboratory evaluation of the Oxylog. The recorded data could then be transferred and stored to disc using an IBM computer and a dedicated Squirrel program.

6.4 ROUTINE USE OF THE OXYLOG

Prior to using the Oxylog for each separate study the equipment (oxygen sensors) was calibrated according to the manufacturers instructions to zero pO_2 (see appendix D). Prior to each individual subject use of the Oxylog the oxygen sensors were calibrated against atmospheric pO_2. The controls were set to record minute $\dot{V}_E$ and $\dot{V}O_2$. The connector was then secured in the Oxylog recorder socket and placed into the receiving socket of the Squirrel.

The subject was then fitted with a face mask supplied by P K Morgan and requested to breathe normally. The face mask was secured by two straps, one placed horizontally around the back of the head and the other placed at 45^0 to the first rising to just below the crown. The straps are tightened to ensure minimal movement of the mask and therefore minimal leakage of air. A digital reading of $\dot{V}_E$ and $\dot{V}O_2$ would usually appear after 2-3 minutes. It was essential to ensure that the minute signals of $\dot{V}_E$ and $\dot{V}O_2$ synchronised exactly with the internal clock of the Squirrel and in turn that both of these measurements

synchronised with the timing of the incremental increases treadmill test. The internal clock of the Squirrel was set exactly against a stopwatch which was used to time the treadmill tests and the increments thereof. It therefore remained for the reading of the Oxylog to be transmitted at exact times. This was ensured by pressing the reset button of the Oxylog (at XX.00 secs on the stopwatch and Squirrel) which effectively 'zeroed' the timing of the signals from the equipment.

6.5 EXAMINATION OF THE VALIDITY OF THE OXYLOG (HEALTHY SUBJECTS

6.5.1 INTRODUCTION

Initially the Oxylog was examined in a group of healthy volunteers to identify and rectify any problems prior to patient involvement. Instead of employing a simultaneous measurement technique we explored the validity of the Oxylog for measuring $\dot{V}O_2$ against the conventional Douglas bag technique, on two separate occasions.

6.5.2 METHOD

Ten students from the department of Physical Education and Sports Science were recruited. The protocol required them to perform two identical treadmill tests. On one occasion measurements were taken with the Oxylog using the face mask supplied by the manufacturers and on the other visit ventilatory measurements were made using Douglas bag techniques (see Chapter 3). The two visits were presented in a randomised balanced design.

On the first visit the subjects height, age and spirometry was recorded (3.1.1 & 3.1.2). For both visits weight was recorded (3.1.3).

For the visit employing the Oxylog the heart rate electrodes were attached and the face mask of the Oxylog placed in the most suitable position. Every attempt was

made to correct any identified leaks of the face mask. The body of the Oxylog and the attached Squirrel were placed on the bench alongside the treadmill. The subject was instructed to breathe normally and the readings of the equipment were co-ordinated.

The subjects performed an incremental treadmill walking test at a constant speed of 3 mph with increases of the incline from 3% by 3% every 4 minutes for a total of twelve minutes. The test was sub-maximal in an attempt to review the Oxylog in a range of measurements appropriate to patients with CAL. Subjects were asked to report their perceived rate of exertion (Appendix B) during the final minute of each incline.

The Douglas bag test employed the same protocol except that expired air was collected in Douglas bags during the final minute precisely, of each stage.

6.5.3 RESULTS

All the healthy subjects completed both the exercise test with relative ease. The physical characteristics of the group are shown in Table 6.1.

After preliminary testing a discrepancy was identified in the values of ventilatory measurements of the Oxylog compared to the Douglas bag in three of the subjects. It was thought that a problem existed with the face masks and their fitting. The facial features of one of the three was small and eventually a small mask was obtained from the manufacturer. The small mask did not appear to solve the problem of leakage in the other two subjects and as an alternative chiropody felt was applied around the bridge of the nose to block any potential leaks. The ventilatory values improved considerably with these modifications and these are the results presented.

TABLE 6.1 Some physical characteristics of the group (mean and SD). N=10.
4 males, 6 females

	mean	SD
Age (yr)	31.1	8.1
Height(m)	1.70	0.08
Weight(kg)	63.00	6.66
FEV_1 (l)	3.83	0.36
FVC (l)	4.80	0.74

The expressed volume ($l.min^{-1}$) of air measured with the Oxylog is the inspired air at ambient pressure, temperature and 50% relative humidity is assumed. The volume of air measured using the Douglas bags is expired air and is expressed as S.T.P.D. It was therefore necessary to convert the Oxylog measurements to S.T.P.D using the formula

$$\dot{V}I_{STPD} = \dot{V}I \times \frac{273}{273+t} \times \frac{(PB - WVP_t)}{760}$$

t = temperature (°C)
PB = barometric pressure (mmHg)
SWVP = saturated water vapour pressure (mmHg)

A subsequent calculation was necessary to convert the expired air volume of the Douglas bag to an inspired volume ,ie equivalent volume to the Oxylog. $\dot{V}I$ can be determined from $\dot{V}E$ using the relative change in nitrogen via the 'Haldane transformation'.

$$\dot{V}I_{STPD} = \dot{V}E_{STPD} \times \frac{\%N_{2E}}{\%N_{2I}}$$

The values at each of the four stages of the exercise test are shown in Table 6.2 for $\dot{V}O_2$ and in Table 6.3 for $\dot{V}I$ using both the Oxylog and Douglas bag techniques. The values are plotted in Figure 6.1. and 6.2. The level of agreement and the Pearson Product moment correlation of the $\dot{V}O_2$ measurements are detailed in Table 6.4 . There was no significant difference in the $\dot{V}O_2$ values at the third stage of the exercise test. There was however a significant difference at the first, second and forth stages. The mean difference in $\dot{V}O_2$ values recorded were -2.3, -1.8 and 1.3 $ml.min^{-1}.kg^{-1}$ greater with the Oxylog than the Douglas bag for stages one, two and four respectively.

The ventilatory measurements, however, present a different scenario from that described above (Table 6.5). The corrected values of $\dot{V}I$ reveal a significantly lower measurement with the Oxylog at the end of stages two, three

TABLE 6.2 Mean (SD) values measured in normals for $\dot{V}O_2$ (STPD) $ml.min^{-1}.kg^{-1}$. n =10.

Stage	Oxylog	Douglas bag
1	14.5 (1.6)	12.2 (0.8)
2	18.3 (1.0)	16.5 (0.5)
3	22.4 (1.5)	21.3 (1.0)
4	27.8 (1.2)	26.4 (0.8)

TABLE 6.3 Mean (SD) values measured in normals for $\dot{V}_I$ (STPD) $l.min^{-1}$. n =10.

Stage	Oxylog	Douglas bag
1	19.7 (2.7)	21.5 (3.85)
2	25.0 (3.2)	28.3 (3.6)
3	30.7 (4.0)	34.5 (4.3)
4	38.1 (5.9)	40.9 (4.6)

FIGURE 6.1 The relationship between the mean (SEM) $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) measurements with the Oxylog and Douglas bag at each stage of the exercise test.

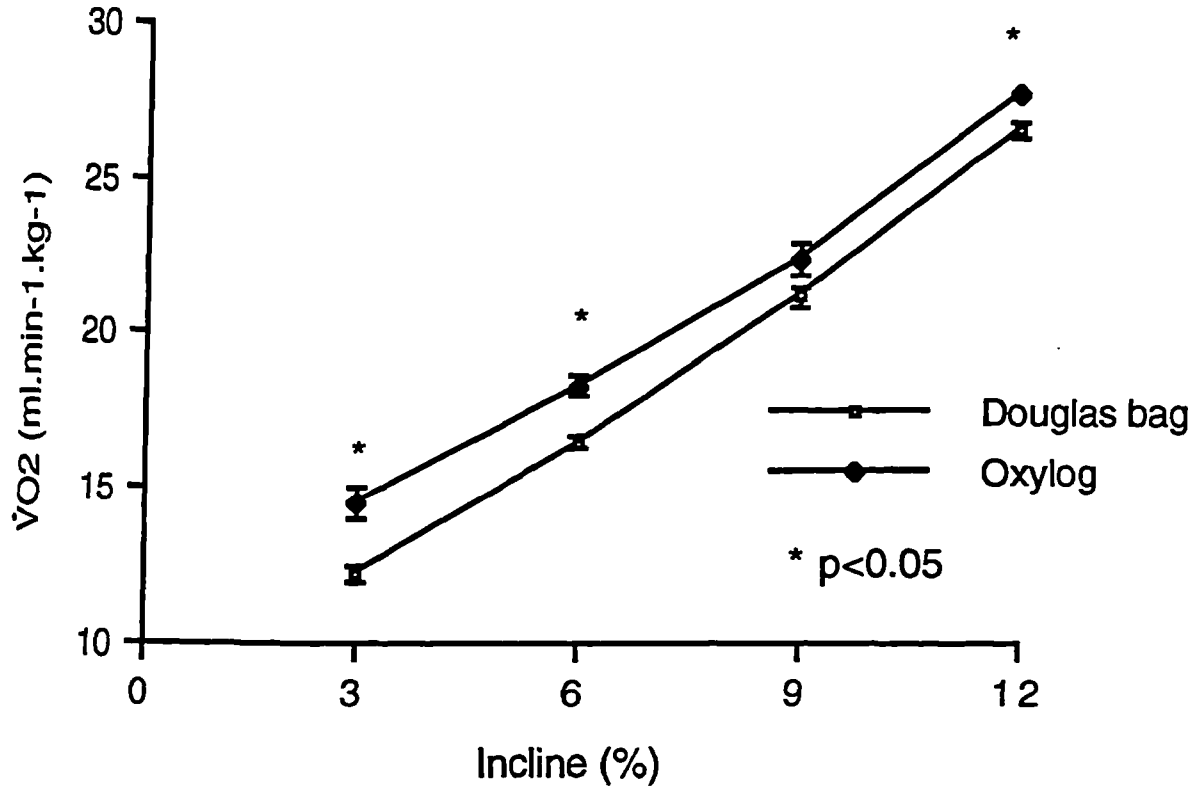


FIGURE 6.2 The relationship between the mean (SEM) $\dot{V}_I$ ($l.min^{-1}$) measurements with the Oxylog and Douglas bag at each stage of the exercise test.

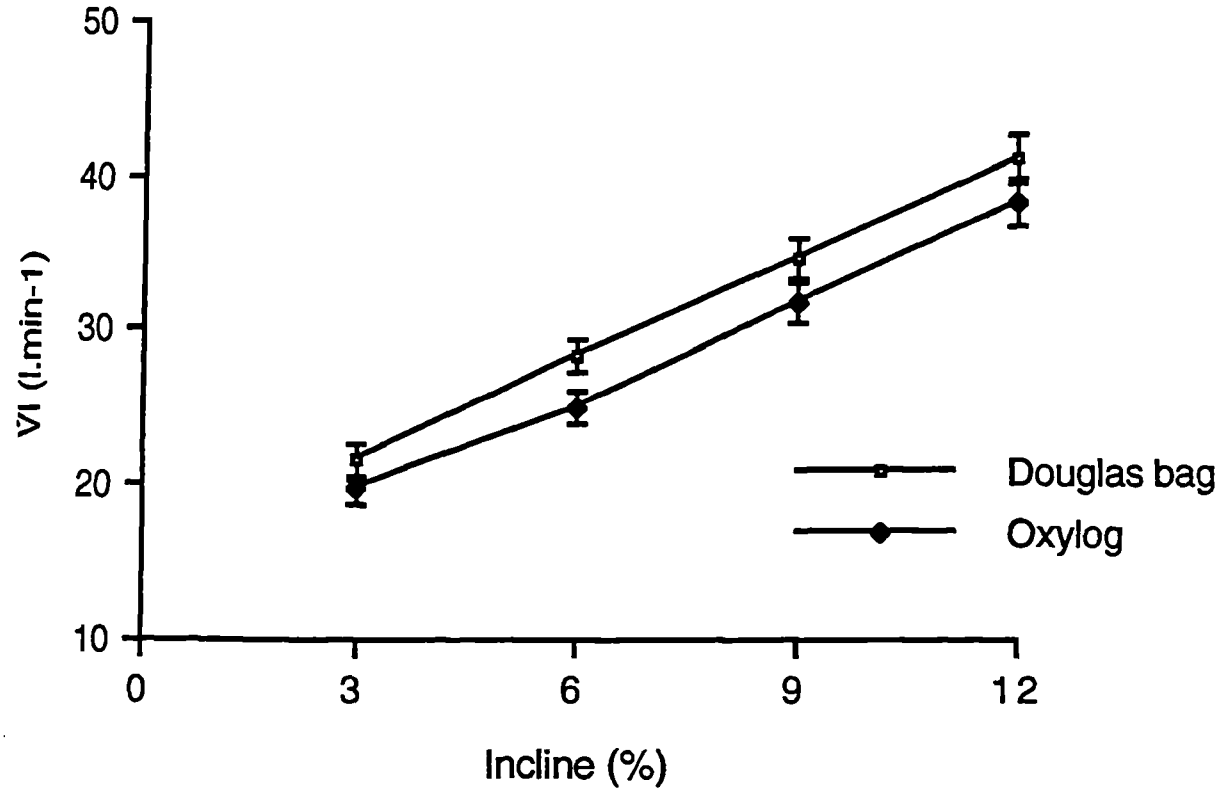


TABLE 6.4 The mean differences and the 95% confidence intervals of the Douglas bag and Oxylog measurements at each stage for $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) and the Pearson Product Moment correlation.

Stage	X difference	SD	95% confidence interval	r
1	-2.3	1.9	-3.7 to -0.9	-0.15
2	-1.8	1.0	-2.5 to -1.0	0.22
3	-1.1	2.1	-2.6 to 0.4	-0.43
4	-1.3	1.6	-2.5 to - 0.2	-0.24

TABLE 6.5 The mean (SD) differences and the 95% confidence intervals of the Douglas bag and Oxylog measurements at each stage for $\dot{V}_I$ (l.min $^{-1}$) and the Pearson Product Moment correlation.

Stage	X	SD	95% confidence interval	r
1	1.8	3.0	-0.3 to 4.0	0.27
2	3.3	2.1	1.8 to 4.8	0.71
3	3.8	3.2	1.5 to 6.1	0.50
4	2.9	2.9	0.8 to 5.0	0.78

and four. A significant difference was not found between stage one ($p>0.05$). The percentage differences in the measurements of $\dot{V}O_2$ exhibit a systematic decrease in the magnitude with an increase in the intensity of exercise. At stage one the difference is 14.5%, this value decreases (9.6% level 2, 5.0% level 3) to 3.8% at level 4. The corresponding values of $\dot{V}I$ do not demonstrate the same pattern. The largest difference is at stages 2 and 3 (11.7 and 11.0% respectively) whilst levels 1 and 4 reveal a slightly lower difference of 8.4% and 6.8% respectively.

The mean R values obtained from the Douglas bag measurements for each stage of the protocol are shown in Table 6.6. (NB the Oxylog assumes an R value of 1). These values represent a significant difference from 1 for all Four stages. The greatest difference is observed at stages one and two where the mean R value was measured to be 0.89 (range 0.83 to 0.96) and 0.93 (0.85 to 0.98) respectively. If it is assumed that with repeat testing an individuals ventilatory response produces the identical R values then this deviation from an R value of 1 during the Douglas bag test would lead to a underestimation of the inspired volumes by approximately 1.8% with the Oxylog.

The mean maximal heart rate at each level for both the Oxylog and Douglas bag are shown in Table 6.7. Each individual responded with an incremental increase in the heart rate. There was no significant difference between the two different methods of testing, see Figure 6.3.

The mean Borg exertion score for each increment is represented in Table 6.8 and plotted in Figure 6.4. These values increased with the increased intensity of the exercise test but represent no significant difference between measurement techniques.

The individuals who participated in the trial are

TABLE 6.6 Mean and standard deviation of R values measured at each stage during the Douglas bag measurements.

Stage	mean	SD
1	0.89	0.04
2	0.93	0.04
3	0.95	0.03
4	0.97	0.02

TABLE 6.7 Mean (SD) heart rate (beat.min^{-1}) recorded at each stage of exercise with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bag
1	94 (11)	94 (9)
2	107 (12)	106 (11)
3	118 (14)	120 (14)
4	133 (16)	134 (17)

No significant difference at any stage.

FIGURE 6.3 Mean (SEM) heart rate (beat.min^{-1}) at each stage of exercise with the Oxylog and Douglas bag.

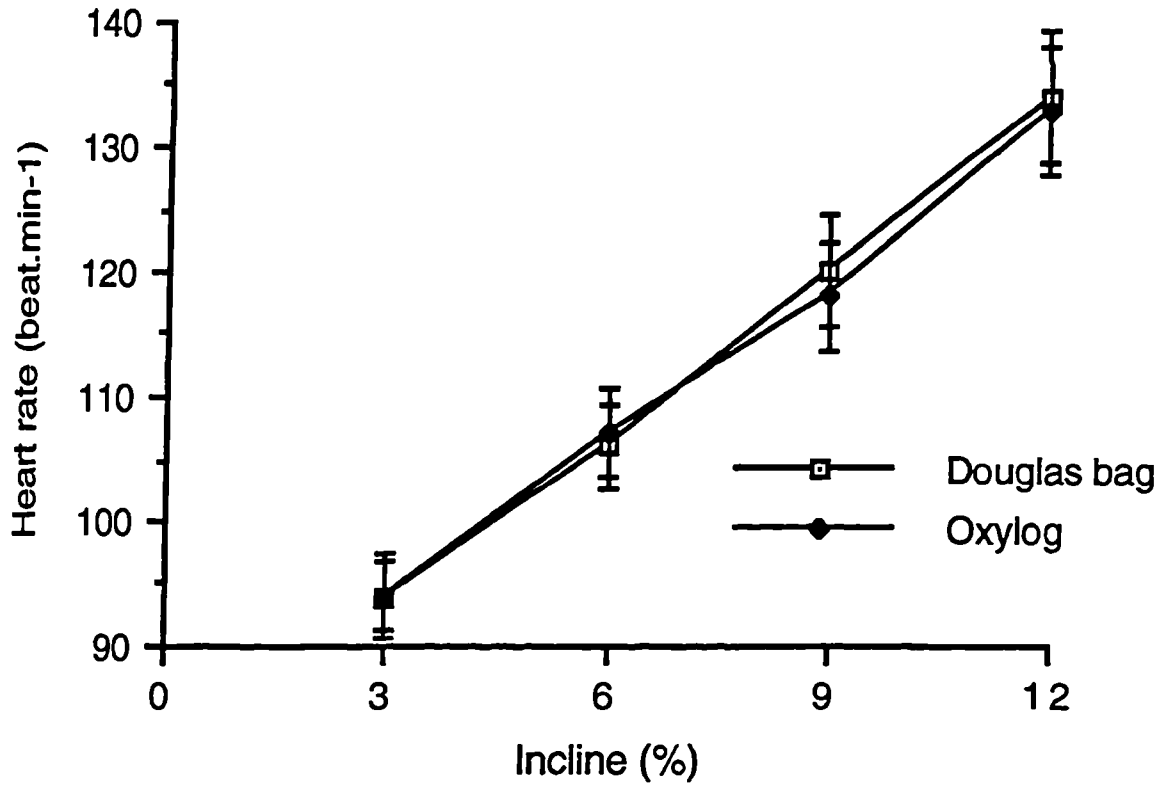
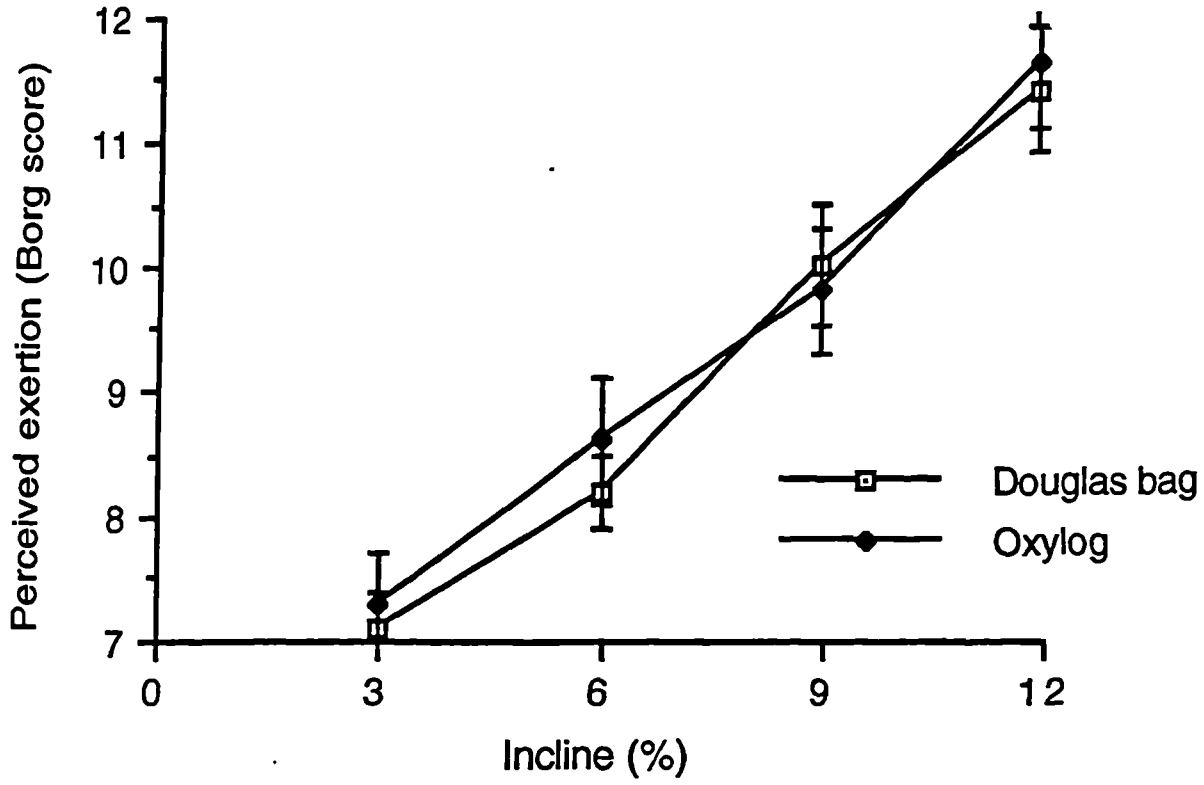


TABLE 6.8 Mean (SD) Borg exertion scale recorded at each stage of the exercise test with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bags
1	7.3 (1.2)	7.1 (0.9)
2	8.6 (1.6)	8.2 (1.1)
3	9.8 (1.7)	10.0 (1.6)
4	11.6 (1.7)	11.4 (1.6)

No significant difference at any stage.

FIGURE 6.4 Mean (SEM) Borg exertion score reported at each stage of exercise with the Oxylog and Douglas bag



familiar with physiological measurements but reported that the face mask was uncomfortable because it had to be a tight fit and some reported that they felt claustrophobic. Another important point raised was the inability to communicate effectively and consequently subjects felt slightly wary that if a problem arose they could not convey this to the operator and the mask was difficult to remove. A handful of subjects felt that it may have altered their breathing pattern during exercise, particularly as Douglas bag measurements demand mouth breathing and these subjects felt the Oxylog for some unexplained reason compelled them to breathe through their nose.

6.5.4 DISCUSSION

The results of this initial study using the Oxylog reveal that the equipment provides a method for ventilatory measurement that corresponds moderately well to the measurements of the Douglas bag. This result is in agreement with the work of both Ballal & McDonald (1982) and Jones et al (1987) but conflicts with that of Harrison and colleagues (1982). The former two studies on healthy subjects identified a significant underestimation of ventilation by the Oxylog compared to their usual gas analysis equipment (Douglas bag and computerised equipment respectively). Ballal and McDonald (1982) incorporated an RAF face mask in their Oxylog system to decrease the possibility of leaks although the underestimation of ventilation by the Oxylog persisted. Harrison et al (1982) incorporated a mouthpiece in to the Oxylog system found no significant differences in the measurements of either $\dot{V}O_2$ or $\dot{V}E$ except at the highest work rates. At stages prior to this the authors had identified no significant differences in the measurements of the Oxylog with an RAF face mask compared to their gas analysis equipment (mass spectrometer) at all but the lowest work rates.

Examining the individual results there were three subjects who recorded higher levels of $\dot{V}_I$ at stage 1, none at stage two, one at stage three and two at stage four. Correcting the volumes by approximately 1.8% at levels two, three and four would decreased the difference but it would be unlikely to account for all of the difference. The discrepancies in the $\dot{V}_I$ measurement are believed to be in part due to undetected leaks in the system occurring seemingly in the majority of subjects. Every effort was made to correct leaks but this was obviously inadequate. It is possible that the negative pressure generated during inspiration would in fact enhance the leaks by dislodging the face mask slightly as it was not adequately secured. On expiration the magnitude of the leaks may have decreased with the expired air forcing the mask against face. difficulties were encountered with the variety of facial anatomy presented. The weight of the hosing was also thought to lift the mask away from the face and the head straps did not provide adequate support.

The measurements of $\dot{V}O_2$ by the Oxylog revealed a different pattern of results being consistently higher at each stage of exercise compared with Douglas bags. The oxygen consumption results are in partial agreement with the work of McNeill et al (1987) who identified overestimation by the Oxylog of both $\dot{V}_I$ and $\dot{V}O_2$ and that of Harrison and colleagues (1982) (using the mouthpiece) who demonstrated that the Oxylog consistently overestimated $\dot{V}O_2$ significantly so until the final stages of the exercise. The consistently higher $\dot{V}O_2$ of the Oxylog may be erroneously elevated due to the additional work created by breathing through a meter or may in part be due caused by the differing patterns of breathing required by the mouthpiece and mask.

It should be noted that a fundamental difference in this study design compared to those documented above is the use of consecutive measurements as opposed to simultaneous

which therefore overcomes day to day variation. The natural physiological variation that occurred with repeat testing on $\dot{V}_E$ and $\dot{V}O_2$ employing Douglas bag techniques was studied by Hardman (1982, unpublished). The results revealed a coefficient of variation of 1.5 - 4.6% for measurements of $\dot{V}O_2$ and 2.7 - 7.4% for the corresponding $\dot{V}_E$ values on an incremental cycle test, performed on successive days (n= 10). The magnitude of the difference between the Oxylog and Douglas on the whole exceed these values. The natural physiological variation may in part account for the measurement differences. Nonetheless it would be unwise to hypothesise that the measurement errors were due to a biological factor rather than to a systematic difference associated with the equipment.

Perhaps the most important difference to consider when comparing other studies is that all except the present relied on simultaneous measurements of the Oxylog and gas analysis equipment connected in series to the patient with the Oxylog communicating directly with the patient. This should however (excluding natural physiological variation) make very little difference to the overall results unless the two pieces of equipment employed for the present study provoked different patterns of breathing. The Douglas bag was connected to the expiratory port of the Oxylog and unless there were expiratory leaks as well, then the volume passing to the Douglas bag would include that volume of air by-passing the Oxylog flow meter and be comparable to the volume expired into the Douglas bag in present study.

The underestimation of $\dot{V}_I$ has not translated into an underestimation of $\dot{V}O_2$ (the reader is referred back to equation in section 6.2). This could possibly be explained by the increased work (and cost) of breathing associated with the Oxylog. This is secondary to the greater resistance of the equipment compared to the Salford valve employed with the Douglas bag. Alternatively, but unlikely,

an error may have occurred at the site of the oxygen sensors despite careful calibration of the equipment. The reader is again referred back to the equation documented in section 6.2. If the oxygen sensors were not correctly calibrated or were unstable over even a short time period the under estimation of the inspired volume may, theoretically be adjusted for in the equation by erroneous measurements of the partial pressures of inspired and expired oxygen concentrations. Alternatively an error in calculations may arise because of the assumption that the response of the oxygen sensors is linear to the actual oxygen consumption.

Both the heart rate data and the Borg ratings reveal no significant difference at any stage of the exercise test between the two methods of analysis, suggesting that the two methods presented a comparable physiological strain both subjectively as well as objectively.

Overall, the Oxylog appeared to provide a reasonable estimation of individual's $\dot{V}_I$ and $\dot{V}O_2$ and was worthy of examination in a patient group. The option of the Oxylog was pursued especially in view of difficulties with alternative methods of gas analysis.

6.6 EXAMINATION OF THE VALIDITY OF THE OXYLOG IN PATIENTS WITH CAL (SUB-MAXIMAL)

6.6.1 INTRODUCTION

Having concluded that the Oxylog provides a relatively valid method of assessing ventilatory parameters in normal subjects it was necessary to repeat the validation procedure in a patient group. In the previous study (6.5) a possible cause of error in the Oxylog and face mask system was identified. It was important to be confident that the equipment would perform well in a group of patient with altered respiratory mechanics before applying it to the field environment. A 2-stage sub-maximal exercise test was adopted, at a speed that all the patients in this study group would be able to perform.

The aim of this study was to assess the validity of the Oxylog in a group of patients. The test was sub-maximal to ensure that an adequate number of equivalent data point were generated.

6.6.2 METHOD

Five patients were recruited for this stage of the trial and were required to make an initial visit to the hospital for baseline measurements as detailed in 2.2.2. During the same visit patients equipped with the Sports Tester performed a sub-maximal test on the treadmill. It was necessary to gauge a speed appropriate for all five patients that would allow them to complete the test at two separate increments, 0 and 3%. The speed selected was 2 mph. Each increment lasted for 4 minutes, allowing the patient to reach 'steady state'. At this stage the patients also experienced the two forms of gas analysis equipment. The Oxylog with the face mask and the standard Douglas bag measurements.

The two subsequent visits to Loughborough were presented

in a randomised balance design and were performed with full medical cover at intervals of one week. The Oxylog was set up as described above 6.4 and all measurements were taken as described above. The heart rate and Borg breathlessness rating was recorded in the final minute.

6.6.3 RESULTS

The physical characteristics of the patients are shown in table 6.9. There was no significant difference in their lung function values for the three visits ($p>0.05$). Employing the analysis proposed by Guyatt et al (1987) there was a marked change in one patient's response to the CRDQ in the dyspnoea, emotion and fatigue component. The patient however assigned this to the menopause. Overall there was no significant statistical difference in the results of the CRDQ for the three visits ($p>0.05$).

Tables 6.10 and 6.11 shows the mean $\dot{V}O_2$ and $\dot{V}I$ recorded at the two levels represented in Figures 6.5 and 6.6. The mean difference and 95% confidence interval at the 0% gradient was 1.90 $ml.min^{-1}.kg^{-1}$ (0.1 to 3.7) greater using the Oxylog for the $\dot{V}O_2$. The mean $\dot{V}E$ was 2.84 $l.min^{-1}$ (5.49 to 0.19) higher with the Douglas bag. Comparable differences were also recorded at 3%, the $\dot{V}O_2$ was 2.1 $ml.min^{-1}.kg^{-1}$ higher with the Oxylog whilst the mean $\dot{V}I$ was higher with the Douglas bag, 2.62 $l.min^{-1}$ (5.95 to -0.71). Applying the Wilcoxon test for matched pairs no significant difference was identified in the measurements of the $\dot{V}O_2$ or $\dot{V}E$ at either level of exercise.

The mean R values of the Douglas bag tests were 0.87 and 0.88 for stages one and two respectively. These values would translate to an underestimation of $\dot{V}I$ with the Oxylog of approximately 1.8% below that of the Douglas bag.

The mean heart rate at each stage is shown in Table 6.12. The values represent no significant difference between the

TABLE 6.9 Some physical characteristics of the patient group, n=5, [mean (range)].
4 males, 1 females.

	1	Oxylog	Douglas bag
Age (yr)	64.4 (52-79)	-	-
Height(m)	1.69 (1.59-1.70)	-	-
Weight(kg)	-	65.33 (49.55-67.8)	65.41 (49.20-67.60)
FEV_1 (l)	1.31 (0.78-2.25)	1.23 (0.75-2.35)	1.23 (0.8- 2.15)
FEV_1 % predicted	47.6 (25.3-93.0)	45.3 (24.4-97.1)	45.0 (24.8-86.8)
FVC (l)	2.82 (2.16-3.03)	2.75 (1.92-3.05)	2.63 (2.10-2.97)

TABLE 6.10 Mean (range) $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) measurements at the two stages of exercise with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bag
1	10.6 (7.9-12.9)	8.7 (5.9-10.4)
2	12.1 (9.8-13.7)	10.0 (8.0-11.1)

TABLE 6.11 Mean (range) $\dot{V}_I$ ($l.min^{-1}$) measurements at the two stages of exercise with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bag
1	17.4 (11.7-22.4)	20.3 (14.4-22.5)
2	21.0 (15.3-26.0)	23.6 (15.7-26.8)

FIGURE 6.5 Mean (SEM) $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) measurements at the two stages of exercise with the Oxylog and Douglas bag.

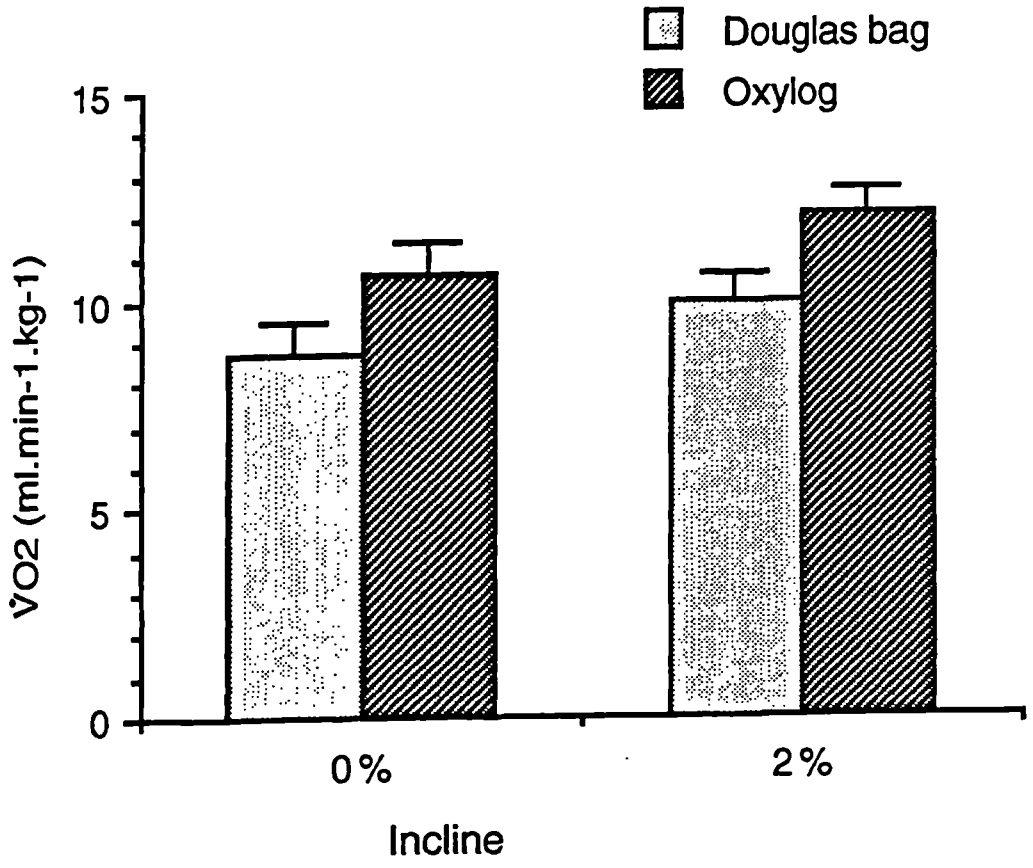


FIGURE 6.6 Mean (SEM) $\dot{V}_I$ ($l.min^{-1}$) measurements at the two stages of exercise with the Oxylog and Douglas bag.

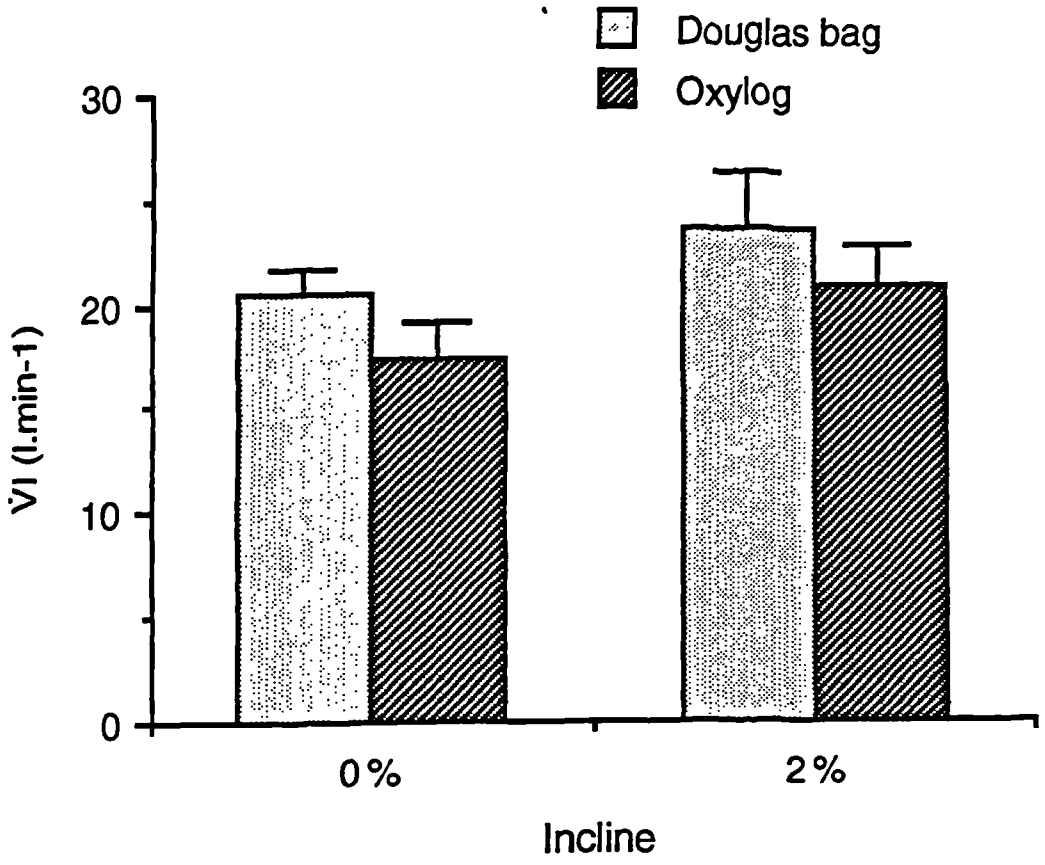


TABLE 6.12 Mean (range) heart rate (beat.min^{-1}) measurements at the two stages of exercise with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bag
1	107 (91-123)	104 (84-127)
2	115 (96-130)	110 (88-126)

two stages with a mean difference of 3 and 5 beat.min^{-1} higher using the Oxylog. These differences were not significantly different.

Examination of the relationships between the two ventilatory measurements at the two stages revealed a Spearman rho of 0.30 and 0.70 for the two measurements of $\dot{V}O_2$ and rho = 0.70 and 0.97 for the $\dot{V}I$ measurements.

The mean Borg scores (Table 6.13) at the end of each stage were 1.9 and 2.3 for the Oxylog and 1.1 and 2.0 for the Douglas bag. This represents a mean difference of 0.8 and 0.3 for stages one and two respectively, these values do not constitute a significant difference at either level.

TABLE 6.13 Mean (range) Borg breathlessness scores recorded at the two stages of exercise with the Oxylog and Douglas bag.

Stage	Oxylog	Douglas bag
1	1.9 (0.5-3)	1.1 (0.5-2)
2	2.3 (0.5-4)	2.0 (0.5-3)

6.6.4 DISCUSSION

Initially six patients were recruited but one of the subject withdrew unable to tolerate the face mask. The other five patients were tolerant of the face mask and we endeavoured to obtain an adequate fit using either a small or medium face mask (P.K.Morgan).

The spirometry and CRDQ indicate the patients were clinically stable for the duration of the study. The heart rate data and the Borg scores indicate that the patients worked to the same level for both modes of testing

Patients consistently reported a preference for the Douglas bag system, not least because they were required to endure the mouthpiece for just the final minute of each stage of exercise whilst the face mask worn throughout the exercise test was intimidating and claustrophobic. Patients also found it difficult to identify possible causes of air leaks. The ventilatory measurements indicate a satisfactory level of agreement between the two methods of measurement. The results present a similar trend to that identified in the normal group, an overestimation of $\dot{V}O_2$ despite an underestimation of $\dot{V}I$. The magnitude of the difference in the patient group is comparable to the difference documented in the healthy volunteers. As the values recorded for the patients are lower this translates into a greater percentage error, although this did not correspond to a significant difference. The possible reasons for this are as described for normal subjects (6.5.4). There is a natural biological variation in oxygen requirements and the efficiency of oxygen utilisation during a repeated exercise test, however these results deviate in a common direction indicating a real difference in the two measurement techniques. Swinburn and colleagues (1985) documented no significant difference in the measurement of $\dot{V}E$ or $\dot{V}O_2$ over the range of work rates patients could achieve compared to computerised equipment.

Because patients found the face mask unacceptable and the inherent difficulties encountered with providing an adequate sealing a viable alternative was sought that could be incorporated into the Oxylog system.

6.7 EXAMINATION OF THE USEFULNESS OF THE OXYLOG INCORPORATING A MOUTHPIECE (HEALTHY SUBJECTS)

6.7.1 INTRODUCTION

As a consequence of the problems identified with the fitting of the mask and possible leaks (also considering the results described in the patient group) it was proposed to assess the usefulness of a mouthpiece and nose-clips. It was thought that a mouthpiece would ultimately be more acceptable to the patients; the group of students use to exercise testing were very co-operative regarding the identification of leaks and it was felt that unless the leak was large patients would not be able to do so. Although RAF face masks appeared to provide an adequate seal they were reported to be cumbersome (Harrison et al 1982). Secondly, being compared with the Douglas bag technique (employing a mouthpiece) it was felt more appropriate to assess comparable equipment as far as possible. A mouthpiece was therefore incorporated into a modified Oxylog system and its reliability examined in the original group of healthy subjects.

6.7.2 METHOD

For this stage the treadmill protocol was as described above 6.5.2. However it was possible to recruit only eight of the original ten subjects for the exercise test. The mouthpiece was constructed in the Cardio-respiratory department at Glenfield General Hospital. It contained the components of a nebulising chamber and two one way valves connected in series. It allowed a mouthpiece to be fitted, the flow meter to be attached with a connector [sealed with adhesive tape (sleek)] and the tubing to pass from the mouthpiece to the body of the Oxylog. For the treadmill exercise test the mouthpiece, which protruded laterally approximately 10-12 cm, was supported by the operator as there was a tendency for the mouthpiece to be dislodged with the weight of the flow meter.

6.7.2 RESULTS

The physical characteristics of the eight subjects is shown in Table 6.14.

The inspired gas volumes were subject to the same conversions applied above (6.5.3). The mean values obtained for the ventilation and $\dot{V}O_2$ at the end of each level are shown in Tables 6.15 and 6.16. The measurements for the $\dot{V}O_2$ are again consistently higher for the Oxylog with the mouthpiece than the Douglas bag, the values are significantly higher, except for the first stage of exercise ($p>0.05$), the mean difference values range from 2.6 to 3.5 $ml.min^{-1}.kg^{-1}$. The values for the mouthpiece were slightly higher for than the face mask although these differences were not statistically significant ($p>0.05$). The mean differences between the Oxylog (mouthpiece) and the Douglas bag and the 95% confidence intervals are expressed in Table 6.17. The values for the two techniques are plotted in Figure 6.7. The relationship was considerably stronger between the Douglas bag measurements using the Oxylog and mouthpiece than the face mask.

The values of $\dot{V}I$ using the mouthpiece underestimated the volume of air inspired (Table 6.18). The values for the two techniques are plotted in Figure 6.8. The difference between the mouthpiece and the Douglas bag is significant at all levels, including level one where the mean difference was just 1.7 $l.min^{-1}$. This difference rose to a mean value of 5.6 $l.min^{-1}$ at stage four. The values of $\dot{V}I$ using the mouthpiece and face mask were not significantly different, except at level 2. The mean differences and 95% confidence intervals between $\dot{V}O_2$ values measured using the Oxylog with the mouthpiece compared with the Douglas bag are presented in Table 6.18.

TABLE 6.14 Some physical characteristics of the group (mean and standard deviation). n=8. 3 males, 5 females

	mean	SD
Age (yr)	31.2	7.9
Height(m)	1.67	0.07
Weight(kg)	61.80	6.95
FEV_1 (l)	3.77	0.36
FVC (l)	4.63	0.70

TABLE 6.15 Mean (SD) values measured in normals for $\dot{V}O_2$ (STPD) $ml.min^{-1}.kg^{-1}$. n=8.

Stage	Oxylog	Douglas bag
1	15.6 (1.3)	12.1 (0.7)
2	19.7 (0.7)	16.5 (0.5)
3	23.8 (1.0)	21.1 (1.1)
4	29.1 (2.1)	26.3 (0.8)

TABLE 6.16 Mean (SD) values measured in normals for $\dot{V}_I$ (STPD) $l.min^{-1}$. n=8.

Stage	Oxylog	Douglas bag
1	19.1 (1.5)	20.7 (2.7)
2	23.8 (2.0)	27.7 (3.3)
3	28.6 (2.9)	33.9 (3.7)
4	34.6 (3.9)	40.3 (5.1)

TABLE 6.17 Mean (SD) differences and the 95% confidence intervals of the Douglas bag and Oxylog measurements at each stage for $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) and the Spearman rank order correlation.

Stage	X	SD	95% confidence interval	rho
1	-3.5	1.8	-5.0 to -1.9	0.88
2	-3.2	1.1	-4.1 to -2.3	0.79
3	-2.6	1.7	-4.1 to -1.2	0.69
4	-1.3	2.3	-3.3 to 0.6	0.43

FIGURE 6.7 Mean (SEM) values of $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) at each stage for the Oxylog and Douglas bag.

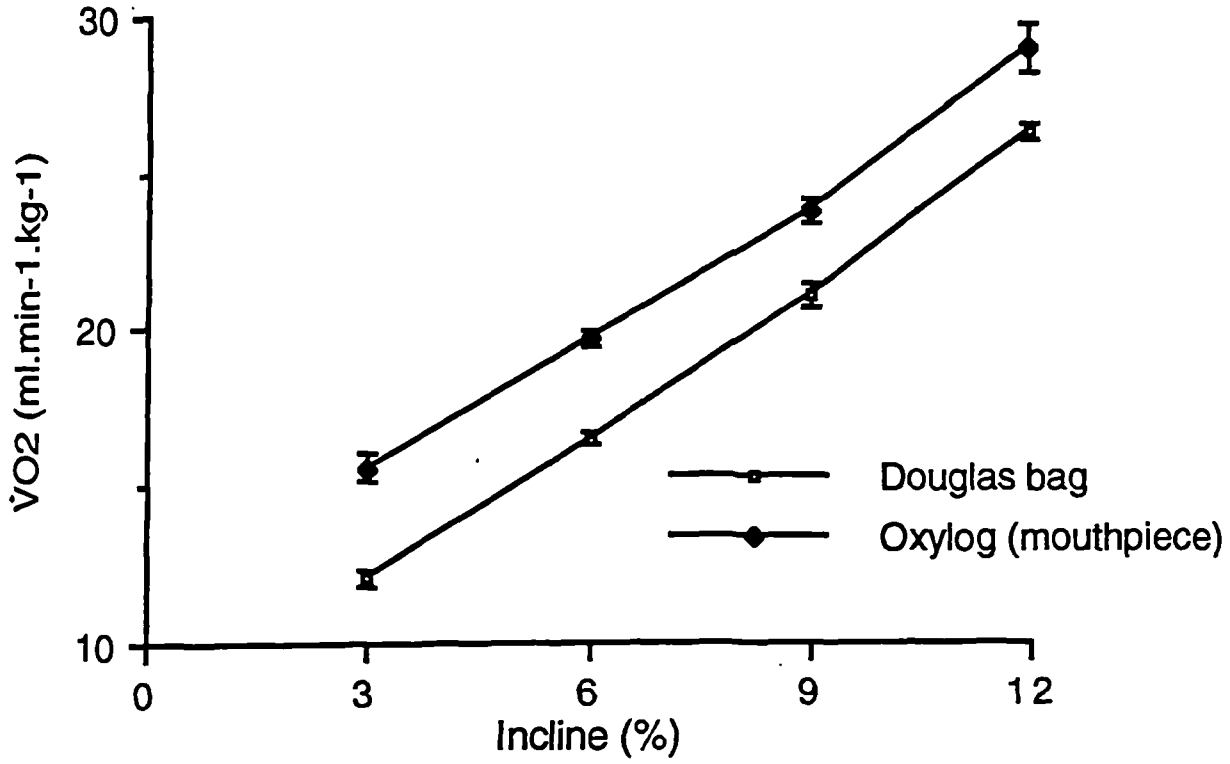
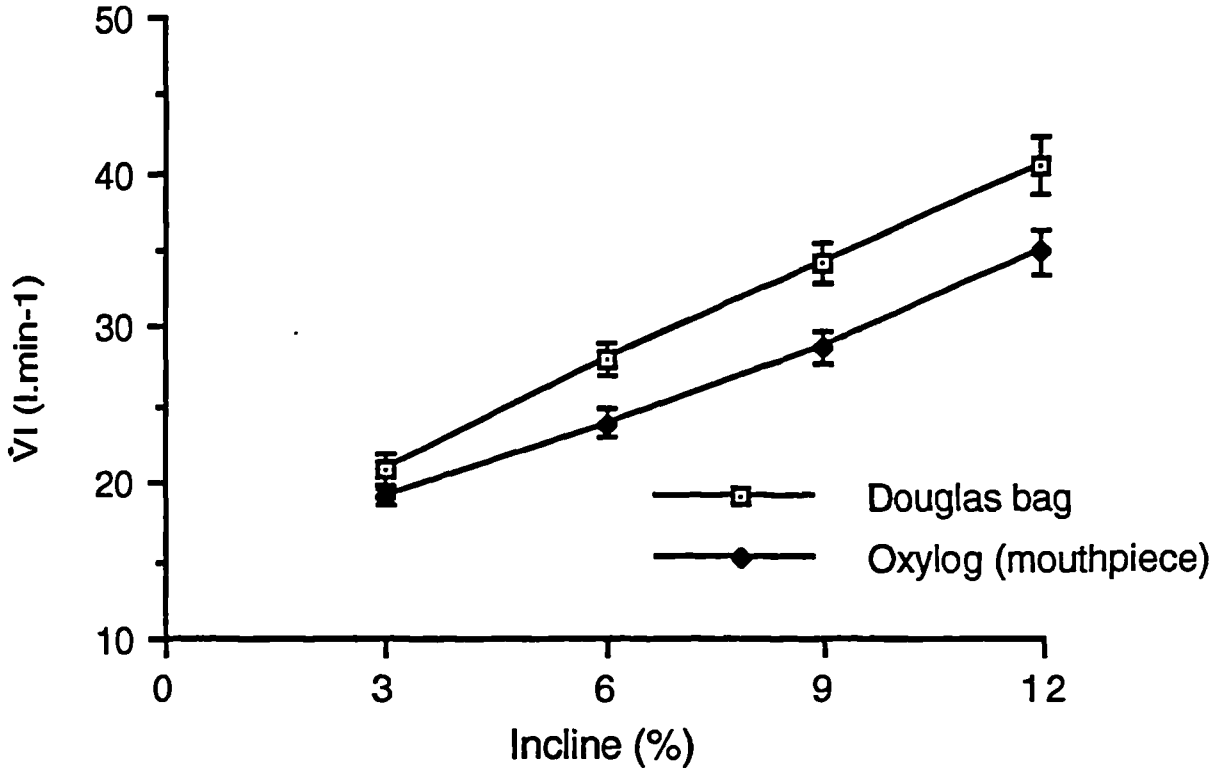


TABLE 6.18 *The mean (SD) differences and the 95% confidence intervals of the Douglas bag and Oxylog measurements at each stage for* $\dot{V}_I$ *(l.min^{-1}) and the Spearman Rank Order* correlation.

Stage	X	SD	95% confidence interval	rho
1	1.7	2.3	-0.3 to 3.6	0.48
2	3.9	1.8	2.3 to 5.5	0.69
3	5.4	2.0	3.7 to 7.1	0.78
4	5.6	4.1	2.1 to 9.1	0.72

FIGURE 6.8 Mean (SEM) values of $\dot{V}I$ ($l.min^{-1}$)
at each stage for the Oxylog and Douglas bag.



The mean R values, 0.88, 0.92, 0.94 and 0.96 for levels 1,2 3 and 4 respectively represent a significant difference from 1.0 at each stage ($p<0.05$). Although this difference translates into the Oxylog underestimating the volume of inspired air by a mean value of less than 1.8%.

The heart rate data and the Borg scoring were again not significantly different.

Finally the subjects reported less discomfort with the mouthpiece of the Douglas bag which was more compact and lighter than the mouthpiece of the Oxylog.

6.7.3 DISCUSSION

The measurements generated are in agreement with Ballal & McDonald (1982) producing lower values for $\dot{V}_I$ and greater values of $\dot{V}_{O_2}$ for the Oxylog compared to the Douglas bags. Harrison et al (1982), using a mouthpiece, identified no significant difference between the two methods except at the highest work rate where the $\dot{V}_{O_2}$ was significantly lower. Overall the use of the mouthpiece does not correct the discrepancy in the values for $\dot{V}_I$ or $\dot{V}_{O_2}$ of the face mask compared to the Douglas bag, in fact the difference between the two measurement techniques increased slightly. The oxygen cost of the exercise with the modified (mouthpiece) equipment was even higher than with the original face mask. This was a genuine increase in the 'cost' of exercise /breathing and not as a result of the increased ventilation being recorded (see equation, section 6.2). The increased cost of breathing was thought in part to be due to the modification of the equipment increasing the external resistance to breathing.

For half of the subjects the mouthpiece appeared to approximate Oxylog measurements to the Douglas bag

measurements, whilst the other half did not. This second group of subjects can be further divided into those subjects who had a consistently lower reading at all stages of exercise with the mouthpiece compared to the Oxylog with the face mask and those who just had a lower reading at the fourth stage of exercise. The reading for this second group at this fourth stage were lower than the Oxylog and mask readings (mean 4.1 $l.min^{-1}$ n=2). As the first three stage measurements of these individuals matched it can be assumed that there was some movement around the mouthpiece to facilitate the passage of air around the mouthpiece and by-pass the flow meter. For the other half of this group the measurement error using the mouthpiece appeared to be systematic, increasing with the intensity of exercise. This could be accounted for (as the subjects described) by the unsatisfactory mouthpiece and its inherent instability that appears to increase with the intensity of exercise. The technique required to secure the plastic mouthpiece was reported to be quite demanding in comparison with that of the Douglas bag and may in part account for the increased V_{O_2}. Added to which the jaw was not relaxed and may have provoked an unfamiliar ventilatory pattern.

Despite the overall acceptability of the mouthpiece certain problems presented during the course of the study. Due to the weight of the flow meter (despite attempts to support it) the subjects felt awkward. A further criticism was of the actual mouthpiece, due to the aperture of the inspiratory limb of the valve a plastic mouthpiece was attached. This mouthpiece was not only difficult to secure safely by the patient because of the short flanges but the plastic moulding made it difficult to retain in one position successfully. In addition the subjects were required to bite the mouthpiece to maintain its position, quite a different technique to the mouthpiece of the Douglas bag.

Despite these difficulties it was decided to pursue the option of a commercially available mouthpiece. This decision was based upon a number of points -

- the initial problems sealing the face mask and identifying leaks [equal to 25-30% in initial study results not reported 6.6)], despite co-operative subjects.
- communication difficulties for the patient.
- patient discomfort.
- comparable technique to Douglas bag measurements.
- more acceptable to the patient.

Finally it was proposed that the resistance of the modified mouthpiece developed may have had a greater resistance to breathing than a commercially available mouthpiece.

6.8 EXAMINATION OF THE VALIDITY OF THE OXYLOG (& MOUTHPIECE) DURING MAXIMAL EXERCISE TESTING IN PATIENTS WITH CAL

6.8.1 INTRODUCTION

The final stage of this investigative procedure was to address the validity of the Oxylog during maximal testing in patients with CAL incorporating the commercial mouthpiece. The ultimate aim being to examine precisely and confidently the physiological response to the shuttle walking test (sub-maximal measurements), culminating in a symptom limited maximum measurement.

6.8.2 METHOD

Six patients with stable CAL volunteered to participate. Again three visits were required, a practice visit to Glenfield and the following two 'test' visits to Loughborough University. At Glenfield [after consent had been obtained and baseline measurements recorded (4.2.2)] an appropriate treadmill walking speed was gauged to evoke a symptom limited maximum performance at Loughborough. The speed was assessed individually for each patient and based upon heart rate and the Borg breathlessness response. The test at Loughborough was at a constant speed with increases from the flat, of 2.5% in inclination every two minutes. The Oxylog and Douglas bag measurements were made as previously described. The mouthpiece employed with the Oxylog was a Hans Rudolph 27 -1400 light weight (272 g), low resistance valve. The mouthpiece had two, one way valves and incorporated a saliva trap. The flow meter of the Oxylog was attached to the inspiratory side of the valve with a connector and the expiratory port was attached to the tubing to the Oxylog. The tubing was slightly narrower than had been previously used allowing an adequate seal around the valve. The valve was supported with a head harness (Hans Rudolph). The actual mouthpiece was of rubber (P.K.Morgan) with slightly enlarged flanges to help secure

it in the patients mouth.

6.9.3 RESULTS

The physical characteristics of the six patients are shown in Table 6.19.

The mean FEV_1 values represent 44%, 47% and 48% of predicted for the practice, Oxylog and Douglas bag trials respectively, indicating a moderate impairment to respiratory function.

The mean speed the patients walked was just 2.6 mph. The mean time for each treadmill test was 7.7 minutes for the Oxylog and 7.3 minutes for the Douglas bag. The mean difference in time was 0.4 minutes, ($p>0.05$).

The mean maximal heart rate attained during the two exercise tests was 131 beat.min^{-1} and 130 beat.min^{-1} for the Oxylog and Douglas bag respectively. This represents approximately 76% of predicted maximal heart rate. The mean difference and 95% confidence interval was 1.2 beat.min^{-1} (-8.0 to 10.2) higher in the Oxylog trial than the Douglas bag.

The Borg ratings were not significantly different for either test, the two mean maximal values were 5.5 for the Oxylog and 5.6 for the Douglas bag test, the mean difference and 95% confidence intervals was -0.17 (-0.96 to 0.62).

The mean $\dot{V}O_2$ and mean $\dot{V}I$ are expressed in Table 6.20. The mean differences and the 95% confidence intervals are shown in Table 6.21. The values for the $\dot{V}O_2$ are not significantly different ($p>0.05$), unlike the values for the $\dot{V}I$. The relationship between the two values for the measurement of $\dot{V}I$ and $\dot{V}O_2$ are relatively strong having a Spearman Rank order correlation of 0.83 and 0.59

TABLE 6.19 Some physical characteristics of the patient group, mean (range).
N=6, 3 males, 3 females.

Trial	1	Oxylog	Douglas bag
Age (yr)	58.0 (50.3-68.6)	-	-
Height(m)	1.72 (1.63-180.0)	-	-
Weight(kg)	-	73.78 (56.50-98.80)	73.35 (56.00-97.90)
FEV_1 (l)	1.42 (0.90-2.80)	1.55 (1.0- 3.1)	1.47 (1.0-2.8)
FEV_1 % predicted	43.8 (31.4-74.3)	47.3 (34.8-88.2)	47.9 (34.8-71.6)
FVC (l)	2.72 (2.20-4.00)	2.73 (2.10-4.15)	2.66 (2.10-3.7)

TABLE 6.20 Mean (range) maximal measurements of $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) and $\dot{V}I$ ($l.min^{-1}$) for the Oxylog and Douglas bag at the patient's maximum.

	Oxylog	Douglas Bag
$\dot{V}O_2$	12.6 (7.9-16.6)	14.0 (8.5-18.8)
$\dot{V}I$	28.3 (15.5-51.3)	39.6 (26.5-65.3)

TABLE 6.21 Mean differences, standard deviation and the 95% confidence intervals of the maximum Douglas bag and Oxylog measurements values for $\dot{V}O_2$($ml.min^{-1}.kg^{-1}$) and $\dot{V}I$ ($l.min^{-1}$) and the Spearman Rank Order correlation.

	Mean	SD	95% confidence interval	rho
$\dot{V}O_2$	1.7	3.0	-1.4 to 4.9	0.59
$\dot{V}I$	11.3	4.6	6.4 to 16.1	0.83

respectively. The R values of the Douglas bag measurements have a mean value during the final minute of the exercise test of 0.96(0.10) which if similar in the Oxylog trial would lead to no error measurement of $\dot{V}_I$.

6.8.4 DISCUSSION

The patients for this stage of the trial were both physiologically and psychologically stable and the two tests appear to have presented a comparable physiological strain assessed both objectively and subjectively.

Overall the mouthpiece and the head harness was more acceptable to the patient than the face mask.

There was only moderate agreement between the measurements of $\dot{V}O_{2\,peak}$ using the Oxylog and Douglas bags in these patients. The values obtained for ventilation were more closely related, although there was a systematic difference. The values for both $\dot{V}O_2$ and $\dot{V}_I$ that were obtained in the present study are of a similar magnitude to those reported by Swinburn et al (1985) who also employed the Oxylog for a clinical trial. Swinburn et al (1985) reported a mean maximal $\dot{V}O_2$ and $\dot{V}_E$ during three exercise tests ranged from 0.8 - 1.0 $l.min^{-1}$ and 26 -31 $l.min^{-1}$, his group had severe airways limitation with a mean FEV_1 of 0.8 l. Both Belman et al (1991) and Zuwallack et al (1991) employed treadmill testing and quote similar levels for VO_2 (further discussion on this topic regarding relative and comparative measurements is located in chapter 5.4) As with this present study and other reported trials, the number of subjects is small and it is therefore inappropriate to draw any conclusions regarding the population as a whole.

As the measurements of the 'gold standard' $\dot{V}O_2$ are comparable for the two techniques it is proposed that the

subjects may in fact adopt an alternative breathing strategy for the Oxylog, which may account for the differences observed in the $\dot{V}_I$. This does not, however, exclude the possibility of leaks (not exclusive to the Oxylog system) or the possibility that the Oxylog system may inhibit maximal ventilation by increasing resistance to breathing. To confirm this suggestion further investigations into the properties of the Oxylog and associated mouthpiece would be required.

At any given work rate prescribed for an individual patient the energy requirements will be comparable (providing the O_2 cost of breathing is the same), this is confirmed by the $\dot{V}O_2$ measurements (regardless of the $\dot{V}_E$ response). Patients will adopt a breathing strategy to ensure an adequate extraction of oxygen and as a consequence, ventilatory volumes may alter slightly. This however is unlikely to account for all the difference in $\dot{V}_I$ which is observed, as is natural physiological variation. It appears that the system leaks and although it was assumed that the source of the leak was around the mouth this was not confirmed. In addition, as described above, the ventilatory response of the patients may have been constrained by the system, increasing the work of breathing to prevent maximal ventilation. Examining the individual data, there appears to be a systematic increase in the magnitude of the error with the increasing intensity of exercise for 4/6 patients. For the remaining two the error remained stable. The resistance to breathing caused by the system is likely to increase with increasing flow and would account for the observed variation in 4 of the 6 individuals tested.

The calculation of $\dot{V}O_2$ by the Oxylog derives a total $\dot{V}_I$ from the flow rate and the partial pressure of O_2 from a small sample of each breath. It appears that despite the underestimation of $\dot{V}_I$ the value of $\dot{V}O_2$ is not distorted.

Despite the difference in $\dot{V}_I$ measurements it was proposed primarily on the basis of the $\dot{V}O_2$ measurements (demonstrating a strong agreement between the maximal measurements of the Douglas bag measurements and the Oxylog) that the Oxylog was worthy of use in a field study examining the response to the shuttle walking test. This decision was reinforced by the fact that Douglas bags were impractical and that the limitations of the Oxylog by this stage were already documented and, at least in part understood.

6.9 INVESTIGATION OF THE RESISTANCE TO INSPIRATION OF THE OXYLOG AND DOUGLAS BAG

6.9.1 INTRODUCTION

Examining the results presented in the proceeding sections it appeared that the Oxylog equipment (with the original mask and the two subsequent adapted mouthpieces) presented measurement difficulties compared to the Douglas bag system. On initial testing (unreported data) it appeared that a loss of measurable ventilation was occurring around the face mask and this was overcome to some extent by correcting the leaks (6.5). It was obviously unreasonable to expect patients to identify leaks and the option of a mouthpiece was pursued. This appeared to be satisfactory, although ventilation continued to be underestimated and $\dot{V}O_2$ overestimated (6.7). The use of the Hans Rudolph valve (in series with the Oxylog) in the patients (6.8) resulted in the underestimation of both the ventilation and the $\dot{V}O_2$.

This section of the thesis therefore reports studies undertaken to examine the resistance to inspiration of the Douglas bag valve and the individual Oxylog systems. An alteration in the measured resistance to breathing with each modification of the Oxylog compared to the Douglas bag (incorporating the Salford valve) may explain some of the differences observed in the results.

The resistance of breathing apparatus comprises laminar and turbulent components. When the flow is laminar, the resistance is mainly dependent upon the diameter of the tubing, rising sharply as the diameter decreases. The resistance due to local turbulence arises in the region of constrictions and sharp bends (Mushin & Jones 1987). Resistance is measured in units of pressure drop (cmH_2O) per unit flow ($l.min^{-1}$).

6.9.2 METHOD

Resistance to airflow was measured using a water manometer connected across the inspiratory port and breathing port of each valve. Resistance to flow was defined as the pressure drop across the two ports and expressed in cm of H_2O in a range of 10-100 $l.min^{-1}$ (at 10 $l.min^{-1}$ increments), ie cmH_2O per $l.min^{-1}$, ($cmH_2O.l^{-1}.min$). The air flow was generated by a flow calibration set (Model 19116, Gould Inc). A continuous flow rate was used in the place of the intermittent breathing of patients. A series of adaptors were made to allow fixation of the valves to the flow generator. The measurements were taken in duplicate and the mean values presented below. The internal diameter of the valves was also taken using a pair of Philips callipers.

6.9.3 RESULTS

The measurements of the internal diameter of the respective inspiratory valves were

1. Salford valve 2.8 cm
2. Oxylog valve 2.5 cm
3. Hans Rudolph 1.5 cm

The resistance to flow is summarised in table 6.22. There was a strong relationship between the resistance of the Oxylog and the Salford valve and an equally strong relationship between the resistance to inspiration of the Salford valve and the Oxylog valve with the addition of the Hans Rudolph. However, there was a significant difference ($p<0.001$) between the resistance to breathing of the Salford valve compared to both the Oxylog alone and its subsequent modification. The mean (SD) difference between the Salford valve and the Oxylog alone was 0.72 (0.42) $cmH_2O.l^{-1}.min$. over the range 10-100 $l.min^{-1}$. The corresponding mean difference between the Salford valve and the Oxylog with the Hans Rudolph was 2.4 (1.37) $cmH_2O.l.^{-1}.$ min.

TABLE 6.22 Resistance (cmH_2O) of the inspiratory ports of the Salford, Oxylog and Hans Rudolph valves.

Flow ($l.min^{-1}$)	Salford valve	Oxylog valve	Hans Rudolph valve (HR)	HR + Oxylog valve
10	0.20	0.40	0.40	0.90
20	0.30	0.55	0.50	1.20
30	0.45	0.80	0.78	1.70
40	0.55	1.00	0.98	2.10
50	0.65	1.25	1.10	2.55
60	0.68	1.45	1.25	3.10
70	0.73	1.65	1.55	3.70
80	0.80	1.85	1.80	4.45
90	0.87	1.05	2.10	4.95
100	0.93	2.35	2.40	5.50

Figures 6.9 and 6.10 plot the resistance of the valves employed for the studies described in Chapter 6. Analysis of the slopes reveals that the flow versus resistance slope for the Salford valve and Oxylog valve were similar. The mean difference and 95% confidence interval for the differences between the slopes was -0.01 (-0.02 to 0.01) cm $H_2O.l.^{-1}min$. This was calculated using a pooled standard deviation from the deviations about the individual fitted regression lines. This pooled standard deviation was used to calculate the standard error of the differences and then the 95% confidence interval. Since zero difference between slopes is near the middle of the confidence interval there is no evidence that the two population regression lines have different slopes (Gardner and Altman 1989). However, it is more useful to examine the vertical distance between the intercepts ie, the vertical distance between the parallel lines. The mean difference between the fitted y values was calculated using an equation incorporating the original mean x and y values of the two slopes and the gradient of the common slope. The resulting mean (and 95% CI) estimated vertical distance between the slopes is -0.67 (-0.92 to -0.43) cm H_2O. It is apparent from Figure 6.9 that the Oxylog consistently results in a higher resistance to breathing than the Salford valve.

The comparison of the slopes of the regression lines between the Oxylog incorporating the Hans Rudolph valve and the Salford valve produced a mean difference and 95% confidence interval of -0.45 (-0.05 to -0.04)cm $H_2O.l^{-1}.min$. Since zero did not pass through the confidence interval, it can be concluded that the regression lines have different slopes. Any further comparison of the regression lines would be invalid as the slopes are not similar (Altman 1991).

The dead space of the three systems was measured as accurately as possible. The dead space of the Salford valve

FIGURE 6.9 The resistance (cmH_2O) to inspiration (range 10 - 100 $l.min^{-1}$) of the Salford valve and the Oxylog inspiratory valve.

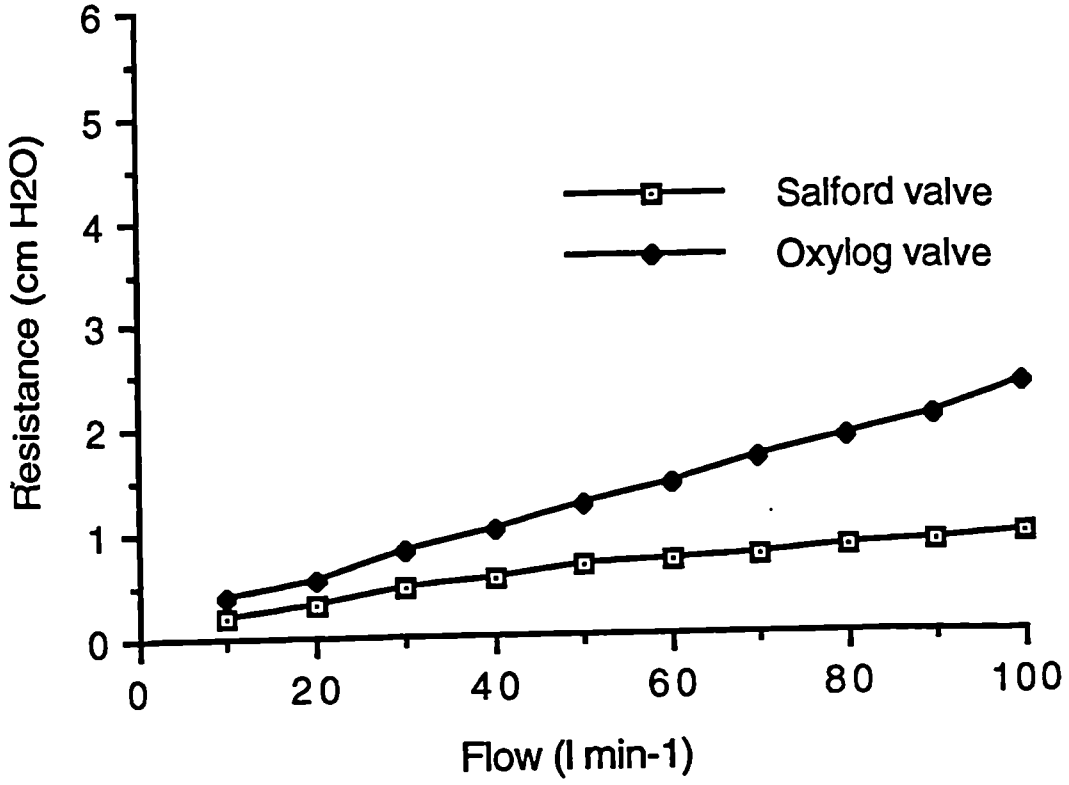
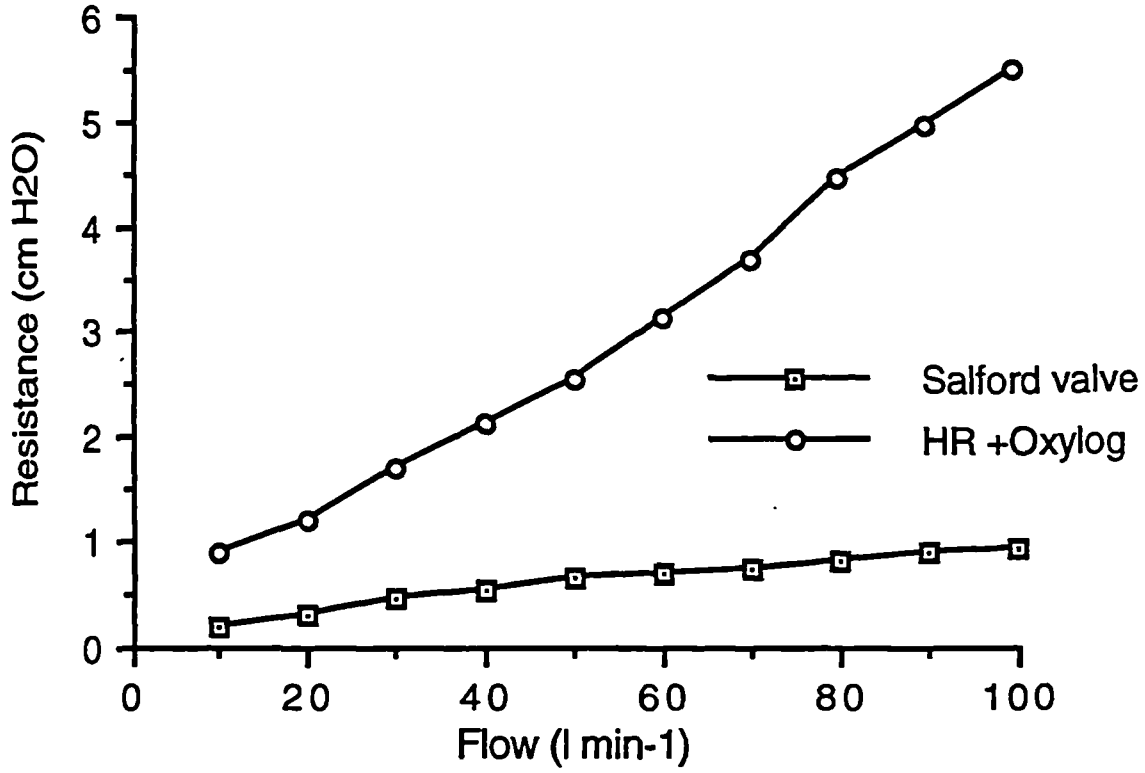


FIGURE 6.10 The resistance (cmH_2O) to inspiration (range 10 - 100 $l.min^{-1}$) of the Salford valve and the Oxylog connected with the Hans Rudolph valve.



is documented to be 80 ml (Jakeman 1979). An approximation (measured in mls of H_2O) of the dead space of the Oxylog face mask employed is 150 ml, whilst that of the Oxylog and Hans Rudolph combination was approximately 280 ml.

6.9.4 DISCUSSION

It has been demonstrated that a reduction of $\dot{V}O_{2\,peak}$ may occur if ventilation is impeded by high resistance introduced into the breathing circuit (Ceretelli et al 1969). The World Health Organisation (Anderson et al 1971) recommend that for the purpose of collecting respiratory gases a low resistance breathing valve (less than 5 cmH_2O at 300 $l.min^{-1}$ ventilation) should be employed into a circuit. Furthermore it is suggested that all biological systems change or adjust their response to external loading and such changes may be undesirable (Butler et al 1986).

It is apparent that the Salford valve offers considerably less resistance to breathing that the other two systems employed in the studies described in Chapter 6. At a rate of 30 $l.min^{-1}$, the mean value for the patients performing a maximal test with the Oxylog and Hans Rudolph equipment (6.8), the resistance increases from just 0.55 cmH_2O to 1.00 cmH_2O to 2.10 cmH_2O using the Salford valve, the Oxylog and the Oxylog with the Hans Rudolph respectively. It can therefore be concluded that for both the final study reported in Chapter 6 (validation of the Oxylog, 6.8) the Oxylog and the Hans Rudolph valves have increased resistance to breathing for the patients. This increase is in the order of 300% compared to the Salford valve.

The initial group of healthy volunteers (6.5) and patients (6.6) employing the mask experienced a small but consistently increased resistance to breathing with the Oxylog as compared to the Salford valve. A zero difference falls outside the 95% confidence interval for the vertical

distance between the two slopes. This indicates that the vertical distance between the slopes is statistically significant at the 5% level (Gardner & Altman 1989). However it remains to be judged whether or not this difference is clinically significant. McGregor & Becklake (1961) demonstrated that resistance breathing (incorporating lengths of 5 mm tubing into the breathing circuit) in normal subjects (n=5) consistently increased the $\dot{V}O_2$ and decreased $\dot{V}E$ in 4 out of 5 subjects. The resistance to breathing is likely to be lower for this present study but the principle remains, increasing the resistance to breathing increases the demand for oxygen but depresses ventilation. A theoretical model proposed by Macintyre and Leatherman (1989) suggest that impedance changes (resistive breathing or disease state) result in a rise in total energy demand, since an increase in muscle stimulation is required to maintain a level of ventilation.

The second comparison of this present study revealed that the Oxylog (with Hans Rudolph valve) had a markedly higher resistance to flow than the Salford valve. This discrepancy increases with increasing levels of ventilation. It is apparent that there is considerable resistance to inspiration in the Oxylog system. At 100 $l.min^{-1}$ the resistance of the Oxylog with Hans Rudolph valve was 5.5 cmH_2O exceeding the WHO recommendations (5 cmH_2O at 300 $l.min^{-1}$). It is therefore reasonable to suggest that the resistance of the latter is clinically significant. The value found for the Salford valve in the present study was similar to that reported by Jakeman and Davies (1979). The manufacturer's measured resistance of the Hans Rudolph valve is 4.1 cmH_2O at 150 $l.min^{-1}$, potentially exceeding the WHO guidelines. Connected in series, the Hans Rudolph and Oxylog valve presented a series of differing diameters to the flow of air. The Hans Rudolph valve was considerably narrower than the Oxylog valve. These variable diameters create turbulence which probably accounts for some of the

resistance. The right-angled bend in the flow of air to the mouthpiece compounds the problem of resistance in a narrow bore tube. The clearly reported increased resistance to breathing measured with the Oxylog valve compared to the Salford valve would theoretically result in a disparity of the oxygen consumption with increasing levels of ventilation. The results documented infact show the reverse. Unfortunately the measurements made reveal no alternative mechanism and there appears to be no ready explanation for the disparity.

The majority of muscular work required for breathing is performed during inspiration, even in patients with CAL (Rochester et al 1979). Therefore the inspiratory muscles are at risk of developing fatigue. If a load is of sufficient magnitude it will result in changes in the muscles' ability to generate force and move the required minute ventilation (Macintyre & Leatherman 1989). It is proposed that respiratory muscle fatigue may represent a 2limiting factor in exercise tolerance (Pardy et al 1981, Fitting 1991) in patients with CAL. Fitting (1991) suggest two reasons for these observations. Patients with CAL have two ways of increasing their ventilation during exercise. Firstly to breathe at higher lung volumes increases the maximum expiratory flow, however this further mechanically disadvantages the inspiratory muscles. The alternative is to prolong expiration to enhance lung emptying. This results in a shortened time for inspiration requiring the inspiratory muscles to contract with an increased velocity. If breathing equipment offers a considerable resistance to inspiration it is apparent that the inspiratory muscles are disadvantaged further and are consequently severely limited in their ventilatory response to exercise. The oxygen cost per litre of ventilation increases with both increasing levels of ventilation and external resistance. Consequently a greater proportion of oxygen is consumed by respiratory muscles. A point is reached when any increase in oxygen

uptake is accounted for by the demands of the respiratory muscles (Collett et al 1985). In patients with CAL the total resistance to breathing is a combination of the external resistance of the equipment employed and the intrinsic resistance of the airways. The added external resistance may be just enough to jeopardise a patient's ability to maintain adequate ventilation, effectively disrupting the already compromised flow volume relationship.

The results of the study of maximal performance in patients with CAL (6.9) are surprising when taking into account the added resistance of the Oxylog and Hans Rudolph system. Overall treadmill exercise performance has not been impaired; there was no significant difference between the Oxylog and Douglas bag trial in total time on treadmill, maximal heat rate or Borg score. However, there was a significantly lower maximal $\dot{V}_E$ but not $\dot{V}O_2$ recorded with the Oxylog. In contrast to the previous studies (6.5 to 6.7), the final study (6.8) demonstrated an underestimation of $\dot{V}O_2$ measured using the Oxylog and Hans Rudolph valve compared to the Salford valve but an underestimation of ventilation was again recorded (6.8). This may be due to considerable leaking of the equipment around the mouthpiece causing a decrease in the calculated $\dot{V}O_2$ [see equation (6.2)] or alternatively a genuine decrease in ventilation because the increased resistance of the equipment inhibits the performance of the inspiratory muscles. This demand for O_2 is met despite the low levels of ventilation.

At a given alveolar ventilation an increase in the resistance to breathing will reduce the amount of oxygen available for non-ventilatory work. This is usually compensated for by an increase in ventilation, but if this resistance increases (airways obstruction, external resistance) performance may be impaired (Collett et al 1985). The problems of the increased resistance of the

equipment described are compounded by the additional dead space. As dead space increases alveolar ventilation decreases (for a constant level of ventilation), ie alveolar hypoventilation. The addition of dead space increases end tidal CO_2, therefore the normal response is to increase the levels of ventilation to maintain $PaCO_2$. In patients with CAL dead space is already increased (V/Q mismatch), however ventilation is increased to maintain or even increase alveolar ventilation (Cherniak 1977), although the magnitude of increase of dead space required to provoke this ventilatory response remains uncertain. Recently, Sridhar et al (1993) demonstrated that the addition of a large dead space (500 ml) resulted in a fall in exercise duration and $\dot{V}O_{2\,peak}$ but no significant changes in $\dot{V}E$.

In this study the healthy subjects and the patients were required to increase their level of ventilation to maintain alveolar ventilation and a stable $PaCO_2$ (blood gas levels were not measured) with increasing levels of exercise. The level of ventilation did not appear to even increase with the system incorporating the largest dead space and is not therefore a contributory factor to the discrepancies in ventilatory measurements between the Oxylog and Douglas bags.

Despite the resistance to breathing encountered with the Oxylog and Hans Rudolph system, the option was pursued for use in the field, primarily because of the practical advantages over the Douglas bags. The mouthpiece was used in preference to the face mask because of the initial problems encountered ensuring a seal. An adequate seal could not be guaranteed with patients despite a variety of mask sizes. The measurement of central importance was $\dot{V}O_{2\,peak}$ and it appeared this measurement by the Oxylog and Hans Rudolph valve was not significantly different from the Douglas bag measurement.

7. THE PHYSIOLOGICAL RESPONSE TO THE SHUTTLE WALKING TEST

7.1 INTRODUCTION

Having examined both the reproducibility (Chapter 4) and the validity (Chapter 5) of the shuttle walking test, the next stage was to examine the physiological responses during and upon completion of the shuttle walking test. To measure the ventilatory response we employed the portable system for measuring $\dot{V}O_2$, the Oxylog (the validity of which had previously been examined Chapter 6).

The aim of this study was firstly to confirm that the shuttle walking test was an incremental exercise test that provoked a graded cardio-vascular and respiratory response to a symptom limited maximum performance. Secondly the data collected would help in understanding the limitation to exercise. There is little information available regarding patients' physiological response to field exercise tests and this is important when examining the limitations to exercise. The majority of data relates to maximal values (McGavin et al 1976, Swinburn et al 1985) and little to the physiological responses during field exercise testing. The limitation to this category of information is a practical one relating to the collection of expired air and heart rate data whilst the patient is moving. The present study attempts to overcome these difficulties by using the Oxylog and the Sports Tester to make ambulatory measurements of heart rate and ventilatory function.

The hypothesis of this study was that the shuttle walking test evoked not only a graded heart rate response but also graded respiratory and metabolic responses.

7.2 METHOD

7.2.1 Patient group

Ten patients were recruited from medical out-patients

clinics. Informed consent was obtained. The selection of patients conformed to the criteria described in Chapter 4 (4.2.2). The patients were required to make three visits to Glenfield Hospital at intervals of one week. The patients, as previously, were requested to withhold relevant medication (4.2.2) and the baseline measurements were as described (4.4.2) for all three visits. Visit one was a familiarisation visit, whilst visits two and three were presented in a random balanced design of a shuttle walk with the Oxylog followed one week later by a shuttle walk without the Oxylog but with pre- and post-exercise capillary blood sample collection for blood lactate concentration analysis. The patients were clinically stable throughout the study.

7.2.2 Familiarisation visit

This first visit allowed the patients to perform a practice shuttle walking test conforming to the previously established protocol (4.2.1.). Heart rate was monitored using the Sports Tester PE3000 (3.1.5) and the Borg breathlessness scale (3.1.6) recorded upon the completion of the shuttle walking test.

7.2.3 The shuttle walking test with the Oxylog

The patients performed a second shuttle walking test (4.2.1) and measurements were made as above (4.2.2). To allow ventilatory measurements the patients were required to carry the Oxylog and the Squirrel data logger (6.2 & 6.4). Unlike the study validating the measurements of the Oxylog (Chapter 6) the patients were required to carry the equipment in a backpack. A backpack (Karrimore), was purchased especially for the study. This was a small backpack that was rested upon the patients thoracic spine, which was considered to be the optimal weight bearing position causing least influence upon the posture of the subject and minimising the effect upon the patients' respiratory pattern. The Oxylog rested in the main

compartment of the backpack while the Squirrel was placed in the outside zipped pocket to allow ease of access to co-ordinate the data recordings with the Oxylog. A hole was cut in the bottom of the backpack to communicate with the expired air port of the Oxylog. Besides carrying the backpack the patients wore the head harness and mouthpiece with tubing connected to the Oxylog and a nose-clip (Chapter 6).

To take the resting measurements values the patients were required to rest (seated) for 4 minutes after the initial values were displayed and the values recorded at the end of the fourth minute were taken to represent resting steady state $\dot{V}_I$ and $\dot{V}o_2$. Heart rate and the Borg scale was also recorded.

The procedure for the test was as described (4.2.2) but meticulous timing was required to co-ordinate the timing of the shuttle walking test with the recording made by the Oxylog. The instructions to the patient were played while they were resting. The four second countdown signal immediately before the triple bleep on the tape was located and the tape stopped after one of the bleeps ie, leaving three seconds before the start of the test. After the 4 minute rest period the patient was positioned for the start of the shuttle test. A stopwatch that had been previously co-ordinated with the time on the Squirrel was used to indicate when the shuttle test tape should begin ie, at x mins and 57 seconds (allowing for the three bleeps remaining of the 4 second countdown), synchronising the recordings of the Squirrel and the Oxylog with the shuttle walking test minute increments.

7.2.3 The shuttle walking test and the collection of capillary blood samples.

The patients performed a routine shuttle walking test (4.2.1) independent of any equipment. The only variation

was the collection of a capillary blood sample pre- and 4 minutes post-exercise.

7.2.4 Capillary blood sampling

Duplicate 20 μl arterialised capillary blood samples were taken from the thumb or index finger using a sterile blood lancet (Baxter Scientific Instruments). The collections were made in 20 μl non-heparinised calibrated micro-pipettes (Boehringer Mannheim). The samples were deproteinised in 200 μl of 2.5% perchloric acid. As a precaution to ensure a free flow of blood and minimise patient discomfort the hand was soaked in warm water for 2 mins and dried thoroughly prior to sampling. The samples were stored at -20°C and assays to determine blood lactate concentration were performed on the supernatant at a later date. The assay method adopted used the fluorometric enzymatic micro technique described by Maughan (1982) (Appendix F).

7.3 RESULTS

The trial taking small blood samples is designated as the lactate trial and the alternative the Oxylog trial.

The patients coped with the Oxylog and backpack satisfactorily but consistently reported that it had inhibited their performance.

The mean FEV_1 of the group and their percentage of predicted values indicate that they were patients severely affected by their airways disease. Five of the patients had FEV_1 values below 40% predicted falling to as low as 20%. The patients' spirometry and other physical characteristics are summarised in Table 7.1. There were no significant changes in lung function values (FEV_1, FVC) throughout the study. Again only a modest correlation was established

TABLE 7.1 Some physical characteristics of the patient group, mean (SD), n = 10.
6 males, 4 females.

	lactate trial	Oxylog trial
Age (yr)	64.4 (7.1)	-
Height(m)	-	1.65 (0.07)
Weight(Kg)	-	69.9 (15.3)
FEV_1 (l)	1.02 (0.38)	1.01 (0.37)
FEV_1 % predicted	40.5 (15.1)	40.1 (14.7)
FVC (l)	2.06 (0.49)	2.06 (0.55)

between FEV_1 values and the distance walked (Oxylog trial), r=0.31.

Examination of the CRDQ revealed that there was no between trial difference of the scoring using the Guyatt et al (1987) analysis. Statistical analysis confirmed the patients emotional/psychological stability.

The mean distances that the patients walked on the Oxylog and lactate trial was 302 (133)m and 375 (137)m respectively. The mean difference and 95% confidence interval and relationship between the Oxylog and lactate trials was 73(32.2)m 95% CI 49.9m to 96.1m, r=0.97. The range of distance that the patient walked (60 - 580 m) represents one level and three shuttles to 8 levels and 8 shuttles. The relationship between the distances walked on all three trials was strong. Figure 7.1 demonstrates the relationship between walk two and three. The decrease in distance walked observed when patients carried the Oxylog is apparent in all the patients. The mean decrease in distance in the male subjects was 76.6 m and 67.5 m in the females.

Analysis revealed no difference in heart rate between the lactate and Oxylog (mean maximal heart rate lactate trial 120 (11) and Oxylog trial 117 (10) $beat.min^{-1}$). The maximal heart rate had a moderate relationship with the distance walked on the two trials, r=0.56 and r=0.50. As reported in previous chapters (4 & 5) there was an overall linear increase in heart rate during the two trials.

The mean resting and post exercise Borg breathlessness scores are shown in Table 7.2.

The mean resting $\dot{V}_I$ and $\dot{V}O_2$ are in Table 7.3, and are expressed at B.T.P.S for the ventilatory measurements and S.T.P.D for the $\dot{V}O_2$ recordings. The measurement of $\dot{V}O_2$

FIGURE 7.1 Relationship between the distance(m) walked on the lactate and Oxylog trials.

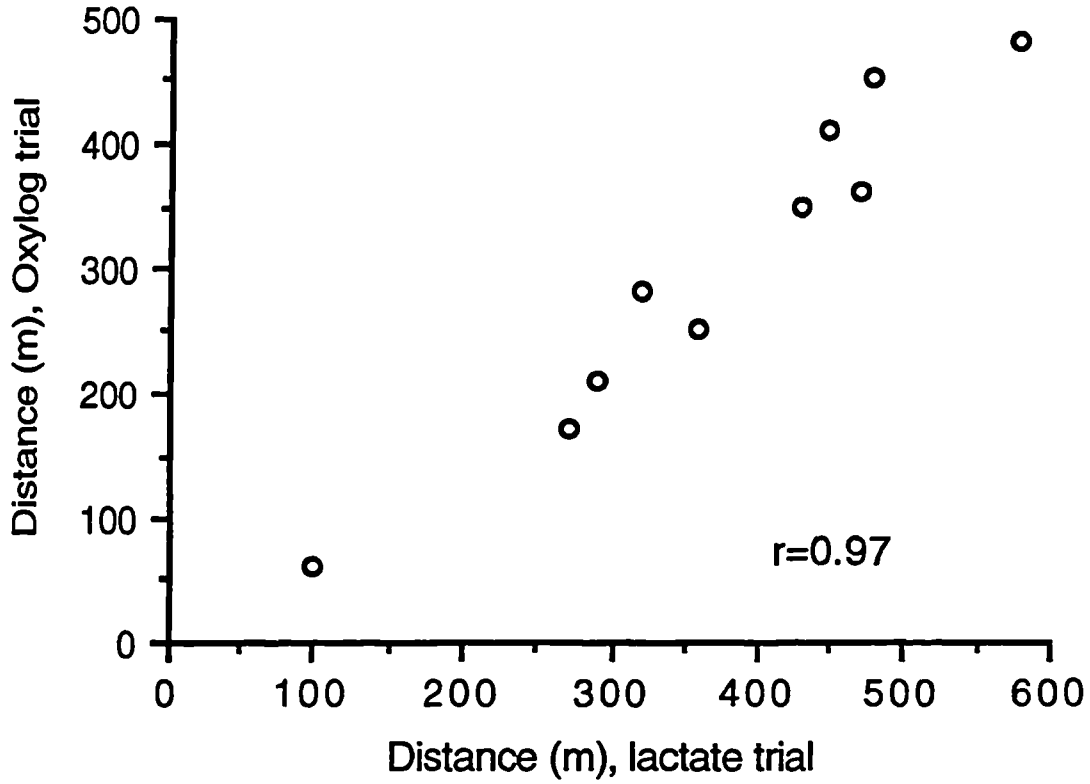


TABLE 7.2 Mean (SD) Borg breathless score at rest and post-exercise.

Trial	Resting score	post exercise score
lactate	1.7 (0.3)	5.5 (0.8)
Oxylog	1.7 (0.3)	5.1 (0.6)

TABLE 7.3 Mean (SD) resting values of ventilation (l.min $^{-1}$) and $\dot{V}O_2$ (ml.min^{-1}.kg^{-1}).

Measurement	Mean (SD)
$\dot{V}_I$ (l.min^{-1}) ATP	7.9 (1.9)
BTPS	9.8 (2.6)
$\dot{V}O_2$ (l.min^{-1}) STPD	0.19 (0.02)
$\dot{V}O_2$ (ml.min^{-1}.kg^{-1})	2.82 (0.61)

expressed as $ml.min^{-1}.kg^{-1}$ do not take into account the weight of the Oxylog (2070 g). This would however make very little difference to the overall values of oxygen consumption.

The corresponding mean maximal exercise values are in Table 7.4. Each patient demonstrated a gradual increase in $\dot{V}_I$ and $\dot{V}O_2$. A linear increase in $\dot{V}O_2$ was demonstrated in each patient with increasing intensity of exercise with progressive levels of the shuttle walking test. Figure 7.2 shows the linear increase of $\dot{V}O_2$ in two representative patients. Patient A demonstrates an increase of 580% from resting values (0.22 $l.min^{-1}$) to a $\dot{V}O_{2\,peak}$ of 1.50 $l.min^{-1}$. The second patient demonstrates an increase of 273%, (0.17 - 0.65 $l.min^{-1}$). The increase in $\dot{V}O_2$ that patients were able to achieve their $\dot{V}O_2$ from their resting values ranged from 127% to 572%. A corresponding linear increase in $\dot{V}_I$ was demonstrated in consecutive levels of the shuttle walking test (Fig 7.3). Such pronounced percentage increases were however not documented, the greatest increase was in patient 5, rising from a resting $\dot{V}_I$ of 12 $l.min^{-1}$ to peak exercise of 46 $l.min^{-1}$ (ATP). Two patients 9 and 10 only increased their $\dot{V}_I$ by 100%. These individuals did also record the lowest FEV_1 values. The mean values of $\dot{V}_I$ and $\dot{V}O_2$ at each level of the shuttle walking test are shown in Figure 7.4 and 7.5 (it should be noted that the number of patients at each level decreases). Figure 7.6 is constructed from plotting the predicted maximal $\dot{V}_E$ (employing the formula 37.5 x FEV_1) against measured $\dot{V}_I$. The maximal $\dot{V}_I$ ranging from just 30% to 97% of predicted (mean 69%). This formula utilises volumes at B.T.P.S, therefore the ventilatory volumes of the Oxylog were manipulated by a conversion factor (Cotes 1979). This increases the mean maximal $\dot{V}_I$ to 24.9 $l.min^{-1}$ (it should be noted that a conversion to $\dot{V}_E$ to allow an entirely legitimate comparison of predicted versus actual $\dot{V}_E$ is not possible with the Oxylog system as expired CO_2 which would allow the values of $\dot{V}_I$ to be subjected to the Haldane transformation is not

TABLE 7.4 Mean (SD) maximal values of ventilation ($l.min^{-1}$) and $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$).

Measurement		Mean (SD)
$\dot{V}_I$ ($l.min^{-1}$)	ATP	20.4 (7.9)
	BTPS	24.9 (9.5)
$\dot{V}O_2$ ($l.min^{-1}$)	STPD	0.74 (0.42)
$\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$)		10.14 (3.90)

FIGURE 7.2 Oxygen consumption response ($ml.min^{-1}.kg^{-1}$) to the shuttle walking test in two representative patients.

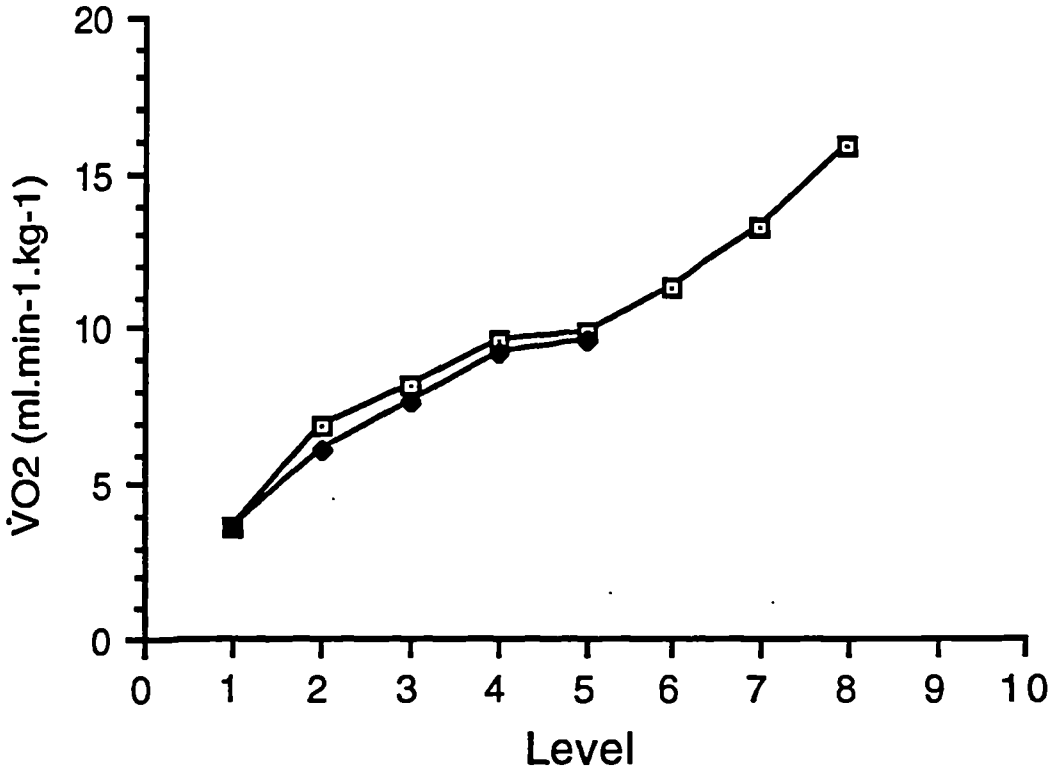


FIGURE 7.3 Ventilatory response ($l.min^{-1}$) to the shuttle walking test in two representative patients.

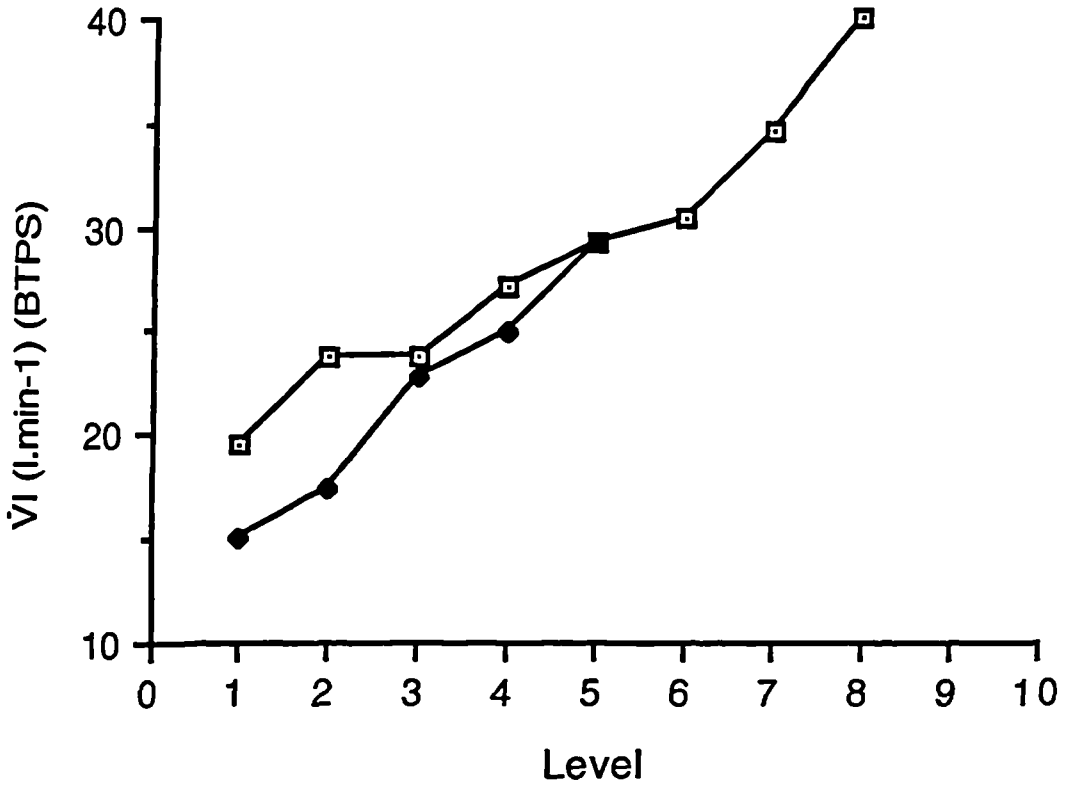


FIGURE 7.4 Mean (SEM) ventilatory response ($l.min^{-1}$) to consecutive levels of the shuttle walking test.

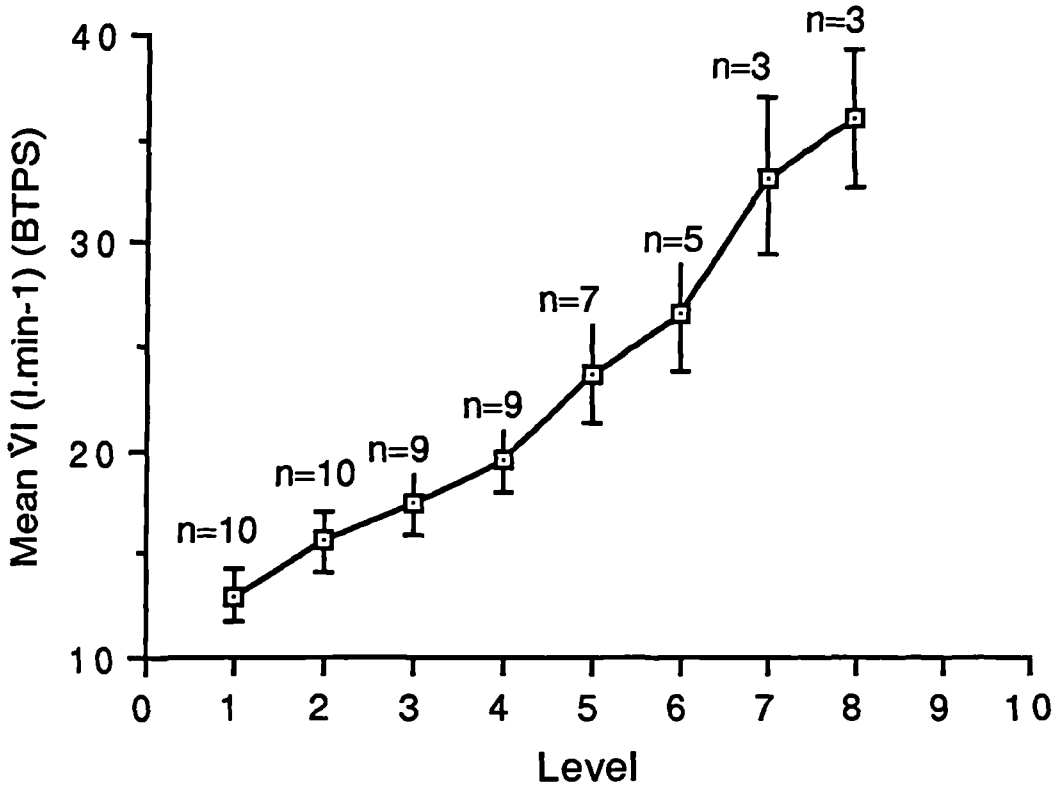


FIGURE 7.5 Mean (SEM) oxygen requirements ($ml.min^{-1}.kg^{-1}$) to consecutive levels of the shuttle walking test.

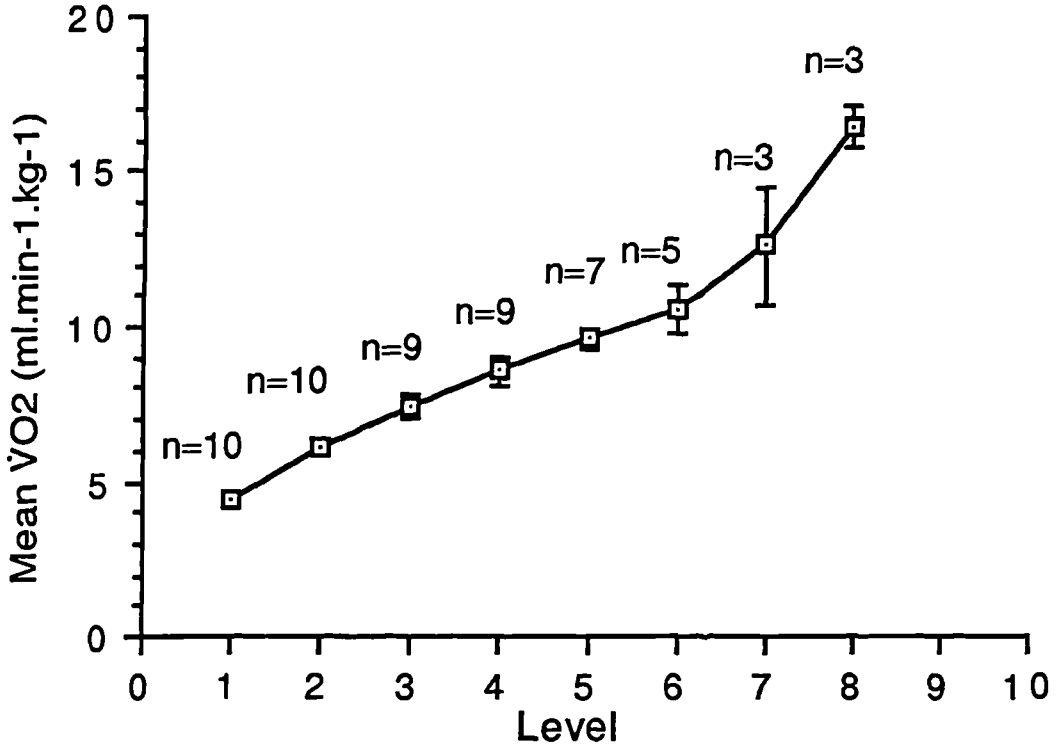
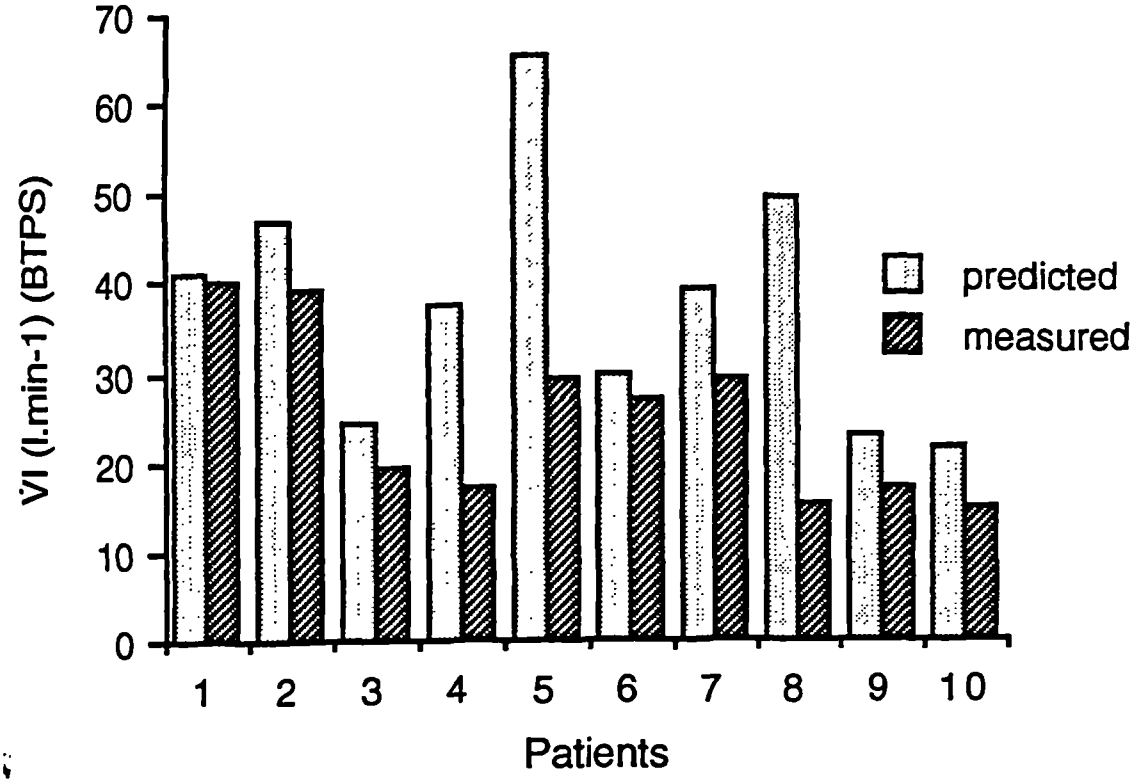


FIGURE 7.6 Predicted $\dot{V}E_{max}$ ($l.min^{-1}$) plotted against measured $\dot{V}I_{max}$ using the Oxylog for the individual patients.



recorded). With this limitation as well as the previously documented underestimation of the Oxylog system (Chapter 6) it is possible that the values presented do in fact underestimate the 'true' maximal ventilation attained during the shuttle walking test.

There was no strong relationship between the percentage of $\dot{V}_I$ attained and the patient's FEV_1 (r= 0.44). The mean resting $\dot{V}_I$ was 9.85 $l.min^{-1}$ (BTPS); patients increased their level of ventilation from their resting values by values ranging from 92% to 208%. The relationship between the maximal $\dot{V}_I$ and the distance attained on that shuttle walking test was moderate (r=0.76). There was however a stronger relationship between the patients' peak $\dot{V}O_2$ and the shuttle distance recorded, r=0.81, Figure 7.7. Employing the regression equation proposed by Bruce et al (1973) to predict $\dot{V}O_{2\,peak}$ Figure 7.8 was constructed to plot the predicted against the measured $\dot{V}O_2$.

Analysis of the blood lactate concentrations pre (mean 1.38 $mmol.l^{-1}$ SD 0.24) and post (1.69 $mmol.l^{-1}$ SD 0.19) shuttle walking test are shown in Figure 7.9. The mean increase (and 95% confidence interval) was significant, ie 0.31 $mmol.l^{-1}$ (0.06 to 0.56).

Figure 7.10 shows the values of $\dot{V}O_2$ measured directly from the Oxylog during the shuttle walk and those values assigned to the performance of the shuttle walking test from the Douglas bag measurements (chapter 5)

FIGURE 7.7 Maximal $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) measured with the Oxylog against performance [distance walked (m)] on the shuttle walking test. n=10.

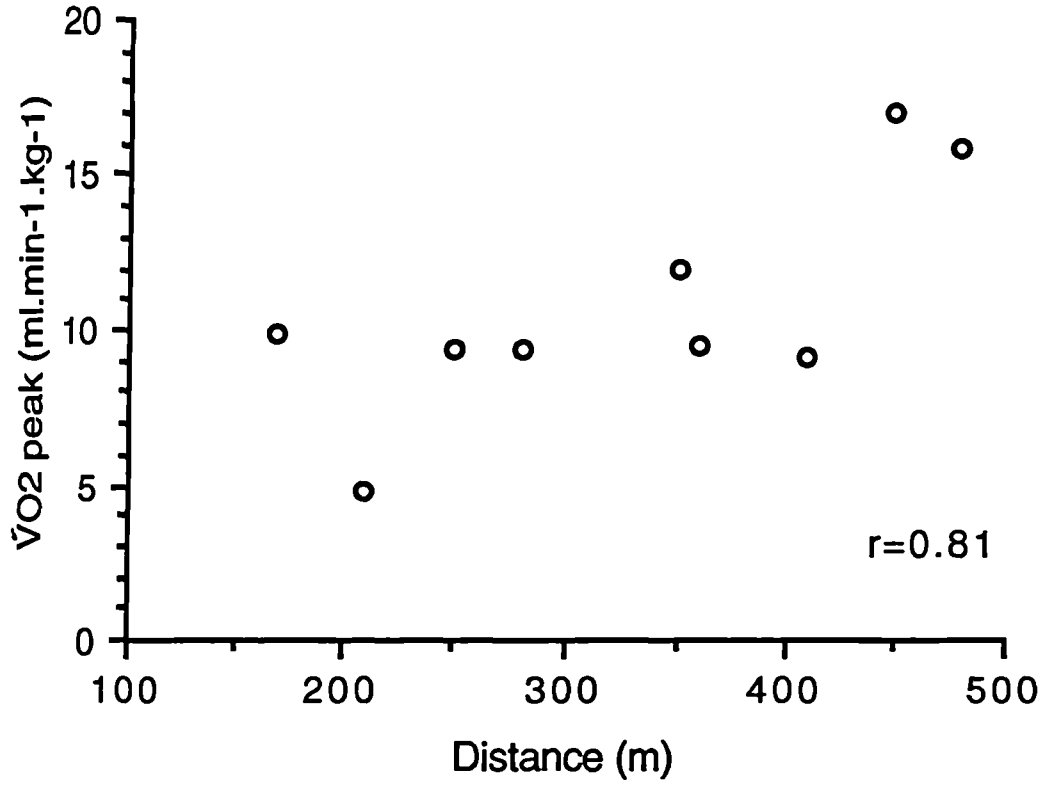


FIGURE 7.8 Predicted $\dot{V}o_{2\,max}$ ($ml.min^{-1}.kg^{-1}$) plotted against measured $\dot{V}o_{2\,peak}$ using the Oxylog for the individual patients.

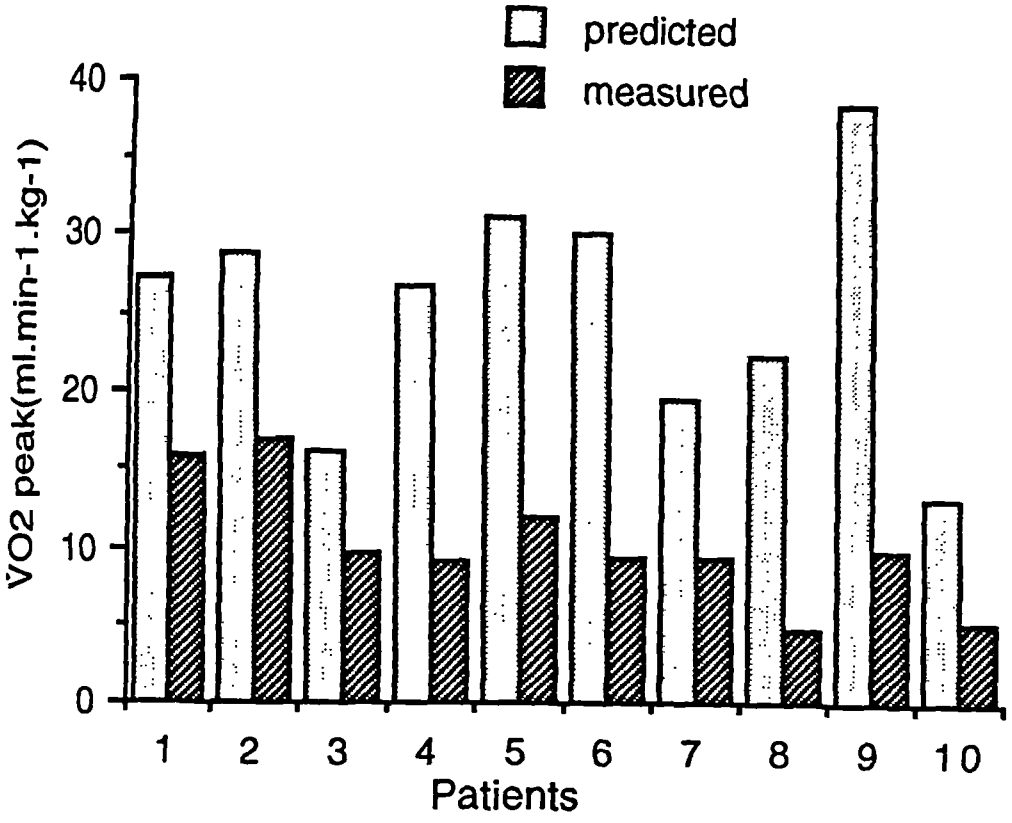


FIGURE 7.9 Mean (SEM) pre and post exercise capillary blood lactate concentrations ($mmol.l^{-1}$)

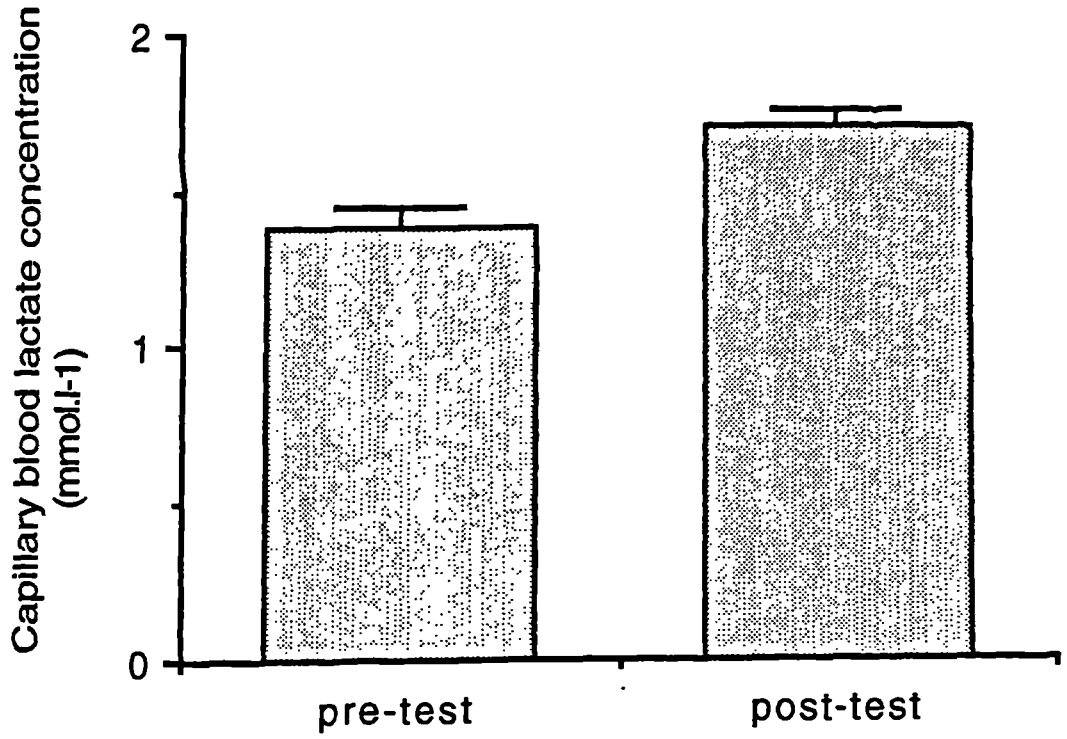
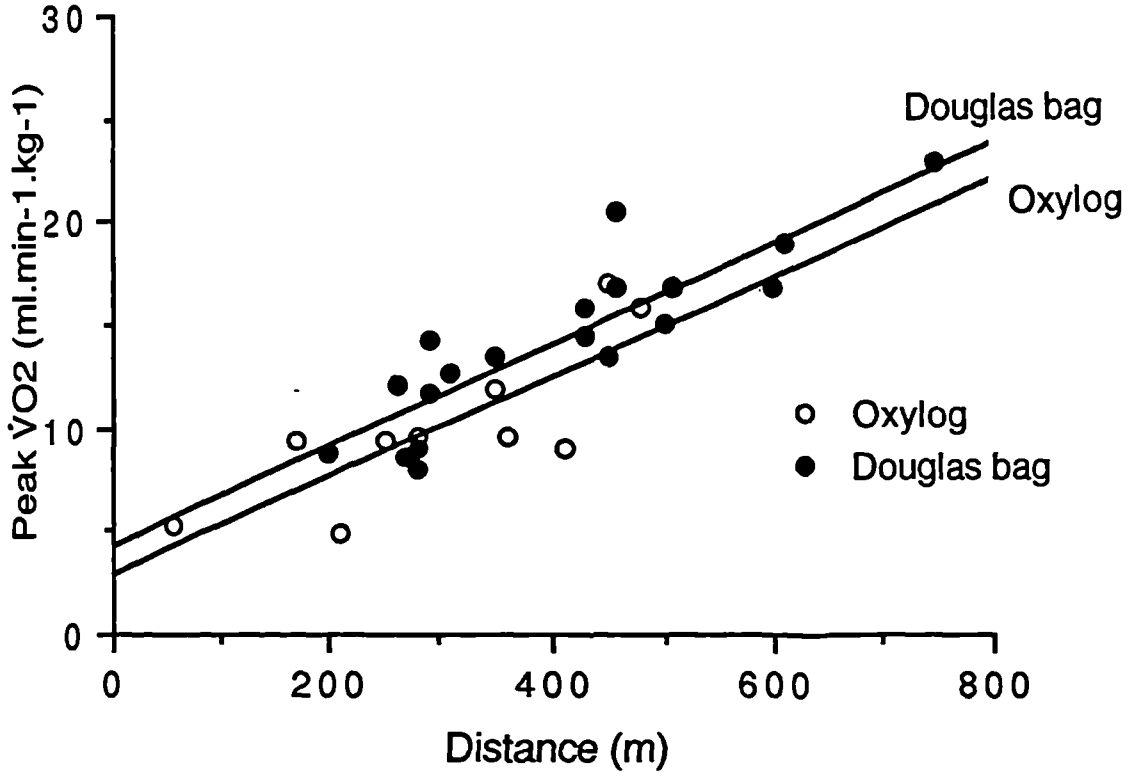


FIGURE 7.10 Values of peak $\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$) measured from the Oxylog during the shuttle walking test and those from the comparison of performance and $\dot{V}O_{2\,peak}$ measured with Douglas bag techniques (Chapter 5).



7.4 DISCUSSION

The group of patients recruited for this study demonstrated a mean FEV_1 of just 1.0 l. Half of the group conformed to the 'severe airways disease category' criteria proposed by the ATS (1986). The patients' clinical and psychological/emotional stability during the period of observation was confirmed with the results of the spirometry and the CRDQ respectively. All patients completed the trial satisfactorily but frequently commented on the weight and general unacceptability of exercising to maximal levels whilst supporting the Oxylog. The issue of the suitability of the Oxylog for this stage of the study was addressed critically. Acknowledging the imprecision of the Oxylog identified in Chapter 6 (with particular reference to the measurement of $\dot{V}_E$) it was felt that this system was preferable to a series of smaller Douglas bags mounted on a back pack. This method would cause considerable disruption to the patients' rhythm if manual intervention was regularly required to collect the expired air and change the bags. The primary physiological marker adopted was the $\dot{V}O_2$, this was shown in Chapter 6 not to be significantly different to the Douglas bag measurements [despite the high resistance to breathing of the Oxylog system incorporating the Hans Rudolph valve (6.9)].

The relationship between the distance walked for the three shuttle tests remained very strong following the results documented in Chapter 4 and 5. Patients attained a similar maximal heart rate on the two trials. The patients managed to walk to a similar degree of physiological stress during the shuttle walk with the Oxylog. The added weight of the Oxylog manifest its effect in decreasing the patients' overall performance. Nevertheless this effect appeared to be systematic and a strong relationship was maintained with the lactate trial (r=0.97).

The maximal heart rate achieved represented 64 - 84% of

predicted. Clearly each of these patients maintained a cardiac reserve. These findings are consistent with a ventilatory limit to functional capacity. The absolute values are consistent with Spiro et al (1975) and Jones et al (1971) in clinically similar groups.

The difficulties with the Oxylog measurements of $\dot{V}_I$ and $\dot{V}O_2$ were documented in Chapter 6; the measurements of $\dot{V}O_2$ do not differ significantly from the 'gold standard' measurements (Douglas bag) but the values of $\dot{V}_I$ reported must be viewed cautiously as the Oxylog and mouthpiece system underestimate volume. This loss of volume, although reducing the overall values for $\dot{V}O_2$ probably does not distort the value in an important way. The linear increase of $\dot{V}O_2$ measured during the shuttle walking test is consistent with the pattern observed during the treadmill test in a similar group of patients (Chapter 5).

In this group of patients there was a 29% variation in the resting $\dot{V}O_2$ and is consistent with the reports of McNeill et al (1987). This variation increased with the increasing intensity of the exercise. In 'normal' subjects the measurement of individual $\dot{V}O_2$ is highly reproducible with a variation of some 7% amongst subjects at any particular walking speed (ACSM 1991, McArdle et al 1991). During the first five levels of the shuttle walking test in patients this discrepancy rose to 37% (level 5). This variation shows that the O_2 cost of comparable exercise varies considerably amongst patients, and that this variation is markedly greater than amongst normal subjects.

The mean $\dot{V}_I$ resting value of 9.85 $l.min^{-1}$ (BTPS) was higher than normal resting values but was considerably lower than the values documented by Matthews et al (1989) in a clinically less severe group and Kirsch and colleagues (1989) in a clinically similar group. The mean resting $\dot{V}O_2$ was again lower than the values cited by the authors above.

It is feasible that the documented ventilatory measurements using the Oxylog are lower than the true $\dot{V}_I$ (the reader is referred to Chapter 6), however the equipment is secure and the patients pursed their lips around the mouthpiece to prevent leakage. The mean maximal values of $\dot{V}_I$ (24.9 $l.min^{-1}$) represent a mean of 69% predicted. The equation employed for this stage of the study was that reported by Carter et al 1987. The present study group closely resembled (FEV_1 values) the group Carter et al (1987) recruited to examine the most useful predictor of $\dot{V}_{E\ max}$ in patients with CAL. The absolute values (STPD) are marginally lower than those quoted by ZuWallack et al (1991), Swinburn et al (1985) and Cotes (1982) in clinically similar groups (judged on the FEV_1 values) and, although useful, a percentage predicted value is often not reported to allow comparison. Overall, the groups cited above appeared to work to similar levels as judged by heart rate response, but as reported in chapter 6 no firm conclusions can be drawn as a variety of test equipment and protocols were employed.

A broad trend of response to exercise response in patients with CAL can be nevertheless observed. Compared to the work of Jones et al (1971) the values reported in the present study are considerably lower for $\dot{V}_{E\ max}$. This may be an artefact of protocol variation or the difference may in fact be due to the Oxylog failing to detect the patients total inspired volume misrepresenting measurements of $\dot{V}_I$. A small additional increase in $\dot{V}_I$ may be accounted for by the variation in the R value at maximal exercise (Oxylog assumes an R value of 1). Two patients exceeded 90% of their predicted $\dot{V}_{E\ max}$, a further two exceeded 80% and another two exceeded 70%. Three patients failed to reach 50% predicted $\dot{V}_{E\ max}$, despite reporting that breathlessness was the limiting factor (Borg scores of 7, 4 and 5). These three patients reached 69, 82 and 63% of predicted maximal heart rate. This low value of $\dot{V}_I$ can in part be accounted for by a lack of motivation in patient 8. Patient 4,

exercising to a Borg score of 7 possibly, has an increased awareness to the sensation of dyspnoea limiting his exercise performance prior to attaining a defined physiological limit. Six of the remaining seven patients reached a maximal $\dot{V}_I$ in excess of 74% predicted. These patients would be approaching a ventilatory limit to functional capacity, consistently reporting breathlessness post-exercise. In view of the results of Chapter 6 it is probable that the maximal $\dot{V}_I$ is underestimated. It is therefore likely that these patients reached a higher maximal $\dot{V}_I$ than these figures suggest, approximating predicted $\dot{V}_{E\ max}$. These values of maximal $\dot{V}_I$ and the assumption of underestimation together suggest that this group of patients reached a true ventilatory limit to exercise. Unfortunately it is not possible to substantiate this comment although the data in Chapter 6 would go some way to supporting this.

The mean value of $\dot{V}O_{2\ peak}$ reported is consistent with that anticipated for a group of severely affected patients. The values are slightly lower than other published data but similar to the values quoted by Swinburn et al (1985) who coincidentally employed the Oxylog. The strong relationship between distance walked and the $\dot{V}O_{2\ peak}$ supports the data reported in Chapter 5. This correlation coefficient is similar to that documented in Chapter 5.

Seven of the patients who participated in this study also completed the study reported in Chapter 5. A $\dot{V}O_{2\ peak}$ measurement was obtained both directly from the shuttle walking test using the Oxylog and indirectly comparing the relationship between performance on the shuttle walking test and the measurement of $\dot{V}O_{2\ peak}$ from a conventional treadmill test. The mean $\dot{V}O_{2\ peak}$ measured in this group of seven patients was 12.9 (3.6) $ml.min^{-1}.kg^{-1}$ during the treadmill test and 11.1(4.2) $ml.min^{-1}.kg^{-1}$ for the shuttle walking test. These two values were strongly related

(rho=0.86) are were not significantly different (mean difference, 1.8 $ml.min^{-1}.kg^{-1}$, 95% CI -0.9 to 4.5). The relationship between the maximal values of ventilation were less strongly related (rho=0.29) but not significantly different. These results suggest that the shuttle test does in fact provoke a symptom limited maximal performance in a similar manner to the conventional treadmill test. The Borg score for these patients in the two studies was not significantly different.

Examining the physiological responses and the Borg scale it is proposed that the shuttle walking test provides an incremental exercise test that provoked a symptom limited maximum performance, and in line with recent work published it appears that not all patients with CAL terminate exercise testing due to the limitations imposed by their respiratory system (Rampulla et al 1992).

The increase in blood lactate concentration was small but significant ($p<0.05$). The mean maximal value of 1.69 $mmol.l^{-1}$ is not consistent with the patients reaching an anaerobic threshold, nor is the accumulation of lactate the likely explanation for the cessation of exercise. This study incorporated patients with severe airways disease and it is well documented that in these patients a lactate accumulation/anaerobic threshold is not commonly identified. Spiro et al (1975) documented a mean maximal lactate concentration of 2.56 $mmol.l^{-1}$ in agreement with the suggestion that these patients do not experience high rates of anaerobic glycolysis in skeletal muscle during exercise. Authors who consistently identify an anaerobic threshold in patients with CAL acknowledge that a group of patients exists with severe airways disease that do not manifest a lactate response at maximal exercise (Sue et al 1988). Belman (1986) extends this issue further by proposing that examining the effectiveness of a training programme in patients with moderate to severe CAL using the conventional

indicator of the anaerobic threshold and $\dot{V}O_{2\,peak}$ relationship is inappropriate because peak levels of exercise in this group are often below threshold levels. Kanarek et al (1979) identified a group of patients from gas exchange ratios who did or did not manifest an anaerobic threshold. The group that did not reach this threshold level utilised 74% of their predicted $\dot{V}E_{max}$. This report is consistent with this present study group. Overall the results of the lactate analysis appear to follow the trends previously observed, that is the more severely affected patients appear not to produce a significant lactic acidosis upon maximal exercise, falling well below anticipated levels observed in a young normal population at $\dot{V}O_{2\,peak}$ (> 8 mmol.l^{-1}). The blood lactate concentrations measured in this study are low but this does not mean that the shuttle walking test does not provoke a symptom limited maximal performance in this patient group but that exhaustion is not necessarily associated with high rates of anaerobic glycolysis in the exercising muscle. The shuttle walking test does appear to provide a gradual stimulus to maximally tolerated levels of exercise.

In conclusion it appears that the shuttle walking test provides an objective measure of disability in this patient group which consistent with the data reported in Chapter 5, relates well to an individual's $\dot{V}O_{2\,max}$. Whilst it appears that ventilatory limitation contributes directly to the cessation of exercise the importance of other factors must not be overlooked. The combined use of the Oxylog and the Sports tester confirmed that the shuttle walking test provoked an incremental cardio-vascular and respiratory response to a symptom limited maximum performance.

8. EXAMINATION OF CAPILLARY BLOOD LACTATE CONCENTRATION IN RESPONSE TO THE SHUTTLE WALKING TEST AND A CONVENTIONAL SYMPTOM LIMITED TREADMILL TEST IN PATIENTS WITH CAL

8.1 INTRODUCTION

In the previous chapter low blood lactate concentrations were observed in response to the shuttle walking test. A considerable rise in the concentration of this metabolite (> 8 $mmol.l^{-1}$) in young healthy subjects is taken as one indicator of a maximal performance. However, this magnitude of response is rarely documented in patients with CAL although some increase in this metabolite has been demonstrated (Spiro et al 1975, Elliott et al 1987). In general it appears that the less severely affected patient is capable of mounting a 'lactate' response, whereas the more severely affected exhibit such reduced exercise capacity that a lactate response may not occur.

The aim of this study was to address more rigorously the question 'Does the shuttle walking test provokes a symptom limited maximum performance which is comparable to a conventional treadmill test?' From the data presented in the previous chapters (5 and 7) it would appear to provide a comparable physiological and subjective response. This study examined the metabolic response to both the treadmill test and shuttle walking test in a group of patients who were less severely affected that the group described in Chapter 7, ie is the low lactate response the test or the patient group. An apparently healthy control group was incorporated into the study. They performed an incremental maximal treadmill test to allow comparison of physiological and metabolic responses to maximal exercise with those observed in the patient group.

8.2 METHOD

8.2.1 Patient Group

Ten patients attending out-patients clinics were recruited for this stage of the study. Informed consent was obtained. The selection of patients selected conformed to the criteria described in Chapter 4 (4.2.2). The patients were required to attend Glenfield Hospital on three separate occasions at intervals of one week (to minimise any training effect), during a period of clinical stability. The patients were instructed to withhold relevant medication for three hours prior to testing. The baseline and exercise test measurements were as described in Chapter 4 (4.2.1 & 4.2.2).

8.2.2 Familiarisation visit

This initial visit introduced the two exercise tests (and the associated equipment) to the patient. The patients were required to perform one practice shuttle walk (4.2.1) and one practice treadmill walk. Between each exercise test there was at least a 45 minute rest period to allow complete recovery.

8.2.3 The treadmill test

The treadmill (Cambridge Medical Instruments 3060) was as described in Chapter 5. The gas analysis equipment was an Oxyconbeta (Jaegar Ltd). The Oxyconbeta allows breath by breath measurements incorporating a fast response differential paramagnetic oxygen analyser and a fast infra red carbon dioxide analyser. Expired air is passed down a sample line located in the mouthpiece to the CO_2 and O_2 analysers. $\dot{V}O_2$ and $\dot{V}CO_2$ were expressed in STPD. A bi-directional digital volume sensor (TripleV volume transducer) is incorporated into the mouthpiece to measure ventilatory volume directly (BTPS). This device basically comprises of a vane suspended inside a tube that rotates with the airflow, interrupting light beams from two LEDs.

Two photo-transistors detect these interruptions and transform the flow into a series of electrical signals. The volume displaced between two signals is fixed. The time between the pulses is a measure of flow. Breath by breath and 8 breath average data was computed and stored on disk.

The speed of the treadmill was calibrated at the beginning of the study. The Oxyconbeta system self-calibrates each time the equipment is switched on. Prior to testing, half way through the study and at the end of the study period the equipment was calibrated with calibration gases (of known concentration 5% CO_2 and 95% N_2) and a 3 litre syringe pump to calibrate volume measurements. At each stage the equipment calibrated accurately with no drift from the standard concentrations or volumes.

The performance of the Oxyconbeta was compared to the conventional Douglas bag in two subjects. Two healthy volunteers were recruited to perform identical sub-maximal incremental exercise tests (3 mph at inclinations of 0%, 2.5%, 5% and 7.5%, 4 minutes stages) on the treadmill at Loughborough University for Douglas bag collection and at Glenfield for the Oxyconbeta trial. The results of this comparison showed little variation in the measurements of volume or gas concentrations. The mean difference of all 4 stages for $\dot{V}_E$ (converted to STPD) was 1.5 $l.min^{-1}$ (5.8%) lower with the Oxyconbeta, and for $\dot{V}O_2$ 1.5 $ml.min^{-1}.kg^{-1}$ (10.5%) higher with the Oxyconbeta.

The symptom limited treadmill test was performed at Glenfield General Hospital. The speed of walking on the treadmill was gauged during the first visit from the heart rate response and the reported Borg breathlessness score. The protocol employed was the same as documented in Chapter 5, ie an individualised speed with increases in the gradient from 0% by 2.5% every 2 minutes until the patient indicated they wished to stop. During the test the

patient's heart rate was monitored as described (3.1.5). A pulse oximeter (Ohmeda) with a finger probe was used to monitor saturation during exercise. Both of these pieces of equipment linked directly to the Oxyconbeta system and the results displayed on the computer screen. For the second treadmill visit resting measurements were made with the patient sitting adjacent to the treadmill. Resting measurements were taken for 4 minutes and between minutes 4 and 5 the patient was directed onto the treadmill and the predetermined walking speed secured before the start of the test at the start. Whilst resting and for the second minute of each increment and patients were requested to report on their perceived level of breathlessness using the Borg breathlessness scale (Appendix B).

Duplicate 20 μl arterialised capillary blood samples were taken from the thumb or index finger using a sterile blood lancet (Baxter Scientific Instruments) as described previously (7.4.2) after both the shuttle and treadmill walking test. The samples were stored at -20°C and assays to determine lactate concentration were performed on the supernatant at a later date.

8.2.4 The second and third visit

These were presented to the patients in a randomised balanced design of one shuttle walking test (4.2.1) (shuttle trial) followed one week later by a symptom limited maximum treadmill walking test (treadmill trial).

8.2.5 The control group

Ten healthy hospital employees were recruited. As far as possible these were age and sex matched. These individuals presented with no significant past medical history and with an FEV_1 greater than 80% of predicted. They performed a maximal incremental exercise test on the treadmill. An initial familiarisation visit allowed the operator to gauge an appropriate speed of walking. An estimated $\dot{V}O_{2\,max}$ was

calculated using the equations of Bruce et al (1973) for sedentary men and women. From this value an appropriate walking speed and inclination was determined using the tables presented in the ACSM handbook (1991). The test on the initial visit was sub-maximal. The appropriate intensity of exercise was assessed from the heart rate response and the reported level of exertion and breathlessness of the Borg scales (Appendix B). For the second visit these individuals followed the same protocol as described above (with the resting measurements), although some commenced at an inclination of 2.5% to limit the time of the test. This group of volunteers were also asked to report on both their perceived level of breathlessness and overall exertion for the second of each of the 2 minute increments. Capillary blood samples were collected as described above.

For each maximal exercise test medical cover was provided.

8.3 RESULTS

No patient/volunteer was excluded from the study because of problems with either the protocol or the equipment used. The results of the CRDQ revealed that the patients were psychologically and emotionally stable throughout the study period.

The physical characteristics of the patient group are summarised in Table 8.1. There were no significant differences in the spirometry values recorded for the patients between the three trials. The same variables recorded in the control group are reported in Table 8.2, for just the second (maximal treadmill) visit.

The mean FEV_1/FVC ratio for the patients for the shuttle and treadmill visits was 51.4% and 52.0% indicating overall moderate impairment (range 39.5% to 68.4%).

TABLE 8.1 Some physical characteristics of the patients, Mean (SD). n=10 (6 male, 4 female)

Visit	1	Shuttle	Treadmill
Age (year)	62.6 (7.6)	- -	- -
Weight (kg)	- -	- -	77.27 (14.31)
Height (m)	1.68 (0.07)	- -	- -
FEV_1 (l)	1.25 (0.44)	1.28 (0.45)	1.27 (0.44)
FEV_1 % predicted	44.9 (13.8)	46.2 (14.0)	45.7 (14.2)
FVC (l)	2.46 (0.59)	2.46 (0.59)	2.41 (0.49)

TABLE 8.2 Some physical characteristics of the control group. Mean (SD). n=10 (6 male, 4 female)

	1
Age (yr)	58.1 (2.6)
Weight (kg)	72.46 (14.31)
Height (m)	1.69 (0.09)
FEV_1 (l)	3.06 (0.77)
FEV_1 % predicted	106.8 (18.8)
FVC (l)	4.09 (0.94)

Table 8.3 reports on the mean difference (95% confidence interval) between these variables for the patients treadmill test visit compared to the control group and their statistical significance.

Again there was a poor relationship between FEV_1, FVC and distance completed (r=0.22 and 0.38 respectively) and in the reported Borg score and distance (rho=0.15). The relationship between maximal heart rate and distance was however slightly higher (r=0.45).

The results of the resting measurements taken immediately prior to the treadmill test are presented in Table 8.4 with the mean differences and 95% confidence interval expressed in Table 8.5. The corresponding results from the maximal treadmill test are summarised in Table 8.6 for both the patients and the control group. The mean differences, 95% confidence interval and level of statistical significance is expressed in Table 8.7.

The speed the patients walked at on the treadmill was 2.36(0.65) mph for a duration of 7.6(3.1) minutes. The peak inclination the patients reached was 10%. The control group walked for a mean duration of 9.5(1.3) minutes at a mean speed of 3.89(0.37) mph. The speed the control group walk was significantly greater than the patient group although the mean time walked was not.

The maximal levels of $\dot{V}E$ were presented as a percentage of predicted maximal (Spiro et al 1975) for the patients and represent a range of 62% to 114% of predicted maximum attained with 4 patients exceeding their predicted values. These four patients were not the four most severely disabled patients (judged by spirometry). Two patients had an FEV_1 equal to or greater than 1.3 l. The patient who attained 114% of predicted $\dot{V}E$ had an FEV_1 of 0.75 l. For the control group, the equation proposed by Jones (1988) was

TABLE 8.3 Mean difference and 95% confidence interval between the physical characteristics of the patient and control groups.

	Mean difference (C-P)	95% confidence interval
Age (yr)	-4.5	-1.1 to 10.12
Weight (kg)	-4.81	-20.84 to 11.22
Height (m)	-0.05	-0.08 to 0.06
FEV_1 (l)	1.79 **	2.39 to 1.19
FEV_1 % predicted	61.00 **	42.9 to 79.1
FVC (l)	1.68 **	2.41 to 0.96

SD** significant difference between patients and controls $p<0.001$

TABLE 8.4 Mean (SD) resting results prior to the treadmill test, for both patients and the control group. (Both n=10).

Measurement	Patients Mean (SD)	Controls Mean (SD)
$\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$)	2.85(0.70)	3.13(0.84)
$\dot{V}E$ ($l.min^{-1}$)	10.60(2.66)	8.59(1.71)
Heart rate ($beat.min^{-1}$)	79(9)	81(12)
Oxygen pulse ($ml.beat^{-1}$)	2.69(0.57)	2.56(0.34)
Oxygen saturation (%)	96.6(2.2)	98.5(1.2)
R	0.83(0.06)	0.90(0.06)
V_D/V_T	0.45(0.03)	0.41(0.04)
Blood lactate concentration ($mmol.l^{-1}$)	0.81(0.49)	0.90(0.48)

TABLE 8.5 Mean difference and 95% confidence interval of the resting results prior to the treadmill test between the patients and control group.(Both n=10).

Measurement	Mean differ -ence	95% confidence interval
$\dot{V}O_2$ ($ml.min^{-1}.kg^{-1}$)	0.25	-0.39 to 0.47
$\dot{V}E$ ($l.min^{-1}$)	-2.01	-4.68 to 0.66
Heart rate ($beat.min^{-1}$)	3	-7 to 12
Oxygen pulse ($ml.beat^{-1}$)	-0.13	-0.53 to 0.74
Oxygen saturation (%)	1.9 *	0.4 to 3.4
R	0.07 *	0.00 to 0.14
V_D/V_T	-0.04	-0.1 to 0.03
Blood lactate concentration ($mmol.l^{-1}$)	0.09	-0.34 to 0.53

* Significant difference between controls and patients $p<0.05$

TABLE 8.6 Mean (SD) treadmill performance and ventilatory results from the treadmill test, for the patients and control groups. (both groups n=10).

Measurement	Patients Mean (SD)	Controls Mean (SD)
$\dot{V}O_{2\,peak}$ ($ml.min^{-1}.kg^{-1}$)	17.1(3.4)	26.0(4.7)
% predicted $\dot{V}O_{2\,max}$	68.9(15.4)	96.6(20.7)
$\dot{V}E_{max}$ ($l.min^{-1}$)	40.9(9.4)	57.4(15.3)
% predicted $\dot{V}E_{max}$	93.9(14.8)	97.1(36.5)
Oxygen saturation	91.7(6.9)	95.7(2.3)
R	0.89(0.09)	1.04(0.06)
Heart rate max ($beat.min^{-1}$)	127(16)	158(24)
% predicted max HR	75.1(9.3)	91.1(14.4)
Oxygen pulse ($ml.beat^{-1}$)	10.3(2.8)	11.9(3.5)
V_D/V_T	0.32(0.08)	0.20(0.03)
Blood lactate concentration ($mmol.l^{-1}$)	1.66(0.95)	4.70(2.39)

TABLE 8.7 Mean difference and 95% confidence interval of the maximal results of the treadmill test between the patients and control group.(Both n=10).

Measurement	Mean difference C-P	95% confidence interval
$\dot{V}O_{2\,peak}$ ($ml.min^{-1}.kg^{-1}$)	8.9 *	4.5 to -13.4
% predicted $\dot{V}O_{2\,max}$	27.7 *	8.0 to 47.4
$\dot{V}E_{\,max}$ ($l.min^{-1}$)	16.5 *	5.4 to 27.6
% predicted $\dot{V}E_{\,max}$	3.1	-25.0 to 31.3
Oxygen saturation (%)	4.00	-1.1 to 9.0
R	0.15 *	0.09 to 0.22
Heart rate max ($beat.min^{-1}$)	30 *	8 to 52
% predicted max HR	16.0 *	3.2 to 28.8
Oxygen pulse ($ml.beat^{-1}$)	1.6	-2.2 to 5.4
V_D/V_T	-0.11 *	-0.16 to -0.06
Blood lactate concentration ($mmol.l^{-1}$)	3.05 *	1.28 to 4.8

* Significant difference between controls and patients $p<0.05$

employed [30.6 x (FEV_1 -29)]. Five of the control group exceeded their predicted maximum (range 52 to 155%).

The predicted values for $\dot{V}O_{2\,peak}$ were calculated from the equations proposed by Bruce et al (1973), the equation employed in Chapters 5 and 7. The patients attained a mean value of 68.9% (range 51.7 to 103.7%) of predicted $\dot{V}O_{2\,max}$, whilst the control group attained a mean value of 96.6% (range 66.3 to 127.2%). These two values were significantly different.

The heart rate data, not significantly different at rest, indicates that the control group were able to not only attain a significantly higher mean maximal heart rate but this also translated into a greater percentage of predicted maximal heart rate attained.

The measurement of capillary blood lactate concentrations shows that at rest there was no significant difference between groups. Post treadmill test, the mean maximal concentration of lactate were significantly higher for the controls compared to the patients, Figures 8.1 and 8.2 show the pre and post treadmill test concentrations of capillary blood lactate for patients and controls respectively. It can be seen that of the ten controls 2 individuals exceeded a post exercise lactate concentration of 8 $mmol.l^{-1}$. A further 4 individuals exceeded 4 $mmol.l^{-1}$, and the remaining 4 exceeded 2 $mmol.l^{-1}$. For the patient group no individual exceeded 4 $mmol.l^{-1}$ and just 2 exceeded 2 $mmol.l^{-1}$. The mean increase in lactate concentration for the control and patient group was 3.80 and 0.85 $mmol.l^{-1}$. This represents a statistically significant increase for both groups. There was no relationship between the patients' spirometry and peak lactate concentration or lactate concentration increase.

The Oxyconbeta system has the function allowing the

FIGURE 8.1 Pre and post treadmill test blood capillary lactate concentration in the patient group (n=10).

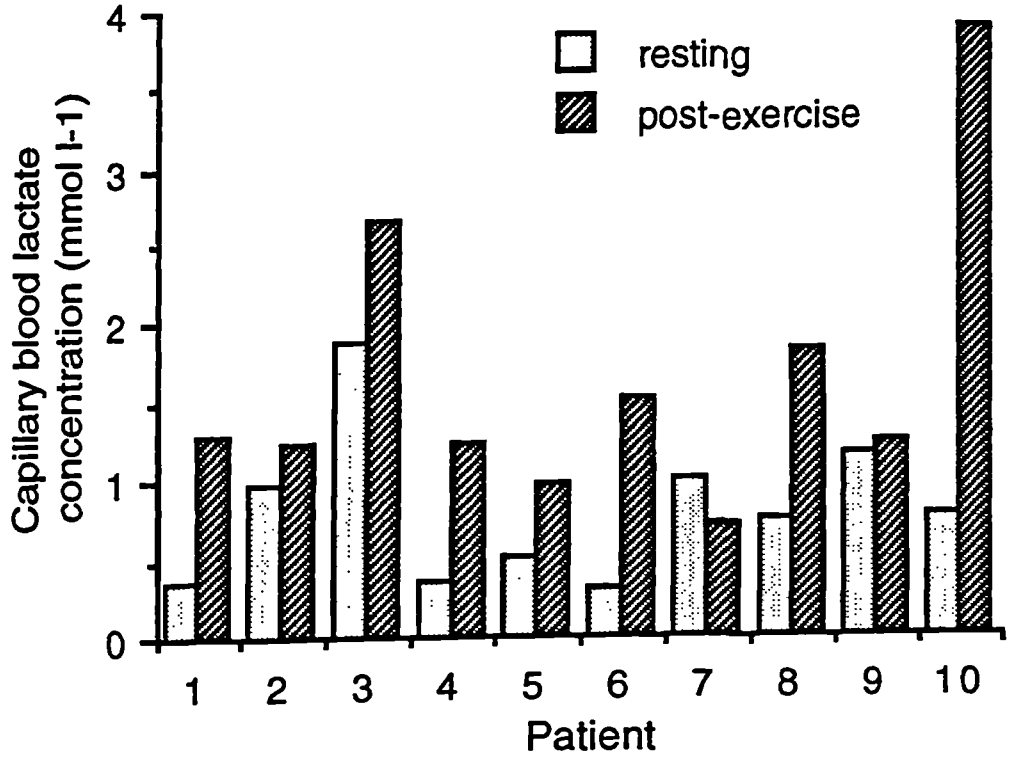
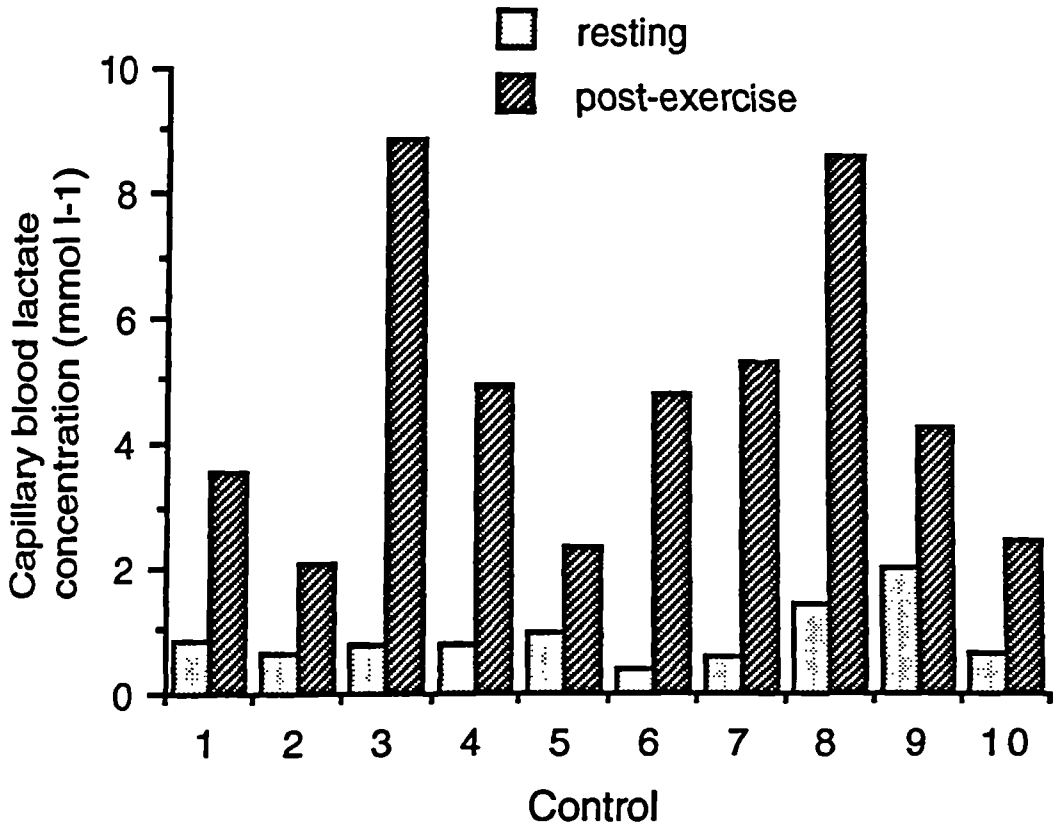


FIGURE 8.2 Pre and post treadmill test blood capillary lactate concentration in the control group (n=10).



identification of an anaerobic ventilatory threshold using the $\dot{V}co_2/\dot{V}o_2$ method described by Sue et al (1988).

For this group of individuals the threshold was reached in 6 patients and all of the control group, as detected by the Oxyconbeta system (Fig.8.3 & 8.4). The mean $\dot{V}o_2$ at which it occurred in the patient group was 0.70 (0.13) $l.min^{-1}$ (representing 54.0% $\dot{V}o_{2\ max}$) and for the 10 control subjects the value was 1.01 $l.min^{-1}$ (equivalent to 49.2% of the $\dot{V}o_{2\ max}$).

The mean maximal Borg breathlessness and exertion scores for the healthy volunteer group were 6.4 (2.4) for breathlessness and 16.8 (1.9) for exertion. The mean difference between the reported Borg breathlessness score post exercise between the patients and the healthy subjects was 1.4 (95% CI -0.45 to 3.25) higher in the control group although this difference was not significant.

On direct questioning, 8 of the ten patients reported stopping exercise because of breathing difficulties, compared to 1 of the control group. Whilst 2 of the patients and 3 of the control group stopped because of overall fatigue (combination of legs and dyspnoea). The remaining 6 of the control group stopped due to leg pain.

Comparing patients' response to both the shuttle walking test and symptom limited maximal treadmill walking test (paired t-test) revealed that there was no significant difference in post exercise capillary lactate concentrations [(1.23(0.98) $mmol.l^{-1}$ post shuttle, 1.66(0.95) $mmol.l^{-1}$ post treadmill). Neither was there any difference in the mean maximal heart rate attained (127 $beat.min^{-1}$ for both the shuttle and treadmill test). Figure 8.5 shows the capillary blood lactate concentrations pre and post shuttle walking test and Figure 8.6 compares the maximum response in the ten patients in both the shuttle

FIGURE 8.3 $\dot{V}CO_2/\dot{V}O_2$ slope with the identification of the ventilatory threshold in 6/10 patients.

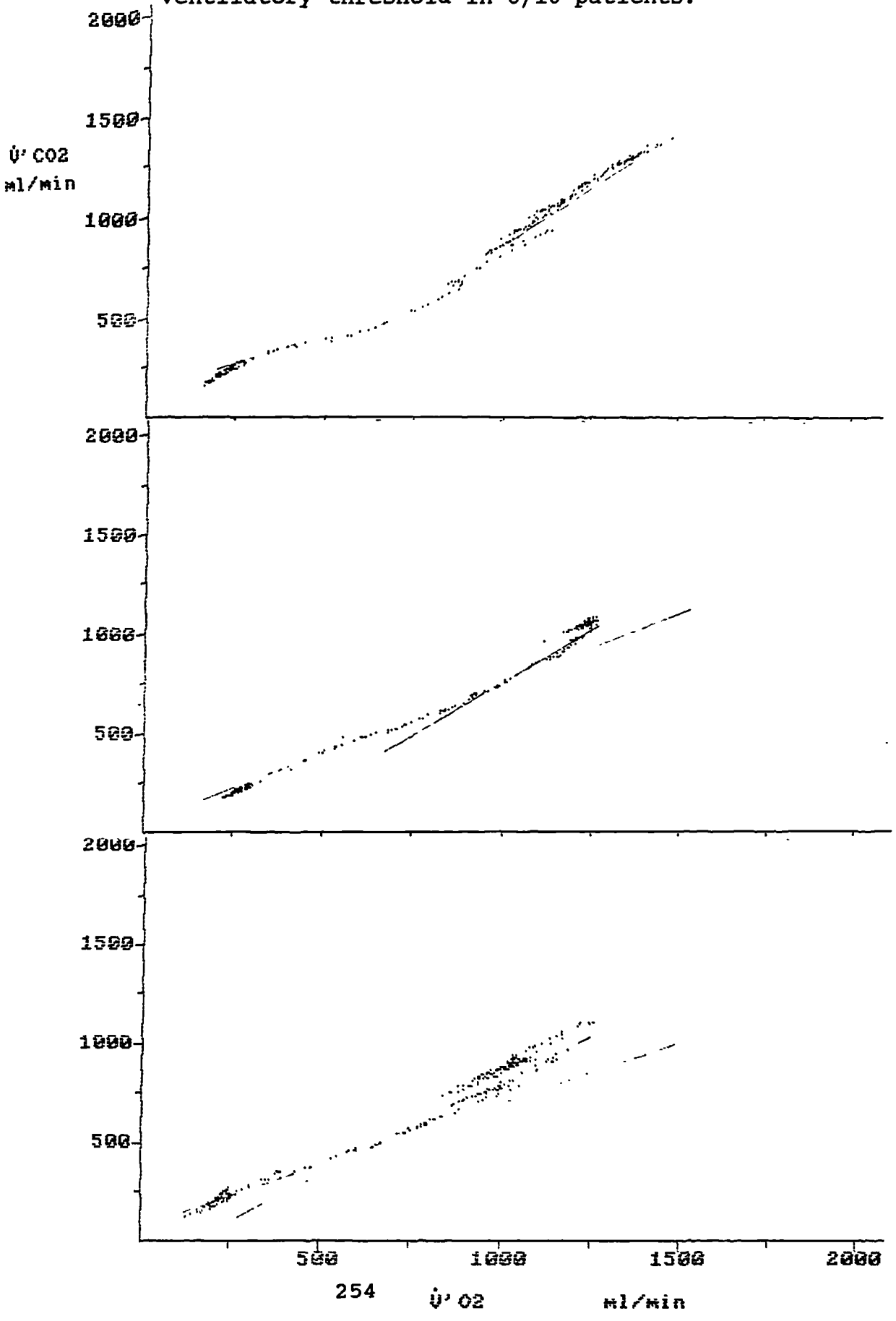


FIGURE 8.3 $\dot{V}CO_2/\dot{V}O_2$ slope with the identification of the ventilatory threshold in 6/10 patients.

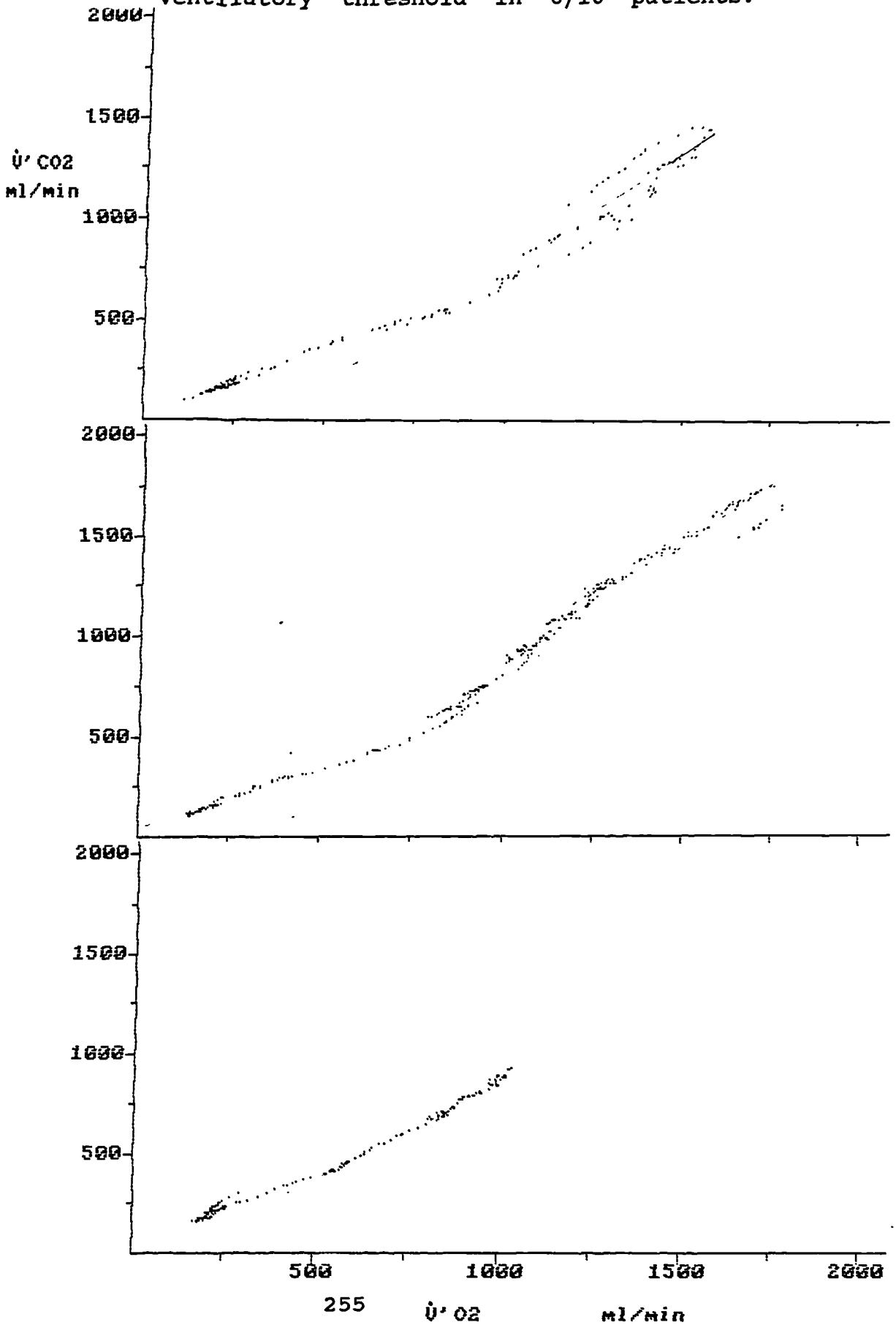


FIGURE 8.4 $\dot{V}CO_2/\dot{V}O_2$ slope for the control group with the identification of the ventilatory threshold. (n=10)

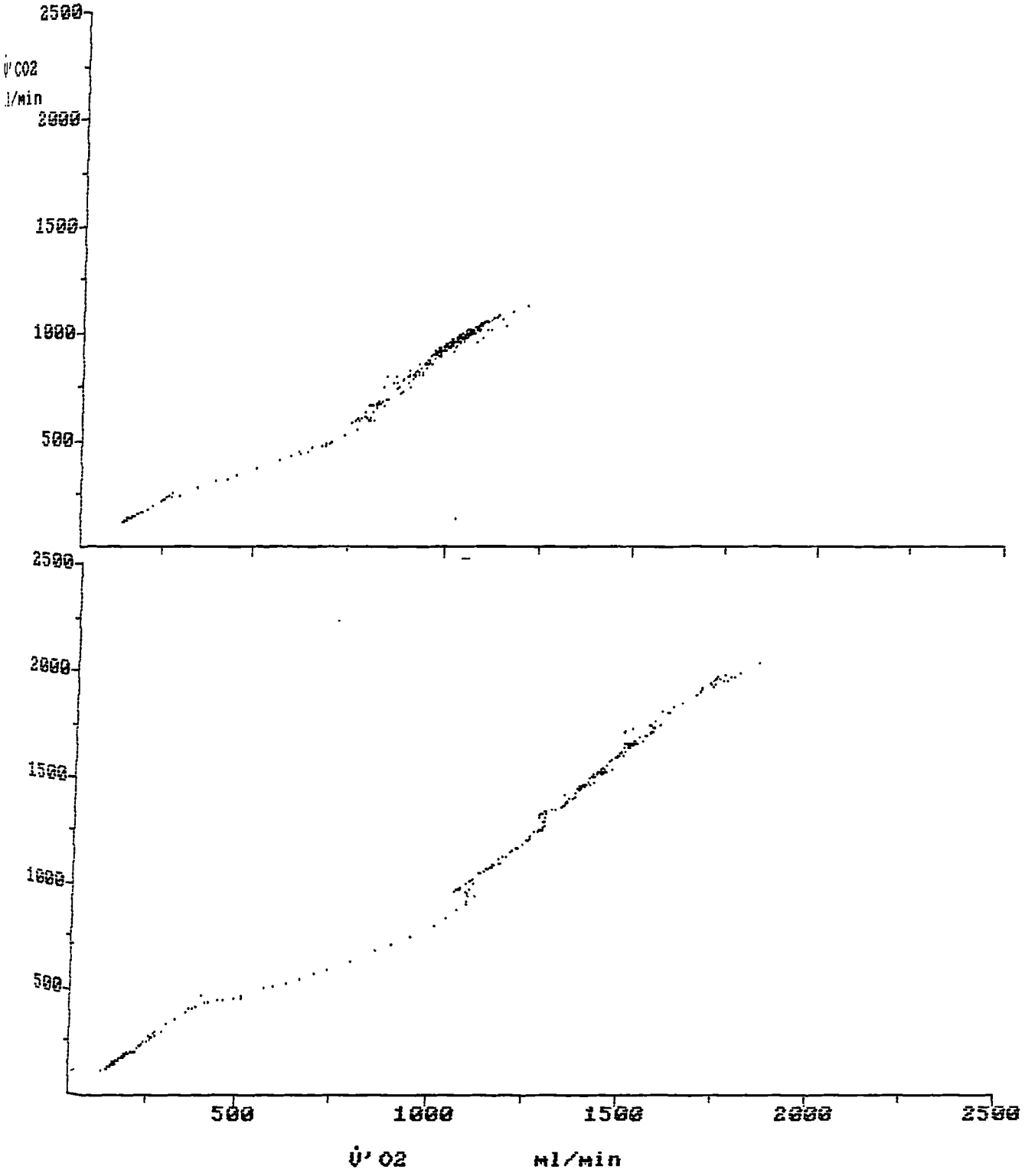


FIGURE 8.4 $\dot{V}CO_2/\dot{V}O_2$ slope for the control group with the identification of the ventilatory threshold. (n=10) (cont'd)

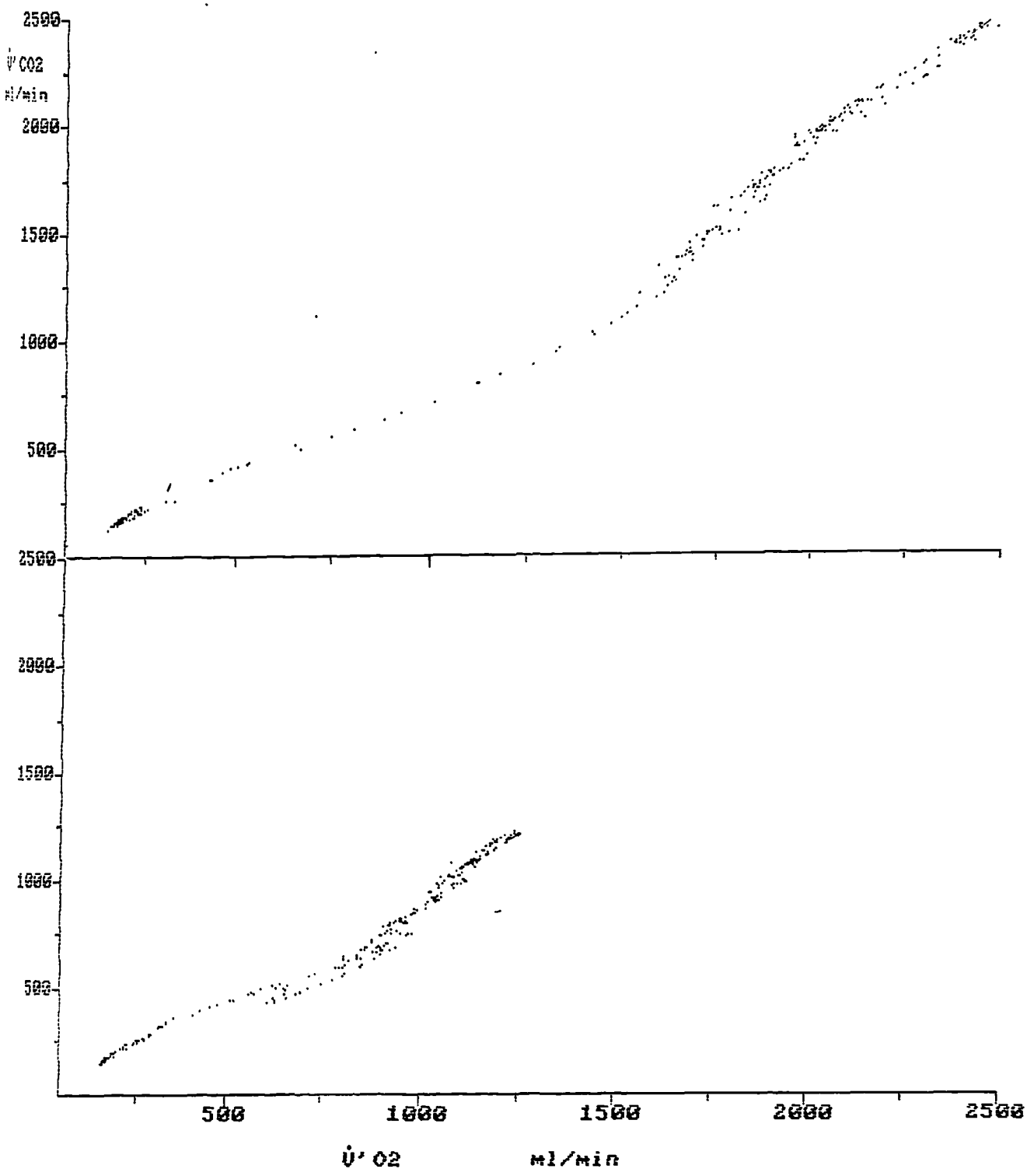


FIGURE 8.4 $\dot{V}CO_2/\dot{V}O_2$ slope for the control group with the identification of the ventilatory threshold. (n=10) (cont'd)

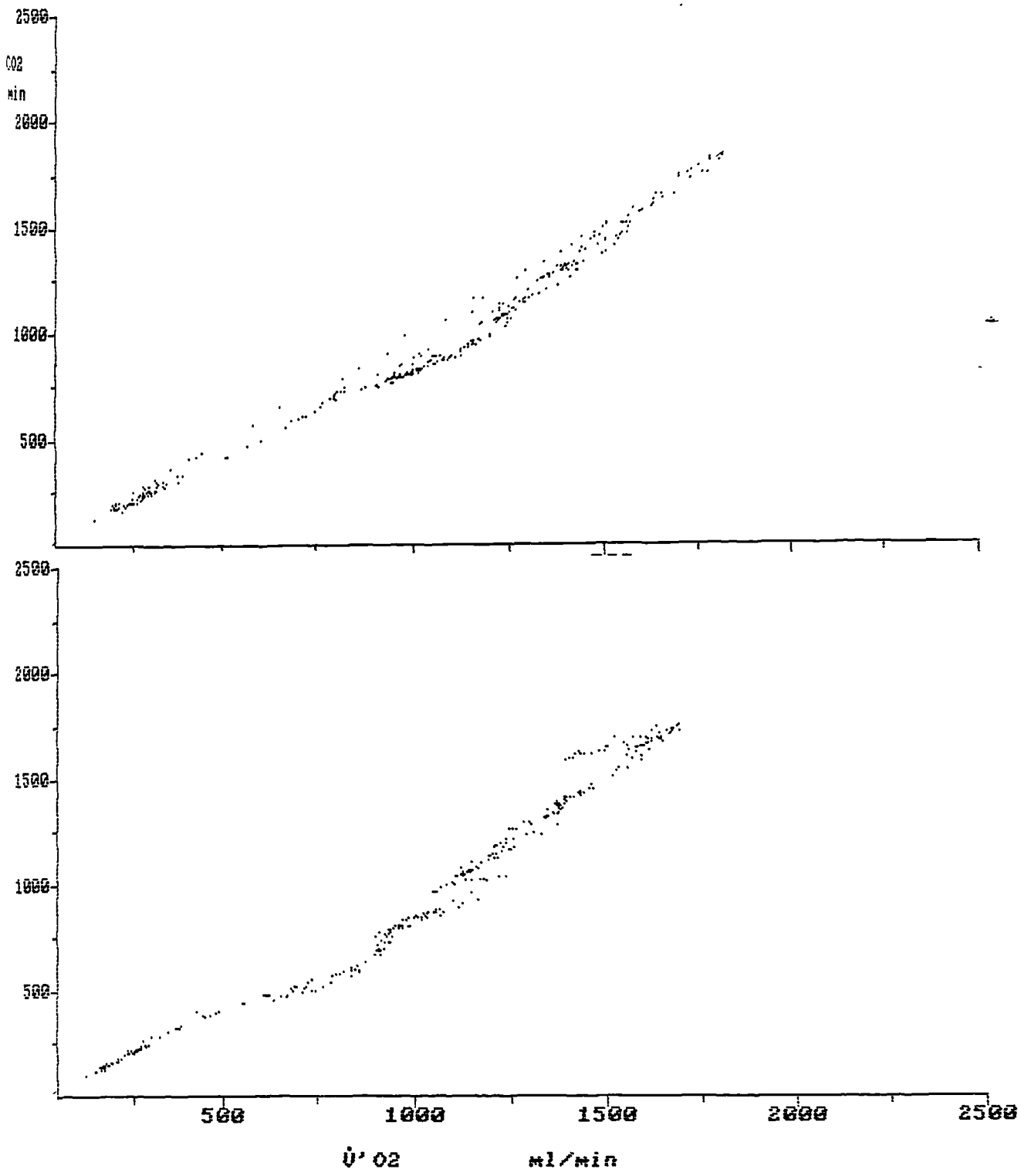


FIGURE 8.4 $\dot{V}co_2/\dot{V}o_2$ slope for the control group with the identification of the ventilatory threshold. (n=10) (cont'd)

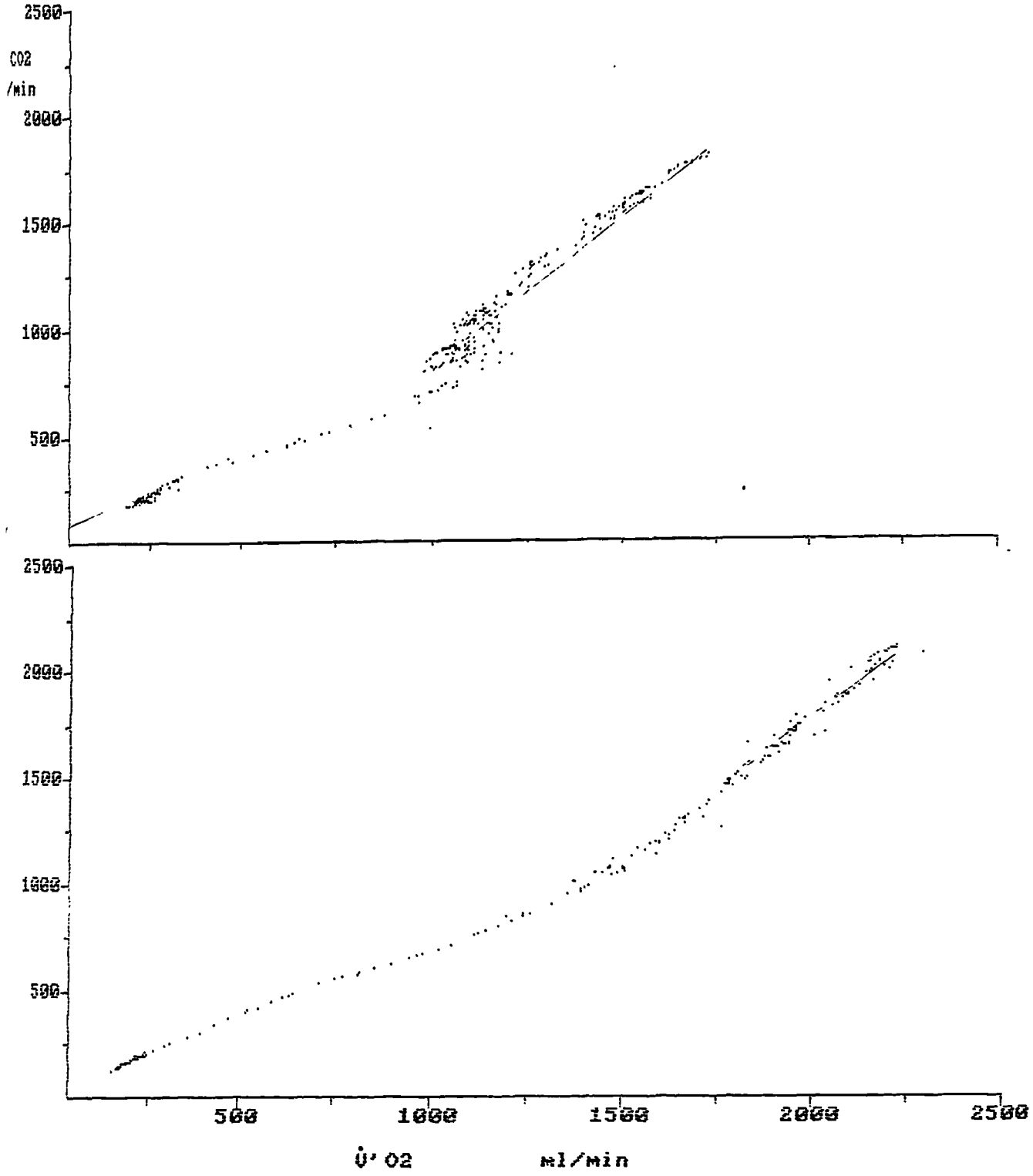


FIGURE 8.4 $\dot{V}CO_2/\dot{V}O_2$ slope for the control group with the identification of the ventilatory threshold. (n=10) (cont'd)

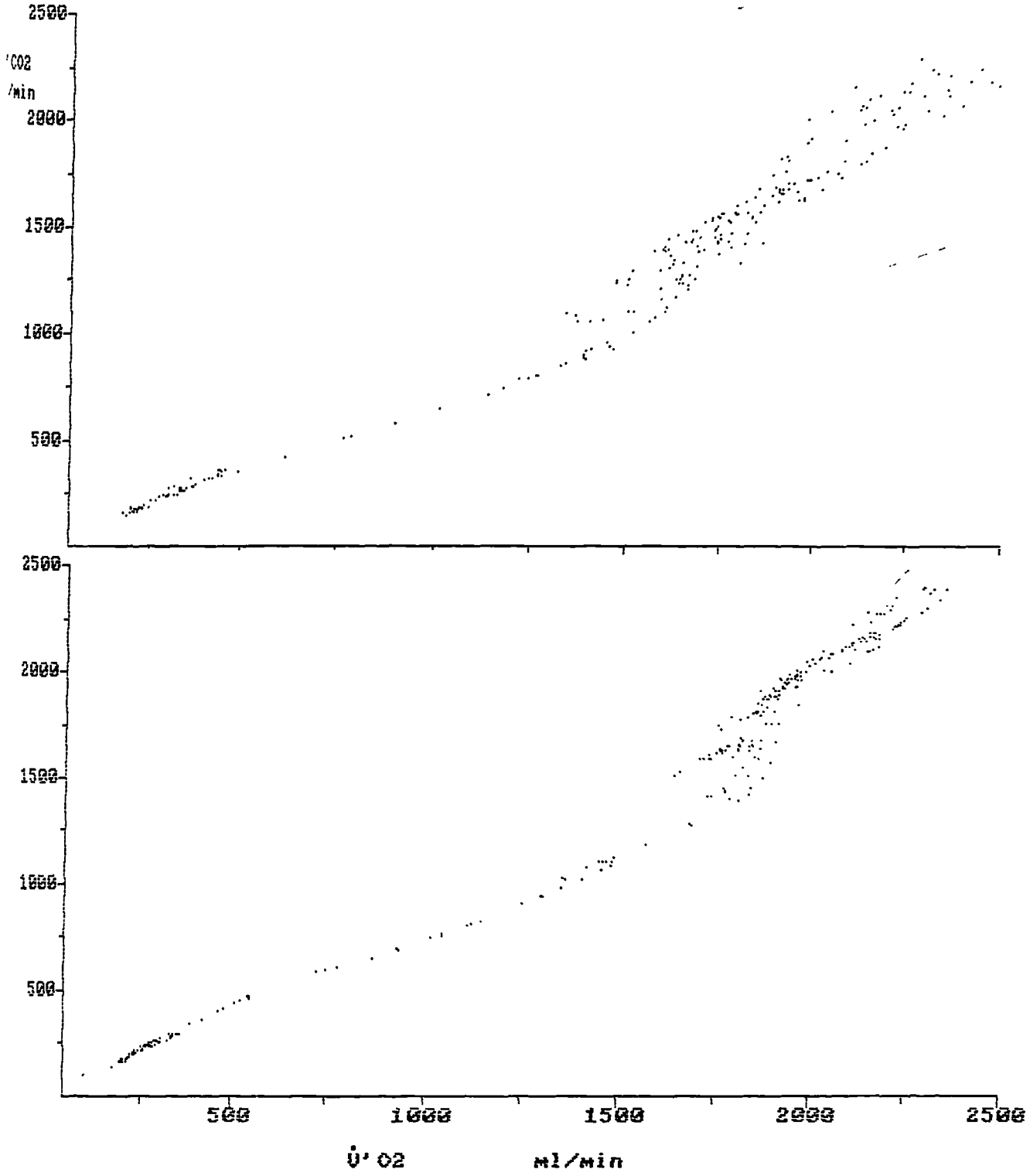


FIGURE 8.5 Pre and post shuttle test blood capillary lactate concentration in the patient group (n=10).

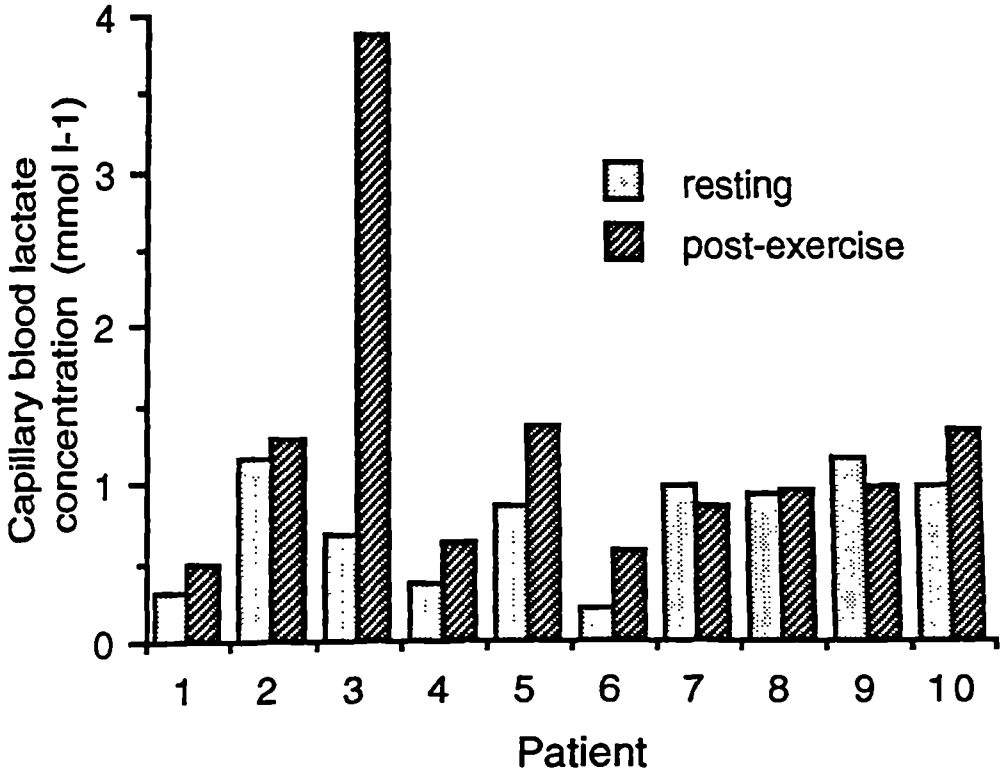
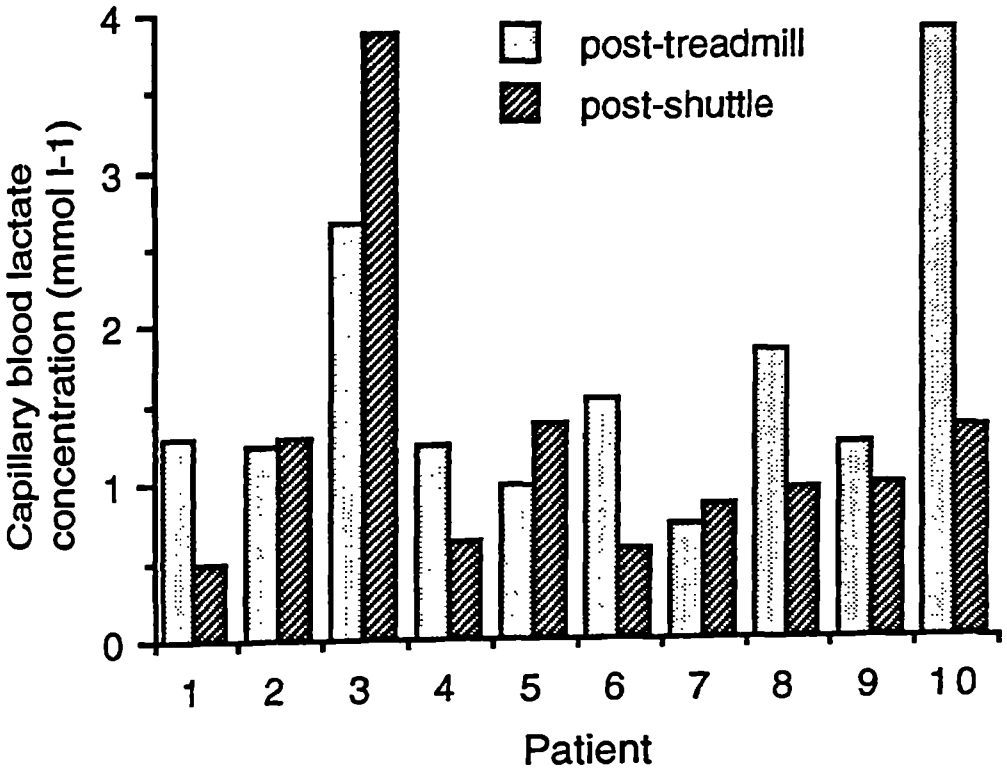


FIGURE 8.6 Comparison of the post exercise capillary blood lactate concentration in the patient group after the treadmill and shuttle walking test. (n=10).



walking test and the treadmill test. One patient (patient 10) produced a considerably higher lactate response to the treadmill than to the shuttle walking test and a greater response when compared to the remaining nine patients. Patient three produced a considerable lactate response after the shuttle walking test and a higher than average response to the treadmill test. These two patients had an FEV_1 of 1.05 l and 1.75 l and reached 62.2% and 103.7% respectively of their $\dot{V}O_{2\,peak}$ and both reached over 90% of their predicted maximum $\dot{V}E$.

The relationship between symptom limited $\dot{V}O_{2\,peak}$ and the distance completed in the shuttle walking test was again strong, r=0.94 (Figure 8.7).

The subjective ratings for the two test for the patient group is shown in Table 8.8, with the mean difference, 95% confidence interval and level of statistical significance shown in Table 8.9.

FIGURE 8.7 The relationship between the symptom limited $\dot{V}O_{2\,peak}$ and the distance completed on the shuttle walking test. (n=10).

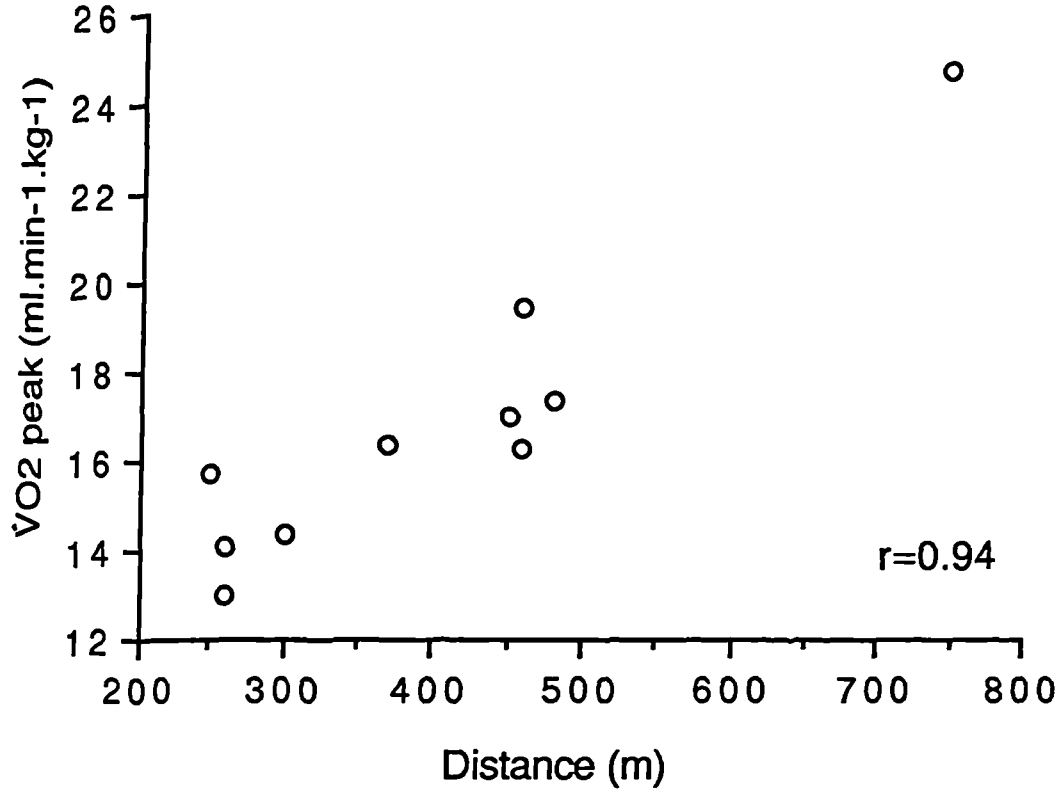


TABLE 8.8 Reported Borg breathlessness score [mean(SD)] at rest and immediately post exercise for the shuttle and treadmill test (n=10).

	Shuttle test	Treadmill test
Resting	1.4 (1.2)	1.2 (1.1)
Post exercise	5.1 (0.8)	5.0 (1.2)

TABLE 8.9 Mean difference, 95% confidence interval and Spearman correlation between the reported Borg breathless score of the shuttle versus the treadmill exercise test.

	Mean difference	95% confidence interval	rho
Resting	0.25	-0.47 to 0.97	0.59
Post exercise	0.10	-0.82 to 1.02	0.46

DISCUSSION

The aim of the study reported in this chapter was to examine the blood lactate response to exercise in patients with CAL and compare the response between the shuttle walking test and a conventional treadmill test. The inclusion of a control group allowed it to be established that the capillary blood lactate measurements were in fact disease related rather than a consequence of increasing age.

The control group did not present with significantly different physical characteristics except for spirometry measurements. The resting physiological measurements prior to the treadmill test for the patient and control group were again not significantly different except for a slightly lower oxygen saturation in the patient group and a slightly increase R value in the control group. This was raised slightly above the *normal resting value of 0.85* (Whipp et al 1984). The latter may be in part due to unfamiliarity with the equipment and resulting hyperventilation (Wasserman et al 1987) (the majority of patients recruited had previously performed laboratory based exercise tests).

Overall the exercise response of the patients with CAL is severely impaired in comparison to the age and sex matched control group. Spiro et al (1975) compared levels of ventilation at a given level of $\dot{V}O_2$, ie the ventilatory equivalent. For this study absolute values were compared as they were in the studies by Nery et al (1983) and Carter et al (1987). The increase in the patients level of ventilation was almost 4 fold while that of the control group was almost 7 fold. These patients were unable to increase their level of ventilation to match the increasing workload primarily due to the abnormal mechanical characteristics of the respiratory system. In addition, it has been suggested that patients have an altered

physiological process; when the set CO_2 point of ventilatory control is depressed there is an increase in the ventilatory requirements of work (Whipp & Wasserman 1988). This results from hypoxaemia and possibly the effects of regional distortion of lung tissue on vagal tone, seen in patients with emphysema. Alternatively, in patients with chronic bronchitis the tendency is for the patient not to ventilate adequately in relation to the metabolic demand of exercise. The CO_2 set point is elevated as a consequence of mechanical limitation to airflow and possibly impaired chemoreflex function (Whipp & Pardy 1986). The hypoxaemia is primarily due, during exercise to the V/Q mismatch. The results of the present study are consistent with the reports of Spiro et al (1975), Nery et al (1983) and Carter et al (1987) when comparison of the exercise response of patients and a control group were examined.

Comparison of performance between the two groups revealed that the patients walked at a slower speed for a shorter duration and achieved a lower peak incline. The $\dot{V}O_{2\,peak}$ was considerably lower in the patient group. A $\dot{V}O_{2\,peak}$ is dependent on a number of factors and a low value in itself does not indicate a ventilatory limit to functional capacity. The lack of a relationship between the $\dot{V}O_{2\,peak}$ and spirometry results are suggestive of a lack of a causal mechanism between impairment (as judged by spirometry) and performance.

The equipment employed at this stage also allowed the examination of the V_D/V_T ratio and the change with exercise. At rest there was no significant difference between the two groups, at peak exercise the ratio was significantly higher in the patient group. The ratio did fall from the resting value but remained higher than normal, consistent with the study by Carlson et al (1991). This is an indication of the patients' limited capacity to increase the tidal volume and the poor gas exchange efficiency as a consequence of the

maldistribution of the V/Q ratios (Jones et al 1985).

The heart rate data shows that the control group were able to reach a much higher maximal heart rate than the patient group. The patient group appear to have a normal incremental heart rate response to the exercise test but at maximal exercise had a considerable heart rate reserve, utilising less than 75% of predicted of their predicted maximum. This would be consistent with a ventilatory limit to performance. In comparison, it would appear that the control group were approaching a cardio-vascular limit to continued performance with little, if any, cardiac reserve.

The lactate response to the treadmill test was significantly higher in the control group than in the patient group. Confirming the results documented in Chapter 7, the lactate response of the patients was low. The results reported are lower than some other published results (Spiro et al 1975, Elliott et al 1987) but not all. The data relating to the measurement of a significant lactate response in this category of patient is both sparse and conflicting. Some authors appear to overlook a low response documented in a proportion of their patients. The patients recruited for the present study were motivated and subjectively reported that they had performed a symptom limited maximum test. This would be confirmed by the minimal ventilatory reserve they were estimated to have post exercise.

Elliott et al (1987) investigated 6 patients with CAL. All 6 produced a lactate response during incremental exercise. The authors suggested that a reliable non-invasive technique to monitor the AT was the systematic increase in the R value. Interpretation of the graphs presented do appear to be somewhat arbitrary. The mean maximal R value was not reported for this study. Kanarek et al (1979) recruited 12 patients with CAL and examined the

incidence of a ventilatory AT. 7/12 patients failed to demonstrate a ventilatory AT. The 5 patients who reached this threshold level did not have greater FEV_1 values (unlike those of Sue et al 1988) but were able to utilise a higher percentage of their predicted ventilatory capacity (FEV_1 x 35). The mean maximal R value was slightly but not significantly higher for the 5 patients (1.10). The AT occurred at approximately 55% of the $\dot{V}O_{2\,max}$, comparable to the present study.

Nery et al (1983) identified a ventilatory AT in 5/7 patients with CAL. Analysis of arterial blood gases revealed a significant drop in pH, a rise in $PaCO_2$ but no significant fall in HCO_3^- , suggestive of a lack of significant rise in blood lactate concentration. Schiffman (1991) states that the inappropriately low minute ventilation during exercise that causes this respiratory acidosis is not due to the decreased respiratory drive but due to the mechanical derangement limiting ventilation and an increased V_D/V_T ratio. Wasserman et al (1987) confirms this proposing that in these patients the limitation to exercise is the inability to clear CO_2 effectively rather than the ability to make O_2 available to the mitochondria.

The patient group in the present study attained a comparable $\dot{V}O_{2\,peak}$ to the previously cited studies above and those in Chapters 5 & 7. Sue et al (1988) did not measure blood lactate concentrations directly (measured a fall in standard bicarbonate ions, HCO_3^-) but identified an 'anaerobic threshold' (AT) in 15/22 patients with CAL. A metabolic AT tended to be identified in patients who utilised a higher percentage of their ventilatory capacity (over about 95% of MVV). Casaburi et al (1989) selected patients for rehabilitation, providing a significant lactate response could be produced. The group selected (n=7) had slightly higher FEV_1 and $\dot{V}O_{2\,peak}$ values. Interestingly, the magnitude of the response did not relate

to their grading of disease severity as has previously been suggested. This poor relationship was apparent in the present study.

In the present study the patient with the greatest lactate response (3.87 $mmol.l^{-1}$) had a FEV_1 of 1.7 l (the 2nd highest of the group) and a $\dot{V}O_{2\,peak}$ of 1658 $ml.min^{-1}$ (the highest female). The mean maximal R value of the patient group was 0.89, not consistent with reaching a true maximal oxygen uptake. The lactate concentration at this threshold value is commonly taken as a value of 4 $mmol.l^{-1}$, although values of 2.5 $mmol.l^{-1}$ are sometimes used. The rise in capillary blood lactate concentration in the control group is consistent with a metabolic AT being exceeded. The mean immediately post exercise R value (1.04) suggests that the control group approached their maximal aerobic capacity. Computer analysis of the breath by breath relationship between $\dot{V}O_2$ and $\dot{V}CO_2$ identified that all the control group also attained a ventilatory AT, using the technique reported by Beaver at al (1986).

Breath by breath analysis of the computed data detected a ventilatory AT in 6/10 patients by the system. It was proposed in the studies by Sue et al (1988), that despite not detecting a ventilatory AT in 10/22 patients, (6 of whom failed to produce a significant HCO_3^- response) this method of detecting an AT was "satisfactory in most individual exercise studies". The identification of the ventilatory AT in the present study of patients occurred at a mean $\dot{V}O_2$ of 0.697 $l.min^{-1}$ (below the value predicted by Wasserman et al 1987), representing a mean value of 54% of the patients $\dot{V}O_{2\,peak}$.

The AT is commonly measured by either blood lactate concentrations or ventilatory measurements. The proposed linking mechanism relies upon the non-linear increase in ventilation being associated with a sharp rise in the

production of lactic acid (the H^+ ions produced by lactate is principally buffered by HCO_3. resulting in an increased production of CO_2 from the dissociation of carbonic acid (H_2CO_3). In an attempt to compensate for the high levels of lactic acid and CO_2 production the respiratory centres are stimulated to increase $\dot{V}E$). The ventilatory response is normally mediated through the carotid bodies.

The detection of a ventilatory threshold in patients with CAL is documented to be hazardous (Belman et al 1992). One important reason is suggested to be a large inter- and intra-observer variability in detecting this point. Other reasons include the sometimes erratic breathing patterns that patients adopt during exercise testing, and a short exercise test generating too few data points to accurately detect a deflection in the plot (Patessio et al 1993).

It would appear that the relationship between these two methods of detection is not conclusive (Loat & Rhodes 1993), as demonstrated in this present group of patients. Patients with McArdles disease (a genetic lack of muscle phosphorylase) fail to produce lactic acid but do demonstrate a normal hyperventilatory response during incremental exercise (Hagberg et al 1982). The most likely mechanism for this was suggested by the author to be signals generated from neural centres that communicate with the respiratory centres of the brain, possibly mediated by increasing levels of circulating catecholamines. An alternative theory suggested by the same author was that working muscles are ideally placed to generate signals via the peripheral afferents to the respiratory centre. In response to these suggestions Whipp (1983), who proposes a causal link between the two methods of detection, replied that the most likely explanation of the ventilatory changes in these patients was the associated muscle pain or anticipation of such pain, a characteristic symptom of McArdles disease.

Neary et al (1985), examined lactate and ventilatory thresholds under normal conditions, under glycogen depletion and previously exercise states. No significant changes were found in the ventilatory threshold measurements demonstrating that lactate accumulation was not responsible for the ventilatory threshold response. This supports the theory that the ventilatory and metabolic AT are coincidentally and not causally linked. Hughes et al (1982) in another study of healthy volunteers also demonstrated that the ventilatory and metabolic AT could be manipulated independently, and therefore uncoupled from the anticipated relationship.

Other factors can contribute to the non linear increase in ventilation with increasing oxygen consumption. Local hypoxia at peripheral chemoreceptors may be more pronounced during severe exercise causing a rise in ventilation independent of any rise in lactate concentrations. Astrand and Rodahl (1986) suggest that impulses from higher brain centres can also modify ventilation particularly if the exercise requires 'mental effort'.

One aim of the present study was to confirm the low lactate response reported in an earlier study (Chapter 7). The lactate response was again low and comparison with the control group allows the conclusion that no measurement error had occurred. This is because the absolute values obtained from the control group were in a range expected from this population. Therefore a low blood lactate concentration after maximum exercise is characteristic of this patient group.

The subjective response to the treadmill test was not significantly different between the two groups, although the control group did report a slightly higher level of breathlessness. This may indicate a psychological adaption by the patients to, what for them, is a common feeling. The

overall level of breathlessness reported by both groups was slightly lower (5.7) than the value (6) reported by Killian (1992) in two similar but larger groups. Patients were not asked to report their perceived levels exertion but 3/10 patients reported overall fatigue as their reason for withdrawal. The study reported by Killian et al (1992) documented that 43% of patients stopped exercising because of leg effort rather than breathlessness. Unlike the present study a cycle ergometer was employed. In a previous study by Killian (1985) a diagram demonstrates that the lower a patients FEV_1 (as a percentage of predicted) the lower is the percentage of predicted $\dot{V}O_{2\,peak}$ attained and the reported Borg breathlessness score. The mean breathlessness score reported by patients with a FEV_1 below 40% predicted was approximately 5, whilst in the 40-60% range this increased to 6. These results are consistent with the present study as they are with the results reported by Rampulla et al (1992) reported in Chapter 5. Two of the control group reported 18 or more as their perceived level of exertion, and another 5 rated it at '17', consistent with a maximal performance (ACSM 1991).

The comparison of results from the patients performing the treadmill and second shuttle walking test allows us to state conclusively that there are no important differences in the metabolic, physiological or subjective response to the two exercise tests. Both constitute an incremental symptom limited maximal exercise test. The strength of the relationship between the two tests is confirmed by the strong correlation between distance walked on the shuttle walking test and the $\dot{V}O_{2\,peak}$ attained on the treadmill walking test, confirming the previously reported correlations in Chapter 5 and Chapter 7. The strength of this relationship allows the observer to make legitimate estimates of an patient's $\dot{V}O_{2\,peak}$ upon completion of the shuttle walking test. This incremental field test, in the present group of patients provides a similar metabolic, cardio-respiratory,

ventilatory and subjective response as the treadmill test. Therefore performance on the shuttle test would allow valid conclusions to be drawn about the patients functional capacity. Obviously the test does not provide all the information that a conventional treadmill test can provide (particularly in comparison to the computerised gas analysis equipment) but it is cheap and simple and provides a reliable alternative that can yield useful information in the assessment of disability in patients with CAL.

9. A COMPARISON OF PATIENTS PERFORMANCE ON THE SHUTTLE WALKING TEST AND THE SIX MINUTE WALKING TEST.

9.1 INTRODUCTION

Studies reported in previous chapters show that the shuttle walking test is a reproducible, reliable and valid field walking test of disability in patients with CAL. The final stage of this project was to compare patients performance on the shuttle walking test with their performance on the well established six minute walking test (6 MWT). The latter is perhaps the most commonly used field exercise test to assess exercise tolerance in this patient group. Although attractive there are several investigators who have expressed concern about the 6 MWT's reproducibility and sensitivity (Swinburn et al 1985, Morgan 1989, see Chapter 3 3.3). The fundamental difference between it and the shuttle walking test is the incremental external pacing of the latter and the self pacing of the 6 MWT.

This final study therefore examines patients' performance and their response to the two exercise tests.

9.2 METHOD

9.2.1 Patient group

Fifteen patients from out-patients clinics were recruited and informed consent was obtained. The selection of patients conformed to the criteria described in Chapter 4 (4.2.2). The patients were required to attend Glenfield Hospital on three separate occasions at intervals of one week (to minimise any training effect), during a period of clinical stability. They were instructed to withhold relevant medication for three hours prior to testing. The baseline and exercise test measurements were as described in Chapter 4 (4.2.1 & 4.2.2).

9.2.2 Familiarisation visit

This visit introduced the two exercise tests to the patient who were required to perform one practice shuttle walk (4.2.1) and two practice 6 MWTs (7.2.3) in an attempt to counteract any learning effect (McGavin et al 1976, Mungall et al 1979, Knox et al 1988). Between each exercise test there was at least a 45 minute rest period to allow complete recovery.

9.2.3 The six minute walking test

The 6 MWT (Butland et al 1982) has no standardised instructions. For the purpose of this study instructions for the patient were written down in an attempt to standardise the procedure. The patient was advised to 'walk up and down the corridor aiming to cover as much ground as possible in the time allowed (6 minutes). You should not be concerned if you have to slow down or stop to rest. The aim is to feel at the end of the test you could not have covered any more ground.'

The test was conducted along a 45 m hospital corridor. The operator sat half way along the corridor in a visible position to the patient. As the patient passed the operator standard instructions were issued, either 'you're doing well' or 'keep up the good work' (Guyatt et al 1984).

9.3 RESULTS

No patients were excluded from the study because they failed to judge their performance appropriately on the shuttle test or the 6 MWT. Likewise no patient was excluded from the shuttle test because he attained 85% of his/her predicted maximal heart rate (this criterion is not commonly employed for the 6 MWT).

The physical characteristics of the group are shown in Table 9.1. The mean FEV_1 of approximately 48% indicates a

TABLE 9.1 Some physical characteristics of the group (Mean, SD), n =15.
10 males, 5 females

	1	Shuttle	6 MWT
Age (yr)	58.4 (7.5)	-	-
Height(m)	1.72 (0.06)	-	-
FVC (l)	2.81 (0.82)	2.77 (0.82)	2.68 (0.81)
FEV_1 (l)	1.42 (0.7)	1.55 (0.8)	1.47 (0.5)
FEV_1 % predicted	48.3 (23.7)	49.6 (23.5)	45.2 (25.5)

moderate degree of airways limitation. There was no significant difference between the spirometry recorded for the three visits.

The distances walked on the two shuttle walking tests and the three 6 MWTs are shown in Figure 9.1. The distances walked for the shuttle walking test ranged from 230 m to 640 m. No patient completed the end of the 12-stage protocol. The maximum distance walked on either trial represented 9 levels and 1 shuttle. The range of distances walked for the 6 MWT on the three trials was 391 m to 591 m, 418 m to 648 m and 414 m to 651 m for trials one two and three respectively (Table 9.2). No patient whilst performing the 6 MWT actually stopped walking although several appeared to decrease their pace considerably. The relationship between the trials and the mean between-test difference is expressed in Table 9.3.

There was no significant difference in the distance walked between the two shuttle walking tests but there was a significant difference between the first and second 6 MWT, the patients walked further on the second walk compared to the first, mean difference -32.1 m ($p<0.05$). There was however no significant difference between the second and third attempt of the 6 MWT. The intraclass correlations between the three 6 MWTs (trial 1 vs 2 R=0.90, trial 1 vs 3 R=0.79 and for trial 2 vs 3 R=0.94, Figs 9.2, 9.3 and 9.4) were good. A strong intraclass correlation between the two shuttle walking tests was identified (r=0.98, Fig 9.5) indicating that these tests are highly repeatable. The third 6 MWT and the second shuttle walking test were used for the comparison between the two exercise tests. The mean difference between the distance walked on the two tests was 54 m. The correlation between the two distances was only moderate (rho=0.68), Figure 9.6. The identified outlier performed equivalently on the three occasions of the 6 MWT.

FIGURE 9.1 Mean(SEM) distances (m) walked on the shuttle walking tests and the six minute walking tests.

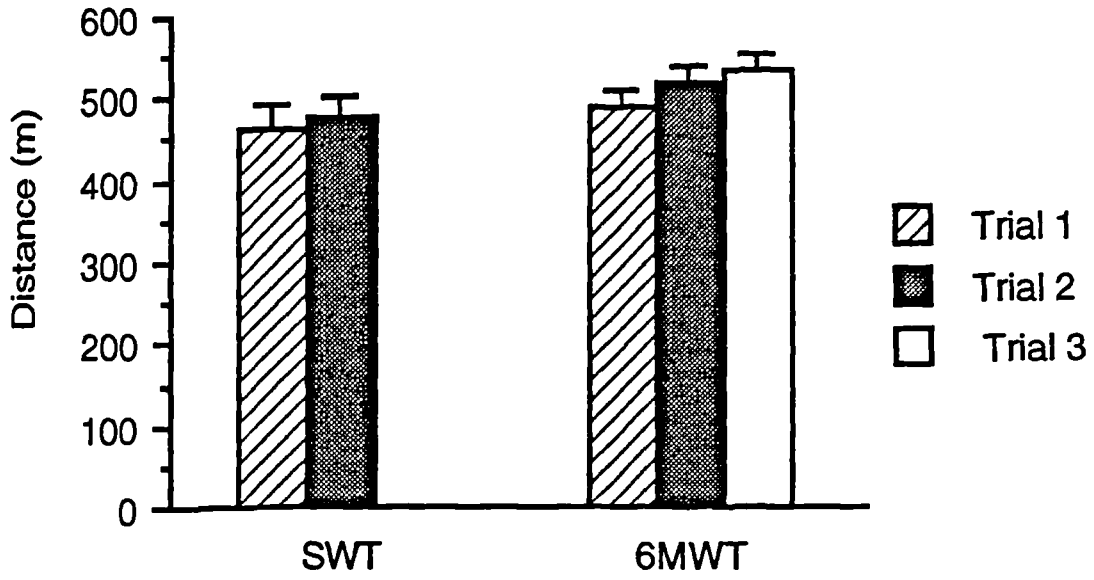


TABLE 9.2 Mean (SD) and range of distances (m) walked on the shuttle walking test and the six minute walking test, n=15.

Test		Mean (SD)	Range
Shuttle walking test	1	461.3 (111.7)	230.0 - 640.0
	2	476.7 (103.8)	330.0 - 640.0
six minute walking test	1	486.5 (68.4)	390.9 - 591.3
	2	518.6 (69.8)	418.2 - 648.0
	3	530.9 (73.1)	414.6 - 651.3

TABLE 9.3 Mean (SD) differences (m) and 95% confidence intervals (m) and correlation coefficients in the distances walked between the two field exercise test.

Test difference	Mean (SD)	95% confidence interval (m)	R/ rho
Shuttle walking test 1-2	-15.3 (29.9)	-31.9 to 1.3	0.98
Six minute walking test 1-2	-32.1 (28.2)	-47.8 to -16.5	0.90
1-3	-44.4 (43.8)	-68.8 to 20.2	0.79
2-3	-12.4 (33.4)	-30.9 to 6.2	0.94
Shuttle walk - six minute test	-54.3 (70.4)	-93.3 to -15.3	rho 0.68

FIGURE 9.2 The relationship between the distance (m) walked on the first and second six minute walking test.

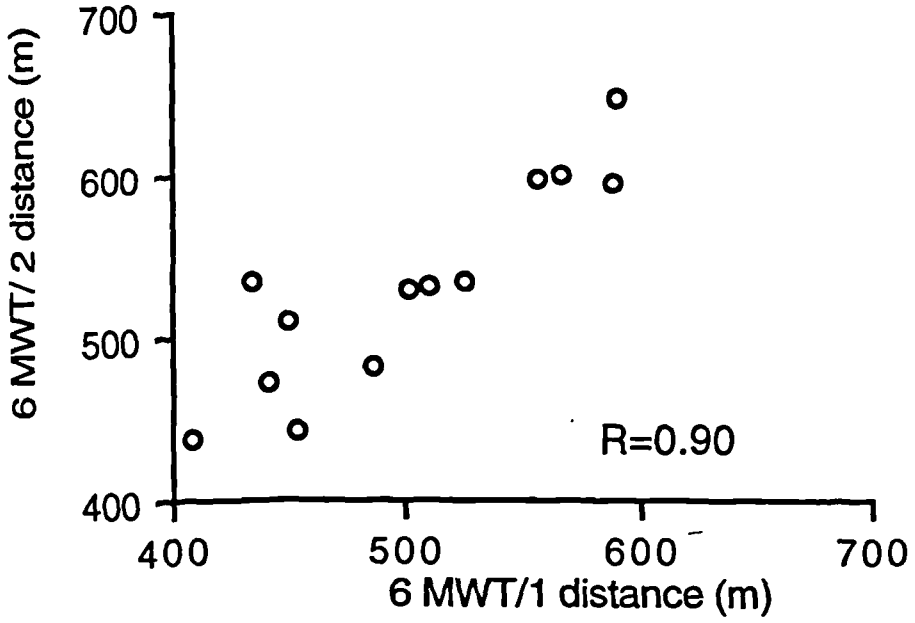


FIGURE 9.3 The relationship between the distance (m) walked on the first and third six minute walking test.

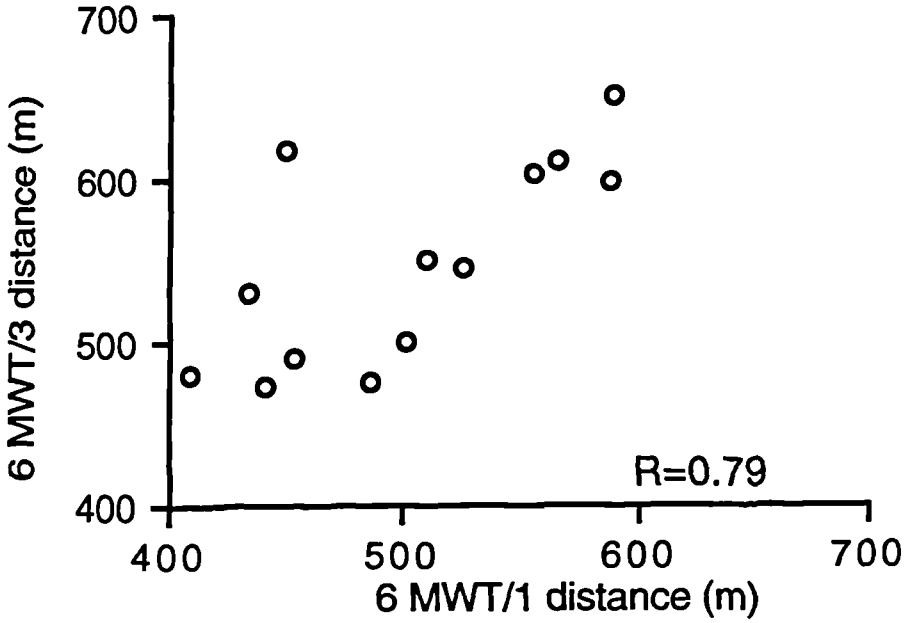


FIGURE 9.4 The relationship between the distance (m) walked on the second and third six minute walking test.

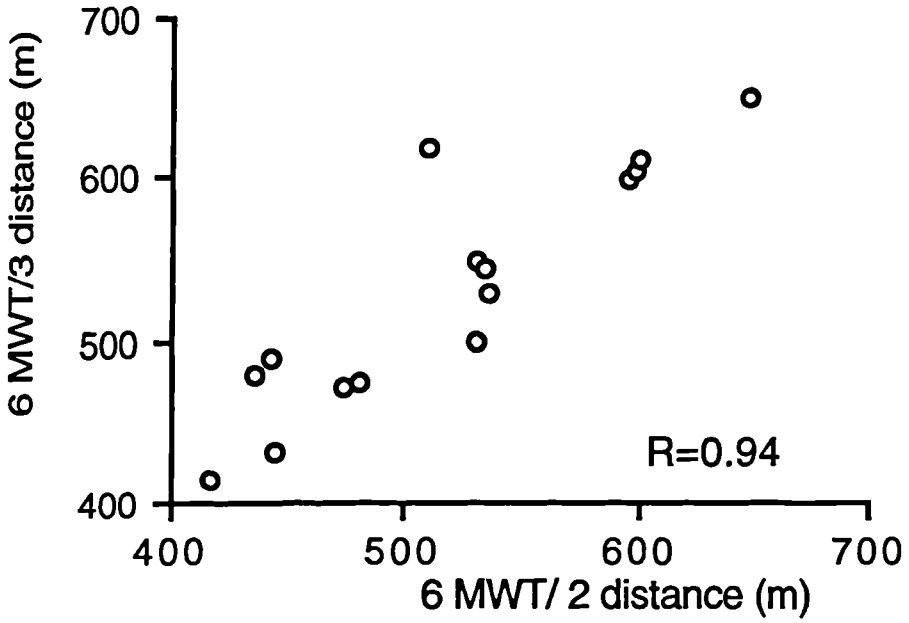


FIGURE 9.5 The relationship between the distances (m) walked on the two shuttle walking tests.

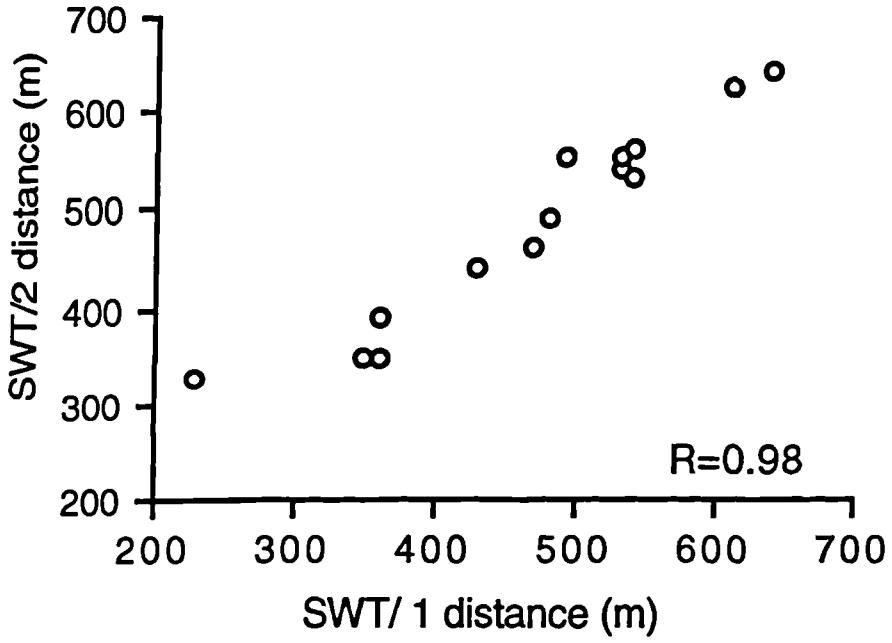
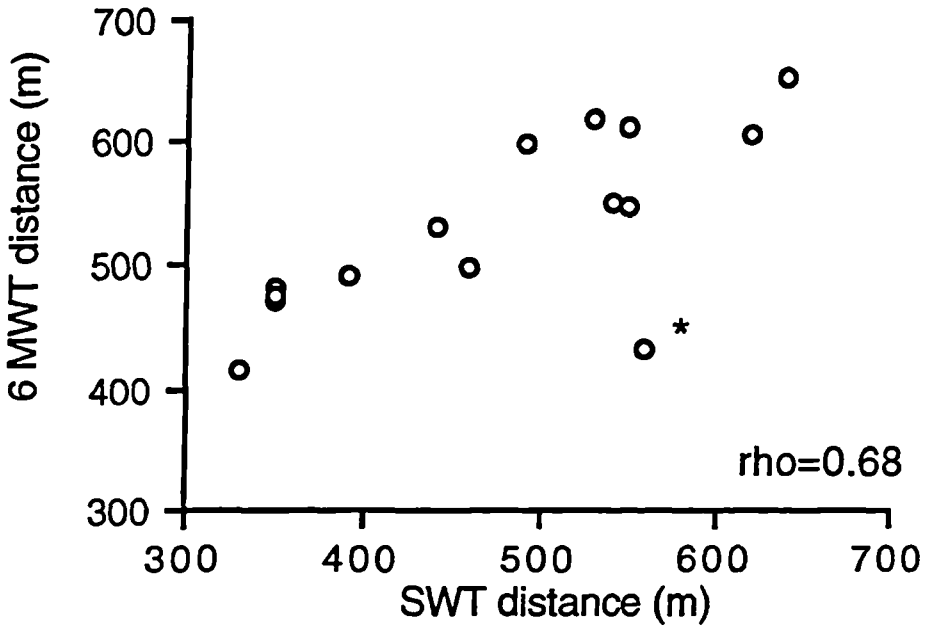


FIGURE 9.6 The relationship between the distances (m) walked on the second shuttle walking test and the third six minute walking test.



Outlier (*)

The mean maximal heart rate data for the two separate walking tests is shown in Figure 9.7. There was no significant between trial difference for either the shuttle or the 6 MWT but, there was a significantly greater mean maximal heart rate recorded at the end of the shuttle walking test than the 6 MWT. There was a moderate correlation between the heart rate values attained at the end of the different protocol (r=0.76). The mean maximal heart rate was 9 beat.min^{-1} (95% CI 1 to 18 beat.min^{-1}) higher in the shuttle walk than in the 6 MWT. The percentage of the predicted heart rate attained was also significantly higher for the shuttle walk compared to the 6 MWT (Table 9.4). The heart rate data confirm that the shuttle test provokes a slightly greater cardio-vascular response than the 6 MWT. The rise from resting levels was significantly smaller for the 6 MWT [41 beat.min^{-1} (range 8 - 86 beat.min^{-1} SD 22)] than the shuttle walking test [55 beat.min^{-1} (range 29-91 beat.min^{-1} SD 21)]. The relationship between the percentage of the predicted heart rate attained and the distance walked is shown in Table 9.5.

The relationship between the distance (m) walked and the percentage of the predicted maximal heart rate attained was strong for both of the shuttle walking tests and equally strong for the third 6 MWT although this relationship was not consistent for all three 6 MWTs. The heart rate data obtained whilst performing the shuttle and 6 MWT is shown in Figure 9.8 and indicates the graded cardio-vascular response to the shuttle walking test presenting an incremental rise in exercise intensity, a response not seen nearly as clearly in the 6 MWT.

The correlation between patients' performance, ie distance walked, and lung function was moderate for the first shuttle walking test. For example, the relationship between FEV_1 and FVC and performance for the first shuttle walk were r=0.57 and r=0.55, respectively. The relationship

FIGURE 9.7 The mean (SEM) maximal heart rate (beat.min^{-1}) attained on the shuttle walking test and the six minute walking test.

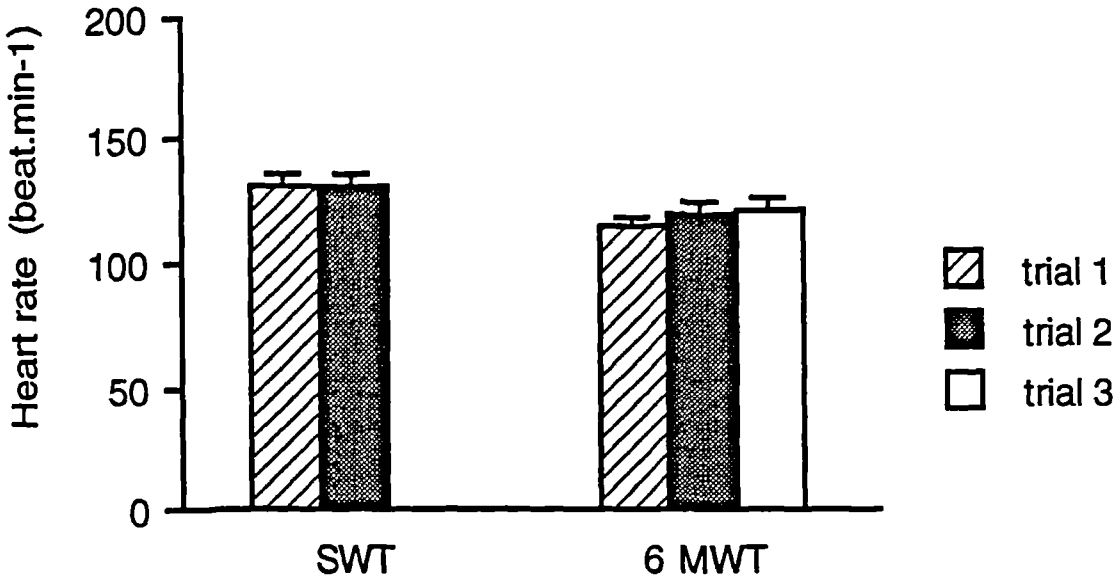


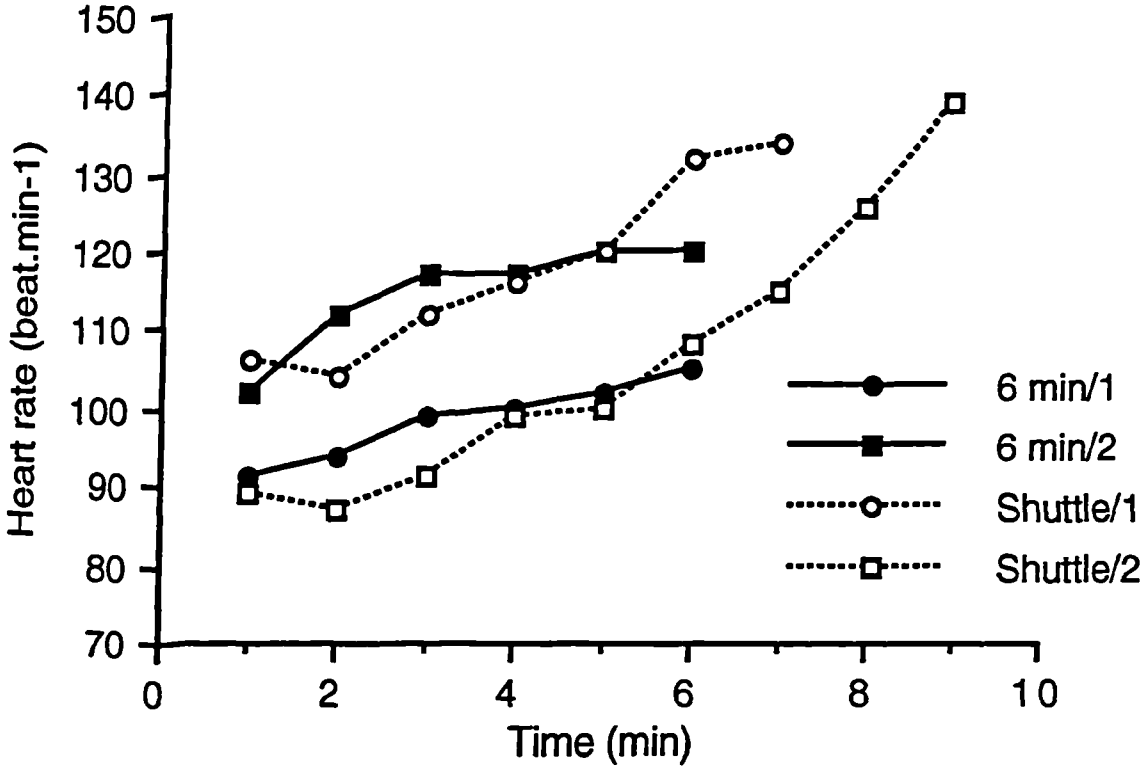
TABLE 9.4 The mean (SD) maximal heart rate (beat.min^{-1}) attained and corresponding mean percentage values on the shuttle walking tests and the six minute walking tests.

Test		heart rate	%
Shuttle walking test	1	131 (5)	77.5 (12.6)
	2	131 (6)	77.7 (14.4)
Six minute walking test	1	114 (5)	67.7 (10.2)
	2	119 (5)	70.7 (13.9)
	3	121 (5)	72.1 (13.7))

TABLE 9.5 The relationship between the distance (m) walked on the shuttle walking test or the six minute walking test with the percentage of maximal heart rate attained, [(210-0.65) x age].

Test		r
Shuttle walking test	1	0.71
	2	0.74
six minute walking test		
	1	0.39
	2	0.54
	3	0.72

FIGURE 9.8 The heart rate response (beat.min^{-1}) to the shuttle walking test and the six minute walking test of two representative patients.



was less strong between the lung function values and performance on the 6 MWT, eg the same values for the first 6 MWT presented r values of 0.45 (FEV_1) and 0.40 (FVC). The correlation coefficients for performance on all the walking test and lung function values are shown in Table 9.6.

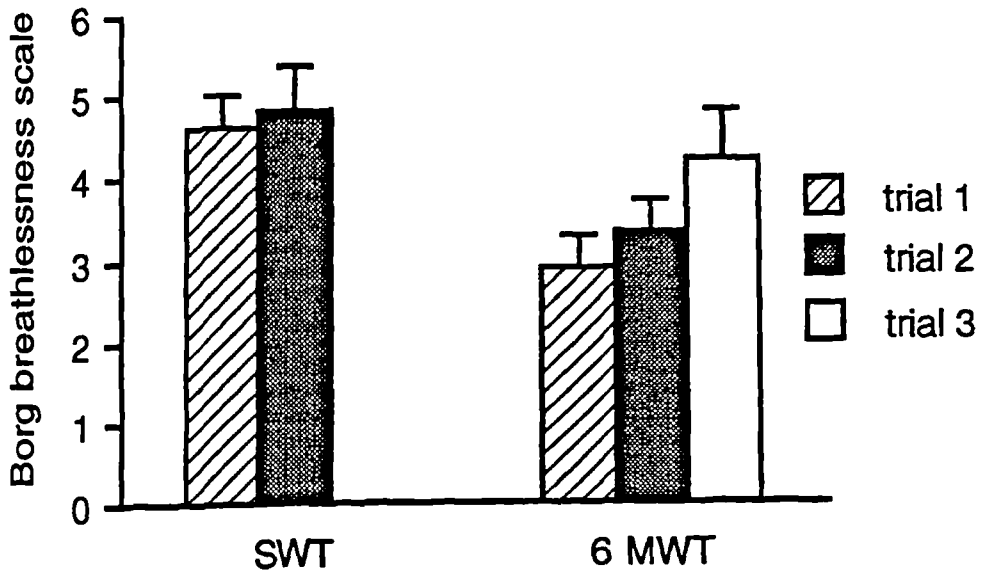
The mean Borg scale reported at the end of each exercise test is represented in Figure 9.9. The mean maximal Borg score recorded was not significantly different between the two shuttle test walks. Friedmans two-way analysis of variance revealed a significant difference between the response at the end of the three 6 MWTs. The response rose from a mean value of 2.9 to 4.2 on trial three. The mean maximal Borg scale was marginally but not statistically greater in the final shuttle walk compared to the final 6 MWT. Nine out of the 15 patients reported to be more breathless upon completion of the shuttle walking test than the 6 MWT. Two patients reported greater breathlessness after the 6 MWT, one of these patients did present with an increased level of breathlessness at rest on the day of the 6 MWT than on the day of the shuttle test. The highest rating after the shuttle test was 9 [very, very severe (almost maximal)] and 7 (very severe) for the 6 MWT. The correlation coefficient for the scoring on these two tests was moderate (rho=0.60).In addition, the mean base resting values recorded for the three visits were significantly different for the first visit compared to the second and third visits, but the resting value was not different for the visit of either the shuttle walk or the 6 MWT alone.

The analysis of the CRDQ responses revealed there was a significant difference between the scores of the mastery component of the questionnaire between the first visit and the visit of the 6 MWT. Otherwise, for all other components on all three visits there was no difference in the scores that could represent a change in the patients overall psychological/emotional status. There appeared to be no

TABLE 9.6 Pearson Product Moment correlations between the distance (m) walked on the shuttle walking test or the six minute walking test with the spirometry results.

Test	FEV_1	FVC
Shuttle walking test 1	0.57	0.55
2	0.52	0.41
six minute walking test 1	0.47	0.39
2	0.45	0.35
3	0.44	0.38

FIGURE 9.9 Mean (SEM) maximal Borg score post exercise for the shuttle walking test and the six minute walking test.



relationship between the distance walked and the scoring on the CRDQ. At best there was a moderate correlation between the dyspnoea score and the distance walked on the first 6 MWT (rho =-0.61).

9.4 DISCUSSION

The results of the present study suggest that the shuttle walking test provokes a symptom limited performance in this group of patients, whilst the 6 MWT although potentially may stimulate an equivalent performance appears not to do so.

The fundamental difference between the two walking tests employed for this study was the element of pacing. The shuttle walking test is an externally paced and incremental test whilst the 6 MWT relies on the patients intrinsic ability to gauge an appropriate speed to provoke a maximal performance. Furthermore, depending upon the manner in which the 6 MWT is conducted and the amount of encouragement offered, the cardio-respiratory system may or may not have been stressed (Fig.9.8). Inconsistencies of this nature probably contribute to the considerable variation in the walking performance reported for clinically similar patient groups between trials (Beaumont et al 1985, Swerts et al 1990, McGavin et al 1978). This makes it difficult to make valid comparisons between studies. The results (mean distance 530.9 m) of the present study do not relate well to previously reported distances in clinically similar groups (Mungall & Hainsworth 1979, mean FEV_1 1.4 l, 12 MWT result 900.6 m, Butland 1982, mean FEV_1 1.3 l, 6 MWT result 413 m). The results of the present study allow the direct comparison not only of patients' response to the shuttle walking test and the 6 MWT but also the comparison of the ranking of the two tests for the patients. Removing the outlier increases the correlation to rho=0.90. Therefore it could be concluded that for most of

the patients in this study performance on the shuttle walking test and the 6 MWT were well correlated. The same two patients performed the longest and shortest distance for both tests. The ranking for the other positions was broadly similar +/- 3 positions but there were two patients for whom the ratings were different. The first patient was ranked third for the shuttle test but fourteenth in the 6 MWT, suggesting that the patient found it difficult to pace himself to perform a symptom limited maximum test for the latter. The second patient was placed second in the 6 MWT but seventh in the shuttle walking test. This patient may have performed maximally during the 6 MWT and not during the shuttle walking test. Alternatively the other patients may have performed sub-maximally on the 6 MWT and maximally on the shuttle test to climb the rankings.

As a result of this self pacing the 6 MWT may be either a sub-maximal or maximal test in any individual at any one time (for the relative merit of these two forms of testing see 2.3). Notable authors on clinical exercise testing (Spiro 1977, Jones 1988) recognise that an incremental exercise test is more likely to reveal a patient's symptoms or limitation to exercise than either a self paced or single rate exercise test. The heart rate data (Fig. 9.7 & Table 9.4) support the proposal that the shuttle walking test consistently provokes an apparently symptom limited maximum performance. For this study there was no significant difference between the distances walked on trial 1 and 2 of the shuttle walking test. The patients stressed their cardio-vascular system equivalently for both trials. This heart rate response is consistent with the trials of Spiro et al (1975) and Carter et al (1987) examining exercise tolerance in patients with CAL and indicative of a ventilatory limit to functional capacity. The mean maximal heart rate recorded for the third 6 MWT was significantly lower that for the second shuttle test as was the rise in heart rate from the resting values. The

heart rate for the 6 MWT was significantly different for trials 1 vs 3 but not for the alternative two comparisons. These data, combined with the distance walked, tends to cloud the issue when considering relative reproducibility and highlights the unpredictability of a self paced test as patients appear to perform to relatively differing capacities of their cardiac reserve for each trial.

The shuttle walking test distance, perhaps not surprisingly, relates more strongly to the percentage of the maximal heart rate attained than the 6 MWT. The external pacing again evokes a consistent relationship whereas the 6 MWT does not appear to do so.

The maximal nature of the shuttle test is further supported by the Borg breathlessness scale rating and the results of the present study are consistent with the previous reports by Silverman et al (1988) and Belman et al (1991). The shuttle test resulted in a reproducible ratings which were higher than those following the 6 MWT (Fig. 9.10). On the other hand the 6 MWT resulted in inconsistent reporting of breathlessness as is often found with a sub-maximal test. Overall these results suggest that the shuttle test provokes a consistent maximal performance as measured both objectively and subjectively and provides a more reproducible exercise test than the 6 MWT.

External pacing allows valid inter and intra-subject comparison. Patients who have completed 500 m in an incremental walking test have experienced a common exercise challenge. This is not necessarily the case for patients completing similar distances in self-paced 6 or 12 minute walking tests so that conclusions regarding their respective functional capacities may be ill founded. It has been suggested that the habitual nature of walking may prevent a self paced test from fully demonstrating the possible beneficial effects of any treatment (Swinburn et

al 1985) and treatment effect may be more apparent with an incremental externally paced exercise test. The shuttle test may enable more effective comparison of different approaches to patient management and therapy than has previously been possible using existing field exercise tests. It is interesting to note that the one patient who performed markedly better on the shuttle test than on the 6 MWT (Fig.9.6) found it difficult to pace himself for the 6 MWT on all three occasions. The extent of his disability was obviously revealed more clearly by the shuttle test than by the traditional 6 MWT.

The defined speeds of walking in the shuttle test ensure that the workload increases in a manner which provides an incremental and qualitatively similar cardio-respiratory stress for all the patients. The heart rate response (Fig.9.9) provides evidence of this graded cardio-vascular response . The shuttle test, unlike the six or twelve minute tests where effort may be maximal from the start, stresses the patient progressively to a symptom limited maximum. This gradual increase in exercise intensity increases the safety of the test.

It has been reported that an externally paced step test is a reproducible and standardised method of assessing functional capacity in normal subjects (Jones et al 1971). However, the performance of patients with severe CAL on a paced step test shows a marked learning effect (Swinburn et al 1985). A 96% improvement in performance over the first four tests has been reported. Because reproducible results are obtained regardless of whether the patient completes just one or all twelve levels the shuttle test is more appealing for the assessment of patients with severe airways disease than the 6 MWT. Morrice & Smithies (1984) reinforced this point in their proposal of the 100 m walk, suggesting that a 6 MWT was too arduous for the severely affected patient. The shuttle walking test, by

incorporating a wide range of walking speeds, allows the monitoring of the progress of all patients using a single exercise test.

Taking the results from a previous study (Chapter 5) and comparing the results with that of McGavin et al (1976) it is apparent that performance on the shuttle walking test relates well to the $\dot{V}O_{2\,peak}$. The original study of the 12 MWT revealed a correlation coefficient of r=0.52, compared to the value r=0.88 for the corresponding value in the shuttle walking test. Swinburn et al (1985) used the 'Oxylog' during the 6 MWT but does not quote a correlation coefficient between the two values. In their study patients were observed to have a lower ventilatory and $\dot{V}O_{2\,peak}$ response than to the self paced walking test than to the paced step test. This indicates that patients tend to select a speed that is comfortable rather than stress themselves to a symptom limited performance. They would consequently fall short of attaining their $\dot{V}O_{2\,peak}$ in a self paced walking test.

In conclusion it appears that the responses to the two walking tests are quite different. The results suggest that the shuttle walking test provokes a symptom limited maximum performance whereas the 6 MWT results in a sub-maximal performance. The shuttle walking test is as acceptable to the patients as the traditional 6 MWT, whilst remaining a simple exercise test for both the patient and operator. It offers distinct advantages to the operator/investigator over the 6 MWT, providing a standardised exercise test that is reproducible and allows valid inter-subject comparison.

10. GENERAL DISCUSSION

The studies described in this thesis were designed to develop and validate a performance test which could be used to assess the functional capacity of patients with CAL.

Patients often present to their doctor with a limitation in their ability to sustain functional activities such as walking, dressing and stair climbing. After symptoms are identified examination is directed towards lung disorders. Further laboratory based investigations focus on identifying the disease process. This process relies heavily on the assumption that the degree of organ impairment closely relates to the inability to perform functional activities (disability) and also the severity of symptoms experienced daily (handicap), ie

Organ impairment → Disability → Handicap.

It has been repeatedly documented in the literature that a patient's static lung function neither predicts nor relates well to his exercise tolerance and consequently his ability to cope with activities of daily living. Frequently exercise testing in some form is incorporated into overall patient assessment. However, to avoid the need for technically demanding exercise testing some investigators continue to use lung function measurements (either simple or complex) to predict a patient's exercise tolerance rather than measure it directly (Carter et al 1987, Carlson et al 1991). Such procedures even require the patient to undergo quite complex respiratory measurements in an attempt to estimate the patient's $\dot{V}O_{2\,peak}$.

Acknowledgment of the importance of the measurement of functional capacity in overall patient assessment has resulted in a wealth of exercise studies proposing a variety of test procedures in both the laboratory and the field (Butland et al 1982, Beaumont et al 1985). This has obviously lead to the measurement of change in exercise

tolerance as an outcome measure in a variety of therapeutic interventions. Surprisingly, much of the literature reporting self paced field exercise test seems to have overlooked the poor relationship which these tests exhibit with $\dot{V}O_{2\,peak}$. Researchers and clinicians continue to use corridor walking tests, assuming them to be an accurate indicator of a patient's functional capacity. The self paced tests are commonly used as a cheap and some would argue effective exercise test. But, self paced and conducted over a fixed period of time they cannot guarantee to provide either a maximal or sub-maximal exercise test. In practice they be either maximal or sub-maximal, depending on the patient group being tested and a variety of psychosocial influences. They cannot claim to provide a sub-maximal endurance test, often the exercise test of choice to indicate an improved exercise tolerance after intervention.

Recognition of the inherent problems associated with the self paced walking tests led to the development of the shuttle walking test described in chapter 1. The subsequent reproducibility studies indicated that the shuttle walking test was equally as reliable, if not more so than the corridor self paced tests giving reproducible results after just one practice walk. In fact, in the study comparing the shuttle test with the 6 MWT there was no significant difference between the first and second shuttle walk, although a small group of patients had performed a shuttle test previously.

The initial study also indicated that although the exercise was to a symptom limited maximum there was a considerable cardiac reserve, suggesting that these patients' exercise tolerance was not limited by cardio-vascular insufficiency. The lactate data (Chapters 7 & 8) excludes a local muscle fatigue as the source of limitation It could of course be argued that maximal testing is very

unreliable in patients with CAL not least because of the motivation required and the difficulty individuals experience judging their individual maximum. In patients this is compounded by the natural variability of the condition. Opinions exist suggesting that this is not necessarily the case and performance on a symptom limited maximum test in patients with stable CAL is consistent (Severa et al 1983, Brown et al 1985).

The data presented in this thesis supports this proposal. The shuttle walking test, a symptom limited maximum exercise test, produced more reproducible test/retest results than the 6 MWT. Furthermore the subjective assessment of breathlessness post shuttle walking test was more reproducible than that post 6 MWT. This data is consistent with the results of Silverman et al (1988) and Belman et al (1991) demonstrating that patients subjective rating of dyspnoea is more reproducible during/after a symptom limited exercise test. Reviewing the individual Borg scores and the maximal heart rate data recorded during the 6 MWT indicated that the group of patients did not approach the 6 MWT uniformly, unlike the approach to the shuttle walking test. As a consequence of this intrinsic variability of the 6 MWT, misleading conclusions as to the patients true exercise tolerance could be drawn.

It is widely recognised that the 6 or 12 MWT do not facilitate comparison of patients' results between centres because of the lack of standardisation and susceptibility to variations in the motivation of the patients and supervisor (Clarke 1991). It is proposed that the shuttle walking test minimises both of these influences. Firstly, the external pacing standardises the test and does not allow the patient to over-ride the signals. Secondly, the instructions are standardised to limit operator effect and the only encouragement that was received by the patient was 'good' as a compliment to their pacing, ie if they turned

around the cone as the bleep sounded. The patient was not encouraged to walk any faster which, until the final stages of the exercise would be inappropriate. It would be interesting to examine the effect of standardised verbal encouragement on patients' performance. However as the shuttle test is on the whole a symptom limited maximal test it is felt that encouragement would be unlikely to alter the patients' perception of breathlessness, the primary end point of the test.

The validation of the shuttle walking test provided strong support for the proposal that this field exercise test did reflect an individual's cardio-respiratory capacity, providing a more objective field measure of a patient's exercise tolerance than has previously available. Reduced exercise tolerance and a parallel fall in $\dot{V}O_{2\,peak}$ is well documented in CAL (Patessio et al 1991). It would therefore seem reasonable to adopt a simple but reliable exercise test that reflects this physiological parameter to monitor the course of the disease and the response to drug therapy etc. This study also allowed the examination of the limitations to exercise in this patient group. It appeared that most patients stopped exercising because they were unable to maintain the level of ventilation demanded for the task, although a minority appeared to stop before this point, consistent with the results previously reviewed by Rampulla et al (1992).

Consideration has been paid to the development of equations based upon resting spirometric measurements to define which patients are ventilatory limited. It is questionable whether any of the resting measures are in fact of any use in this regard (Patessio et al 1991). This issue is further complicated by suggestions that exercise may induce a variable amount of bronchodilation (Sean et al 1989) and a variable increase in the FRC (Dillard et al 1985). The ventilatory requirement for a given level of

exercise is dictated by the equation-

$$\dot{V}E = \frac{K \times \dot{V}CO_2}{PaCO_2 \times (1-V_D/V_T)}$$

(K is a constant)

In CAL patients' ventilation/perfusion mismatching causes hypoxaemia (lung units with a low V/Q) and a high V_D/V_T (reflecting lung units with a high V/Q), the latter a measure of inefficiency of CO_2 exchange. A second cause of high ventilatory requirements is an early onset of lactic acidosis. Employing the Douglas bags techniques reported in Chapter 5 it was not possible to detect a anaerobic threshold using the method proposed by Beaver et al (1986), ie looking for an inflection in the $\dot{V}CO_2/\dot{V}O_2$ slope. However the mean maximal R value for this group exceeded 1.0 consistent with attaining maximal oxygen uptake. It is widely reported that an anaerobic threshold is measured at approximately 55-65% of maximal oxygen uptake, therefore it would be traditionally anticipated that a significant increase in blood lactate concentration should have been observed. This traditional view has been challenged by Brookes (1985) who questioned the notion that the exercising muscle tissue becomes anoxic and therefore becomes anaerobic with significant reserves in cardiac output, muscle blood flow, capillary dilation and arterial-venous O_2 difference. Brookes (1985) then challenges the fact that no proponents of the anaerobic threshold concept have in fact attempted to demonstrate muscle anoxia.The author summarises that " basing the anaerobic threshold on the presumption of an O_2 deficit during sub-maximal exercise is a serious mistake".

The group included for the validation study included a wide range of disease severity. Until recently it has been assumed that the patient most likely to be able to exercise to a level adequate to produce a lactic acidosis is less severely impaired. It has now been proposed that the work

rate at which the anaerobic threshold occurs does not relate well to resting spirometric measurements (Patessio et al 1991). The reason for this, it is suggested, is that the degree of impairment of the pulmonary vasculature does not necessarily relate to the pathological process responsible for the airways obstruction. This pathological mechanism would limit the amount of oxygen supply to exercising muscles more so that the reduction in lung volume. This would certainly be true for the two patients who produced a significant lactate response described in Chapter 8. These patients did not have the highest lung function values, in fact one patient was at the bottom of the range. The development of a significant lactic acidosis depends upon a number of factors, including muscle bulk, muscle fibre type and their pattern of recruitment, the oxidative enzyme capacity of the fibres and the capillary network serving the exercising muscle. It may be suggested that the individuals recruited for this present study did not exercise to a high enough intensity to recruit a high percentage of type II muscle fibres, known to have a high concentration of lactate dehydrogenase, facilitating a more rapid reduction of pyruvate to lactate (Skinner and McLellan 1980).

Interestingly 6/10 patients were judged to attain a ventilatory anaerobic threshold during the treadmill test. The considerable disparity between these two measures ('lactate' anaerobic threshold and 'ventilatory' anaerobic threshold) is worthy of further investigation in this patient group. In sports science there is considerable interest in the coincidental rather than causal relationship between these two variables (Loat & Rhodes 1993) and with the addition of computerised equipment into the larger hospitals it is now possible to investigate this in more depth. It is suggested that the group of patients who will respond to an exercise training programme are those who can mount a lactate response [because these

patients would tend to have more ventilatory drive and hyperventilation in response to exercise, accompanied by a reduced efficiency in gas exchange (Wasserman et al 1989)]. Unfortunately it is likely that this criterion will automatically exclude a large percentage of the population with CAL. It should be remembered that the buffering of lactic acid is not the only cause of increased ventilation with increasing levels of exercise, but also the increased aerobic metabolism and possibly hyperventilation with exercise. The latter may be amenable to modulation.

Interestingly, Wasserman et al (1989) reviewed the work by Sue et al (1989) and concluded that two thirds of the patients developed a significant metabolic acidosis detected either invasively or non invasively and suggested that *exercise* training has the potential to improve exercise tolerance in patients who develop 'metabolic acidosis' (measured using ventilatory or standard bicarbonate parameters). Furthermore he proposes that the V-slope may in fact be preferable to the invasive monitoring of blood lactate concentrations.

Kumagai et al (1982) examined the usefulness of using the ventilatory threshold as an assessment tool in performance evaluation for healthy individuals. Their results demonstrated that the ventilatory threshold related strongly to the individual's $\dot{V}O_{2\ max}$. This principle may also be valid in the assessment of patients with CAL. Further evidence supporting the dissociation between the ventilatory and anaerobic threshold is observed in the adaption of each threshold to training. Gaesser and Poole (1986) reported a greater increase in the lactate threshold that in the ventilatory threshold over a 6 week training period in normal individuals, suggesting that the regulatory mechanism between these two thresholds is different. It is worth considering the implication of these results for patients with CAL. If we accept the measurement

of a metabolic acidosis to be valid by either invasive or non invasive techniques as suggested by Wasserman (1989) the theoretical acceptance rate to pulmonary rehabilitation is automatically increased (by virtue of attaining an anaerobic threshold). It would appear from this results reported in this thesis and alternative studies (Sue et al 1988, Nery et al 1983) that patients do not necessarily manifest a threshold value for both variables. Therefore for the patients who do not produce a significant lactate response an alternative assessment must be sought. In conjunction with evidence suggesting that these threshold values are coincidentally linked it would be worth incorporating assessment of the ventilatory anaerobic threshold pre- and post training patients with CAL.

The results of this thesis and the review of other studies (Sue et al 1988, Hagberg et al 1982, Neary et al 1985, Hughes et al 1982) appear to suggest that the association between lactate and ventilatory thresholds may be coincidental in patients with CAL. Although this relationship has been challenged and investigated in sports science in respiratory medicine the relationship continues to be assumed to be causal. During exercise ventilation is usually driven by a combination of neural and humoral mechanisms. In the absence of, or modified humoral signals (McArdles disease and glycogen depletion), or in response to different input from higher centres or peripheral receptors (eg speed of movement varies) the respiratory centre still produces an appropriate ventilatory response.

The shuttle walking test has the potential be used to estimate an individualised walking speed that would be an effective training level. By judging a patient's performance on the shuttle walking test a high or low intensity training programme can be prescribed. The possibilities of this potentially simple, accessible and

acceptable method of prescribing an appropriate exercise programme warrants further investigation. The efficacy of a brisk walking training programme in healthy middle aged males (Stensel et al 1992) has convincingly been demonstrated and a study of its application to a patient population is required. If a low level training programme proved to be successful in increasing the individual's functional capacity and/or endurance performance the implications for decreasing the level of disability of the patients presenting with CAL would be great. Clinically the efficacy of low level training has been examined by Freeman et al (1990) in a group of cystic fibrosis patients with encouraging results. Unlike the rehabilitation programmes offered in North America (Goldstein et al 1992) consisting often of a six week inpatient intensive training programme a community based walking programme would be more sustainable and acceptable to the European population. Furthermore this type of exercise prescription could be based at district general hospitals that do not possess extensive exercise testing equipment. It would be speculative to suggest that an improvement in shuttle test performance would result from training.

If a patient manifests a true ventilatory limit to exercise performance it is well documented that $\dot{V}O_{2\,peak}$ rarely improves (Neiderman et al 1991, Simpson et al 1992), unlike training a healthy population. Therefore, in theory the performance on the shuttle test may remain static, this however requires further study. On the other hand if the limitation to exercise is not ventilatory (Rampulla et al 1992) but in fact peripheral, a heightened perception of breathlessness (Belman & Kendregan 1981) or psychological (motivation) then an improvement in the shuttle test may be anticipated/observed post training/rehabilitation. It is reported that the individual assessment of breathlessness bears little relationship to either the severity of the airways limitation or the external load (Gottfried et al

1981). Certainly in the present study the reported Borg breathlessness ratings post exercise do not relate well to either the static lung function measurements or performance. Breathlessness, like pain, has both physical and emotional components. Unfortunately it is not known which component is more important in disease (Jones 1992). Dyspnoea potentially impairs an individual's 'quality of life' particularly if the perception is inappropriate to the level of exercise achieved. On the other hand the perception of dyspnoea can be a useful clinical tool warning of deterioration.

Despite initial difficulties with the Oxylog system reported in Chapter 6, their subsequent modification allowed the Oxylog equipment to be incorporated into the protocol described in Chapter 7. This study reaffirmed the assumption of the maximal stimulus to exercise that the shuttle walking test provides (proposed in Chapter 5). The patients demonstrated a strong tendency towards a ventilatory limit. The underestimation of $\dot{V}_I$ of the Oxylog has been reported in other literature. The respective relationship between $\dot{V}O_{2\ peak}$ and performance was r=0.88 (treadmill & Douglas bags vs shuttle test performance), r= 0.93 (treadmill & breath by breath computer gas analysis vs shuttle test performance) and finally r=0.81 (directly measured shuttle test performance with the Oxylog).

The use of the shuttle walking test has already been extended into other areas where exercise testing is appropriate in clinical medicine. Perhaps the most obvious alternative application of the shuttle walking test is into the area of cardiac rehabilitation for patients who are post coronary artery by-pass surgery or post myocardial infarction. The test is presently under examination for its reproducibility and suitability in this group of patients. A further area that the shuttle walking test has been employed in the assessment of fitness of patients with

chronic low back pain. Unpublished data suggest that this is a reproducible measure of exercise tolerance in this patient group, with pain as the limiting factor to an improved performance. The shuttle walking test could easily be incorporated into clinical pharmacological trials. The test has most recently been employed as a measure of functional capacity to examine the usefulness of a newly developed CAL specific quality of life questionnaire. Scoring on the functionally based questionnaire revealed a strong relationship with shuttle test performance (Hyland et al 1993).

In summary, the studies reported in this thesis consistently demonstrate that the shuttle walking test is a reproducible exercise test of functional capacity in patients with CAL. This group of patients have a reduced exercise tolerance in comparison to a healthy age matched control group. Overall it would appear that patients terminate exercise because of a ventilatory limit, ie an inability of the lungs to match the required levels of ventilation. The studies reported in Chapters 4, 5, 7 and 9 exclude both a peripheral muscle fatigue and a cardio-vascular cause for the cessation of exercise. However motivation and tolerance to dyspnoea must not be overlooked in this group of patients. Despite this reduced exercise tolerance the shuttle walking test is sensitive enough to provide an accurate estimation of an individuals $\dot{V}O_2$ max, the traditional reference measure of cardio-respiratory capacity. The shuttle test offers a simple but reliable exercise test that is acceptable to the patients and attractive to the operator primarily because of its inherent standardisation. This allows more valid intra-, inter-subject and multi-centre comparison of patients than has previously been possible with simple exercise tests. The shuttle test can be used in any District General Hospital as a cheap but effective alternative to a laboratory exercise test. The shuttle test does not replace

formal laboratory exercise testing but provides a useful adjunct to current practice in patient assessment and management.

REFERENCES

ACSM. (1991). Guidelines for exercise testing and prescription. (4th ed). Lea & Febiger, Philadelphia.

ADAMS L and GUZ A.(1991). Dyspnoea on exertion. In: Exercise pulmonary physiology and pathophysiology (Lung biology in health and disease series/52).(Ed Whipp BJ & Wasserman K). pp449-494. Marcel Dekker inc., New York.

AITKENHEAD AR and SMITH G.(1990). Textbook of anaesthesia (2nd ed). Churchill Livingstone, Edinburgh.

ALTMAN G. (1980) statistics and ethics in medical research. BMJ;**281**:1336-1338.

ALTMAN G. (1991) Practical statistics for medical research (1st ed). Chapman and Hall, London.

ALTOSE DM. (1985). Assessment and management of breathlessness. Chest;**88**:77s-83s.

AMERICAN THORACIC SOCIETY. (1986). Evaluation of impairment/disability secondary to respiratory disorders. Am. Rev. Respir. Dis;**133**:1205-1209.

AMERICAN THORACIC SOCIETY. (1987). Standards for the diagnosis and care of patients with chronic obstructive pulmonary disease (COPD) and asthma. Am. Rev. Respir. Dis; **136**:225-244.

ANDERSEN KL, SHEPHARD RJ, DENOLIN H, VARNAUSKAS E et al (1971). Fundamentals of exercise testing. World Health Organisation, Geneva.

ASKANAZI J, SILVERBERG PA, FOSTER RJ, HYMAN AI et al. (1980). Effects of respiratory apparatus on breathing pattern. J. Appl. Physiol;**48**:577-580.

ASTRAND P-O and RODAHL K. (1986). Textbook of work physiology. (3rd ed). McGraw hill.

BALKE B and WARE R. An experimental study of physical fitness in air force personnel. U.S Armed Forces M. J;**10**:675.

BALLAL MA and McDONALD IA. (1982). An evaluation of the oxylog as a portable device with which to measure oxygen consumption. Clin. Phys. Physiol. Meas;**3**:57-65.

BAUMGARTNER TA and JACKSON AS. (1987). Measurements for evaluation in physical education and exercise science. (3rd ed). W C Brown, Iowa.

BEAVER WL, WASSERMAN K and WHIPP BJ. (1986). A new method for detecting anaerobic threshold by gas exchange. J. Appl. Physiol;**60**:2020-2027.

BEAUMONT A, COCKCROFT A and GUZ A. (1985). A self paced treadmill walking test for breathless patients. Thorax;**40**:459-464.

BECK CK, BABB TG, STAATS BA and HYATT RE. (1991). Dynamics of breathing during exercise. In: Exercise pulmonary physiology and pathophysiology (Lung biology in health and disease series/52).(Ed Whipp BJ & Wasserman K).pp67-98 Marcel Dekker inc., New York.

BELMAN MJ and MITTMAN C. (1980). Ventilatory muscle training improves exercise capacity in chronic obstructive pulmonary disease patients. Am. Rev. Respir. Dis;**121**:273-280.

BELMAN MJ and KENDREGAN BA. (1981). Exercise training fails to increase skeletal muscle enzymes in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**123**:256-261.

BELMAN MJ. (1986). Exercise in chronic obstructive pulmonary disease. In: Clin. Chest Med.**4**:585-597. (Ed Make BJ). W B Saunders, Philadelphia.

BELMAN MJ, BROOKS LR, ROSS DJ AND MOHSENIFAR Z. (1991). Variability of breathlessness measurement inpatients with chronic obstructive pulmonary disease. Chest;**99**:566-71.

BELMAN M, EPSTEIN LJ, DOORNBOS, ELASHOFF et al. (1992). Noninvasive determinations of the anaerobic threshold, Reliability and validity in patients with COPD. Am. Rev. Respir. Dis;**102**:1028-34.

BERGNER M, BOBBITT RA, CARTER WB and GILSON BS. (1981). The sickness impact file: development and final revision of a health status measure. Med. Care;**19**:787-806.

BLAND JM and ALTMAN DG. (1986). statistical methods for assessing agreement between two methods of clinical measurements. Lancet;**42**:307-310.

BORG GAV. (1982). Psychophysical bases of perceived exertion. Med. Sci. Sport. Ex;**14**:377-381.

BROOKS GA. (1985). Anaerobic threshold: review of the concept and direction for future research. Med. Sci. Sport. Ex;**17**:22-31.

BROWN HV and WASSERMAN K. (1981). Exercise performance in chronic obstructive pulmonary disease. In: Symposium on chronic obstructive lung disease. Med. Clin. N.Amer;**65**:525-545.

BROWN SE, FISCHER CE, STANSBURY DW and LIGHT RW. (1985). Reproducibility of $\dot{V}o_{2\,max}$ in patients with chronic air-flow limitation. Am. Rev. Respir. Dis;**131**:435-483.

BRUCE RA, KUSUMI F, and HOSMER D. (1973). Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. Am. Heart. J;**85**:546-562.

BRUCE RA. (1984). Methods of exercise testing: step test, bicycle, treadmill, isometrics. In: Exercise in cardiovascular health and disease.(Ed.Amsterdam EA, Wilmore JH and DeMaria AN). pp 149-160. York Medical Books.

BURROWS B, FLETCHER CM, HEARD BE, JONES NL et al. (1966). The emphysematous and bronchial types of chronic airways obstruction. Lancet;**1**:930.

BURROWS B. (1991). Epidemiological evidence for different types of chronic airflow limitation. Am. Rev. Respir. Dis;**143**:1452-55.

BUTLAND RJA, PANG J, GROSS ER, WOODCOCK AA and GEDDES DM. (1982). Two-, six- and twelve- minute walking tests in respiratory disease. BMJ;**284**:1607-1608.

BUTLER JP, LEITH D and JACKSON AC. (1986). Principles of measurement: applications to pressure, volume and flow. In: Handbook of Physiology Section 3. The respiratory system (Ed Fishman AP). Volume 3 Part I p15-54 Williams and Wilkins Company, Baltimore.

BYE PTP, ESAU SA, LEVY RD, SHINER RJ et al. (1985). Ventilatory muscle function during exercise in air and oxygen in patients with chronic airflow limitation. Am. Rev. Respir. Dis;**132**:236-240.

CALLES-ESCANDON J and FELIG P. (1984). Fuel-hormone metabolism during exercise and after physical training. Clin. Chest Med.**5**:3-20 (Ed-LOKE J). W B Saunders, Philadelphia.

CARLSON DJ, RIES AL, KAPLAN RM. (1991). Prediction of maximal exercise tolerance in patients with COPD. Chest;**100**:307-311.

CARTER R, PEAVLER RM, ZINKGRAF S, WILLIAMS J and FIELDS S. (1987). Predicting maximal exercise ventilation in patients with chronic obstructive pulmonary disease. Chest;**92**:253-259.

CASABURI R, WASSERMAN K, PATESSIO A, IOLI F et al. (1989). Anew perspective in pulmonary rehabilitation: anaerobic threshold as a discriminant in training. Eur. Respir. J;**suppl 7**:618-623s.

CASABURI R, PATESSIO A, IOLI F, ZANABONI et al. (1991). Reduction in exercise lactic acidosis and ventilation as a result of exercise training in patients with chronic lung disease. Am. Rev. Respir. Dis;**143**:9-18.

CERRETELLI P, RAJINDER S, SIKAND S and FARHI LE. (1969). Effect of increased airway resistance on ventilation and gas exchange during exercise. J. Appl. Physiol;**27**:597-600.

CHERNIAK RM. (1977). Pulmonary function testing. W B Saunders, Philadelphia.

CHINN S. (1991). Repeatability and method comparison. Thorax;**46**:454-456.

CIBA GUEST SYMPOSIUM. (1959). terminology, definitions and classification of chronic pulmonary emphysema and related conditions. Thorax;**14**:286.

CIESLA N. (1989). Postural drainage, positioning and breathing exercises. In: Chest physiotherapy in the intensive care unit. Ed. Mackenzie CF, Imle PC and Ciesla N. Williams & Wilkins, Baltimore.

CLARK CJ. (1991). Strategies for the evaluation of rehabilitation treatment. Europ. Respir. Rev;**1**(suppl 6):475-481.

CLAUSEN JL. (1990). The diagnosis of emphysema, chronic bronchitis, and asthma. Clin Chest Med **11**:363-374 (Ed-Hodgkins JE) W B Saunders, Philadelphia.

COHEN L and HOLLIDAY M. (1982). Statistics for social scientists. Paul Chapman publishing Ltd, London.

COCKCROFT AE, SAUNDERS MJ and BERRY G. (1981). Randomised controlled trial of rehabilitation in chronic respiratory disability. Thorax;**36**:200-03.

COCKCROFT A, BEAUMONT A, ADAMS L and GUZ A. (1985). Arterial desaturation during treadmill and bicycle exercise in patients with chronic obstructive airways disease. Clin. Sci;**68**:327-332.

COLE RB & MACKAY AD. (1990). Essentials of respiratory disease (3rd ed). Churchill Livingstone, Edinburgh.

COLLETT PW, PERRY C and ENGEL LA. (1985). Pressure-time product, flow, and oxygen cost of resistive breathing in humans. J. Appl. Physiol;**58**:1263-1272.

COOPER KH. (1968). A means of assessing maximal oxygen intake. JAMA;**203**:3,135-138.

COTES JE. (1979). Lung function assessment and application in medicine. (4th ed). Blackwell Scientific Publication, Oxford.

COTES JE, POSNER V and REED JW. (1982). Estimation of maximal exercise ventilation and oxygen uptake in patients with chronic lung disease. Bull. Europ. Physiopath. Resp;**18**

(suppl. 4):221-228.

CREMONA G, OTULANA BA, MIST B, SHARPLES L et al. (1991). Twelve minute walking distance correlates with maximal oxygen consumption ($\dot{V}O_2$) max on an incremental treadmill test for patients with pulmonary vascular disease (PVD). Thorax;**46**:297p.

CROFT J and DOUGLAS A. (1981). Respiratory diseases (3rd ed). Blackwell Scientific publications, Oxford.

CUMMINGS G & SEMPLE S. (1973). Chronic bronchitis and emphysema. In: Disorders of the respiratory system. pp327-352. Blackwell Scientific Publications, Oxford.

DANTZKER DR. (1987). Ventilation-perfusion inequality in lung disease. Chest;**91**:5:749-754.

DAVIDSON AC, LEACH R, GEORGE RJD and GEDDES DM. (1988). Supplemental oxygen and exercise ability in chronic obstructive airways disease. Thorax;**43**:965-971.

DILLARD TA, PIANTADOSI S and RAJAGOPAL KR. (1985). Prediction of ventilation at maximal exercise in chronic air-flow obstruction. Am. Rev. Respir. Dis;**132**:230-235.

DILLARD TA, PIANTADOSI S and RAJAGOPAL KR. (1989). Determination of maximum exercise capacity in patients with chronic airflow limitation.Chest;**96**:267-271.

Di PRAMPERO PE. (1992). An analysis of the factors limiting maximal oxygen consumption in healthy subjects. Chest;**101**:188s-191s.

DODD DS, BRANCATISANO T and ENGEL LA. (1984). Chest wall mechanics during exercise in patients with severe air-flow obstruction. Am. Rev. Respir. Dis;**129**:33-38.

DONAHOE M, ROGERS RM, WILSON DO and PENNOCK BE. (1989). Oxygen consumption of the respiratory muscles in normal and malnourished patients with chronic obstructive pulmonary disease. (1989). Am. Rev. Respir. Dis;**140**:385-391.

EDITORIAL. (1965). Definition and classification of chronic bronchitis. The Lancet;April 10:775-779.

ELLIOTT CG, CROMAR B, ADAMS TD, CRAPO RO et al. (1987). Measurement of anaerobic threshold in chronic airflow obstruction. Respiration;**52**:7-15.

FITTING JW. (1991). Respiratory muscle fatigue limiting physical exercise? Eur. Respir. J;**4**:103-108.

FLENLEY DC. Respiratory medicine. (1990). (2nd ed) Balliere Tindall.

FOLGERING H, DEKHUIJZEN R, COX N and VAN HERWAARDEN C. (1991). The rationale of pulmonary rehabilitation. Eur. Respir. Rev;**1**(suppl):464-471.

FREEDMAN S, LANE R and GUZ A. (1987). Breathlessness and respiratory mechanics during reflex or voluntary hyperventilation in patients with chronic airflow limitation. Clin. Sci;**73**:311-318.

FREEMAN W, WIERS DC, SAPIANO SB, WHITEHEAD JE, BURGE PS and CLAYTON RM. (1990). The twenty-metre shuttle-running test: a combined test for maximal oxygen uptake and exercise induced asthma? Resp. Med;**84**:31-35.

FREEMAN W, STABLEFORTH DE, CAYTON RM and MORGAN MDL. (1990). effect of low and high intensity aerobic training on physical fitness in adult cystic fibrosis. Thorax;**45**:781a.

GAESSER GA and POOLE DC. (1986). Lactate and ventilatory thresholds: disparity in time course of adaption to training. J. Appl. Physiol;**61**:999-1004.

GALLAGHER CG. (1990). Exercise and COPD. The medical clinics of N. America;**74**:619-642. (Ed-Posman JA & Cockcroft DW). W B Saunders, Philadelphia.

GALLON A. (1991). Evaluation of chest percussion in the treatment of patients with copious sputum production. Resp. Med;**85**:45-51.

GANONG WF. (1987). Review of medical physiology. (13th ed). Appleton & Lange, California.

GARDNER MJ and ALTMAN DG. (1989). Statistics with confidence - confidence intervals and statistical guidelines. British Medical Journal, London.

GIBSON GJ. (1990). Respiratory function during exercise. In: Respiratory Medicine (Ed.Brewis RAL, Gibson GJ and Geddes DM). pp 162-166 Balliere Tindall.

GOLDSTEIN RS, GORT EH, BROWN DL, STUBBING D et al. (1992).A controlled trial of respiratory rehabilitation. Am. Rev. Respir. Dis;**145**:767a.

GOTTFRIED SB, ALTOSE MD, KELSEN SG and CHERNIAK NS (1981). Perception of changes in airflow resistance in obstructive pulmonary disorders. Am. Rev. Respir. Dis;**124**:556-570.

GRASSINO A. (1989). Inspiratory muscle training in COPD patients. Eur. Respir. J;**2** (suppl. 7):581s-585s.

GRIMBY G, SALTIN B and WILHELMESEN L. (1971). Pulmonary flow-volume and pressure-volume relationship during sub-maximal and maximal exercise in young well

trained men. Bull. Physiopathol. Respir;7:157-167.

GRIMBY G, GOLDMAN M and MEAD J. (1976). Respiratory muscle action inferred from rib-cage and abdominal V-P partitioning. J. Appl. Physiol;41:739-752.

GUYATT GH, PUGSLEY SO, SULLIVAN MJ, THOMPSON PJ, BERMAN LB, JONES NL, FALLEN EL and TAYLOR DW. (1984). Effect of encouragement on walking test performance. Thorax;39:818-822.

GUYATT GH, TOWNSEND M BERMAN and PUGSLEY SO. (1987). Quality of life in patients with chronic airflow limitation. Br. J. Dis. Chest;81:45-54.

GUYATT GH, BERMAN LB, TOWNSEND M, PUGSLEY SO and CHAMBERS LW. (1987). A measure of quality of life for clinical trials in chronic lung disease. Thorax;42:773-778.

GUYATT GH, TOWNSEND M, J KELLER, SINGER J and NOGRADI S. (1989). Measuring functional status in chronic lung disease: conclusions from a randomised control trial. Respiratory Medicine;83:293-297.

HAGBERG JM, COYLE EF, CARROLL JE, MILLER JM et al. (1982). Exercise hyperventilation in patients with McArdles disease. J. Appl. Physiol;52:991-994.

HANSEN JE. (1984). Exercise instruments, schemes, and protocols for evaluating the dyspneic patient. Am. Rev. Respir. Dis;129:suppl s25-s27.

HARRISON MH, BROWN GA and BELYAVIN AJ. (1982). The 'Oxylog' an evaluation. ergonomics;25:809-820.

HICKS CM. (1988) Practical research methods for physiotherapists. Churchill Livingstone, London.

HOGG TC, MACKLEM PT and THULBECK WM. (1968). Site and nature of airways obstruction in chronic obstructive lung disease. N. Engl. J. Med;278:1355.

HOPKIN J. (1991). Genetics and lung disease. BMJ;302:1222-1223.

HOWARD P. (190). Clinical features and management. In: Respiratory Medicine (Ed. Brewis RAL, Gibson GJ and Geddes DM). pp520-533. Balliere Tindall, London.

HOWELL JBL. (1990). Breathlessness. In: Respiratory Medicine (Ed.Brewis RAL, Gibson GJ and Geddes DM). pp 221-228 .Balliere Tindall, London.

HUGHES EF, TURNER SC and BROOKS GA. (1982). Effect of glycogen depletion and pedalling speed on 'anaerobic threshold'. J. Appl. Physiol;52:1598-1607.

HUMPHREY SJE and WOLFF HS. (1977). The Oxylog. J. of Physiol;**267**:12p.

HYLAND M, BOTT J, SINGH SJ and KENYON CAP. (1993). Development and validation of a patient-completed questionnaire for assessing quality of life in patients with chronic obstructive pulmonary disease. Submitted to Health Psychology.

JAKEMAN P and DAVIES B. (1979). The characteristics of a low resistance breathing valve designed for the measurement of high aerobic capacity. Brit. J. Sports. Med;**13**:81-83.

JAKOBSSON Per EJ and JORFELDT L. (1990). Blood fuel metabolites at rest and during exercise in patients with advanced chronic obstructive pulmonary disease with and without chronic respiratory failure. Respiration;**57**:304-309.

JEFFERY PK. (1991). Morphology of the airway wall in asthma and in chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**143**:1152-1157.

JOHNSON AN, COOPER DF and EDWARDS RHT. (1977). Exertion of stair climbing in normal subjects and in patients with chronic obstructive bronchitis. Thorax;**32**:711-716.

JONES NL. Pulmonary gas exchange during exercise in patients with chronic airway obstruction. (1966). Clin. Sci;**31**:39-50.

JONES NL, JONES G and EDWARDS RHT. (1971). Exercise tolerance in chronic airways obstruction. Am. Rev. Respir. Dis;**103**:477-490.

JONES NL and BERMAN LB. Gas exchange in chronic airflow obstruction. (1984). Am. Rev. Respir. Dis;**129**(suppl):581-583.

JONES NL, KILLIAN KJ and STUBBING DG. (1985). The thorax in exercise. In: The thorax (Lung biology in health and disease, Part B vol 29). (Ed Roussos C and Macklem PT). pp627-662. Marcel Dekker inc., New York.

JONES NL. (1988). Clinical exercise testing. (3rd ed). W B saunders, Philadelphia.

JONES NL. (1991). Determinants of breathing patterns in exercise. In: Exercise pulmonary physiology and pathophysiology (Lung biology in health and disease series/52). pp 99-120. Marcel dekker inc., New York.

JONES PW, WAKEFIELD JM and KONTAKI E. (1987). A simple and portable paced step test for reproducible measurements of ventilation and oxygen consumption during exercise. Thorax;**42**:136-143.

JONES PW, QUIRK FH, BAVEYSTOCK CM, COLLIER JG et al. (1990). The St Georges respiratory questionnaire - repeatability and sensitivity to change. Thorax;**45**:811a.

JONES PW. (1991). Quality of life measurement for patients with diseases of the airways. Thorax;**46**:676-682.

JONES PW, QUIRK FH and BAVEYSTOCK CM. (1991). The St Georges Respiratory Questionnaire. Respiratory Medicine;**85**(supp B):25-31.

JONES PW. (1992). Breathlessness perception in airways obstruction. Eur. Respir. J;**5**:1035-1036.

KANAREK D, KAPLAN D and KAZEMI H. (1979). The anaerobic threshold in chronic obstructive lung disease. Bull. Europ. Physiopath. resp;**15**:163-169.

KATZ A and SAHLIN K. (1990). Role of oxygen in regulation of glycoysis and lactate production in human skeletal muscle. Ex. and Sports Science Review. pp1-23. ACSM.

KILLIAN KJ. (1985). The objective measure of breathlessness. Chest;**88**:84s-89s.

KILLIAN KJ, LEBLANC P, MARTIN DH, SUMMERS E et al. (1992). Exercise capacity and ventilatory, circulatory, and symptom limitation in patients with chronic airflow limitation. Am. Rev. Resp. Dis;**146**:935-940.

KIRSCH JL, MURO JR, STANSBURY DW, FISCHER CE et al. (1989). Effect of naloxone on maximal exercise performance and control of ventilation in COPD. Chest;**96**:761-66.

KNOX AJ, MORRISON JFJ and MEURS MF. (1988). Reproducibility of walking test results in chronic obstructive airways disease. Thorax;**43**:388-392.

KUMAGAI S, TANAKA K, MATSUURA Y, MATSUZAKA A et al. (1982). Relationship of the anaerobic threshold with the 5km, 10km and 10 mile races. Europ. J. Appl. Physiol;**49**:13-23.

KUMAR PJ and CLARK ML. (1987). Clinical Medicine. Balliere Tindall, London.

LAMB D. (1990). Pathology. In: Respiratory Medicine (Ed.Brewis RAL, Gibson GJ and Geddes DM). pp497-506 Balliere Tindall, London.

LANE DJ. (1983). The clinical presentation of chest disease. In: Oxford textbook of medicine. (Ed. Weatherall DJ, Ledingham JGG & warrel DA).pp15.25-15.39 (vol.2). Oxford University Press, Oxford.

LANIGAN C, MOXHAM J and PONTE J. (1990). Effect of chronic airflow limitation on resting oxygen consumption.

Thorax;**45**:388-390.

LEAVER DJ and PRIDE NB. (1971). Flow volume curves and expiratory pressures during exercise in patients with chronic airflow obstruction. Scand. J. Dis. Suppl. **77**:23-27.

LeBLANC P, BOWIE DM, SUMMERS E, JONES NL ET AL. (1986). Breathlessness and exercise in patients with cardiorespiratory disease. Am. Rev. Respir. Dis;**133**:21-25.

LÉGER LA and LAMBERT J. (1982). A maximal multi-stage 20m shuttle run test to predict Vo_2 max. Europ. J. Appl. Physiol;**49**:1-12.

LEITCH AG, MORGAN A, ELLIS DA, BELL G, HASLETT C and McHARDY GJR. (1981). Effect of oral salbutamol and slow release aminophylline on exercise tolerance in chronic bronchitis. Thorax;**36**:787-789.

LOAT CER and RHODES EC. (1993). Relationship between the lactate and ventilatory thresholds during prolonged exercise. Sports Medicine;**15**:104-115.

LOCKHART A. (1979). Exercise limiting factors in chronic obstructive lung disease. Bull. Europ. Physiopath. resp;**15**;305-317.

LOKE J, MAHLER D, PAUL-MAN SF, WIEDERMANN et al. (1984). Exercise impairment in chronic obstructive pulmonary disease. Clin. in Chest Medicine;**5**:121-144. (Ed Loke J). W B Saunders, Philadelphia.

MACINTYRE NR and LEATHERMAN NE. (1989). Mechanical loads on the ventilatory muscles- a theoretical analysis. Am. Rev. Respir. Dis;**139**:968-973.

MARITZ JS, MORRISON JF, PETERS J STRYDOM NB et al. (1961). A practical method of estimating an individuals maximum oxygen intake. Ergonomics;**4**:97-122.

MATTHAY RA, ARROLIGA AC, WIEDERMANN HP, SCHULMAN DS et al. (1992). Right ventricular function at rest and during exercise in chronic obstructive pulmonary disease. Chest;**101**(suppl.):255s-262s.

MATTHEWS JI, BUSH BA and EWALD FW. (1989). Exercise responses during incremental and high intensity and low intensity steady state exercise in patients with obstructive lung disease and normal control subjects. Chest;**96**:11-17.

MAUGHAN RJ. (1982). A simple rapid method for the determination of glucose, lactate, pyruvate, analine, 3-hydroxybutyrate and acetoacetate on a single 20ul blood sample. Clin. Chi. Acta;**122**:231-240.

McARDLE WD, KATCH FI, and KATCH VL. (1991). Exercise physiology- energy, nutrition and human performance. (3rd ed). Lea and Febiger, philadelphia.

McGAVIN CR, GUPTA SP and McHARDY GJR. (1976). Twelve-minute walking test for assessing disability in chronic bronchitis. BMJ;**1**:822-823.

McGAVIN CR, ARTVINLI M, NAOE H AND McHARDY GJR. (1978). Dyspnoea, disability, and distance walked: comparison of estimates of exercise performance in respiratory disease. BMJ;**2**:241-243.

McGREGOR M and BECKLAKE MR. (1961). The relationship of the oxygen cost of breathing to respiratory mechanical work and respiratory force. J. Clin. Invest;**40**:971-980.

McKELVIE RS and JONES NL. (1989). Cardio-pulmonary exercise testing. Clin. Chest Med. **10**:277-291 (Ed. Mahler DA) W B Saunders, Philadelphia.

McNEILL G, COX MD and RIVERS JPW. (1987). The Oxylog oxygen consumption meter: a portable device for measurement of energy expenditure. Am. J. Clin. Nutr;**45**:1415-1419.

MIHN Vu-D, LEE HM, VASQUEZ P, SHEPARD JW and BELL JW. (1979).Relation of $Vo_{2\,max}$ to cardiopulmonary function in patients with chronic obstructive lung disease. Bull. Europ. Physiopath. resp;**15**:359-375.

MORGAN AD. (1989). Simple exercise testing. Respiratory Medicine;**83**:383-387.

MORGAN MDL. (1991). Experience of using the CRQ (Chronic Respiratory Questionnaire). Respiratory Medicine;**85**(supp B):23-24.

MORRICE A and SMITHIES T. (1984). The 100m walk: a simple and reproducible exercise test. Br. J. Dis. Chest;**78**: 392-394.

MUNGALL IPF and HAINSWORTH R. (1979). Assessment of respiratory function in patients with chronic obstructive airways disease. Thorax;**34**:254-258.

MUSHIN WM and JONES PL. (1987). Physics for the anaesthetist. (4th ed). Blackwell Scientific Publications, Oxford.

MUZA SR, SILVERMAN MT, GILMORE CG, HELLERSTEIN HK and KELSEN SG. (1990). Comparison of scales used to quantitate the sense of effort to breathe in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**141**:909-913.

MYERS J, BUCHANAN N, SMITH D, NEUTEL J et al. (1992).

Individualised ramp treadmill; Observations on a new protocol. Chest;**101**(suppl):236s-241s.

NAGLE FJ, BALKE B and NAUGHTON JP. (1965). Graduation step test for assessing work capacity. J. Appl. Physiol;**20**:745-748.

NEARY PJ, MaCDOUGALL, BACHUS R and WENGER HA. (1985). The relationship between lactate and ventilatory thresholds: coincidental or cause and effect? Eur. J. Appl. Physiol;**54**:104-108.

NEIDERMAN MS, HENDERSON-CLEMENT P, FEIN AM, FEINSILVER SH et al. (1991). Benefits of a multi-disciplinary pulmonary rehabilitation program. Chest;**99**:798-804.

NERY LE, WASSERMAN K, FRENCH W, OREN A and DAVIS JA. (1983). Contrasting cardiovascular and respiratory responses to exercise in mitral valve and chronic obstructive pulmonary diseases. Chest;**83**:446-453.

PARDY RL, RIVINGTON RN, DESPAS PJ and MACKLEM PT. (1981). Inspiratory muscle training compared with physiotherapy in patients with chronic airflow limitation. Am. Rev. Respir. Dis.**123**:421-425.

PARDY RL, RIVINGTON RN, DESPAS PJ and MACKLEM PT. (1981). The effect of inspiratory muscle training on exercise performance in chronic airflow limitation. Am. Rev. Respir. Dis;**123**:426-433.

PARDY RL, HUSSAIN SNA and MACKLEM PT. (1984).The ventilatory pump in exercise. Clin. Chest Med.**5**:35-50 (Ed-LOKE J). W B Saunders, Philadelphia.

PARE PD, WIGGS BR, JAMES A, HOGG JC AND BOSKEN C. (1991). The comparative mechanics and morphology of airways in asthma and in chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**143**:1189-1193.

PARTRIDGE MR. (1982). Chronic bronchitis and chronic airflow limitation. (2nd ed). Update postgraduate centre series, Update books.

PATESSIO A, CASABURI R, IOLO F, and DONNER CF. (1991). Mechanisms of exercise limitation. Europ. Respir. Rev;**1**(suppl 6):482-485.

PATESSIO A, CASABURI R, CARONE M, APPENDINI et al (1993). Comparison of gas exchange, lactate, and lactic acidosis thresholds in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**148**:622-626.

PETTY TL. (1990) Definitions of Chronic Obstructive Pulmonary Disease. Clin Chest Med **11**:363-374 (Ed-Hodgkins JE) W B Saunders, Philadelphia.

PRIDE NB. (1990). Epidemiology, aetiology and natural history. In: Respiratory Medicine (Ed.Brewis RAL, Gibson GJ and Geddes DM). pp 475-484 Balliere Tindall, London.

PRIDE NB. (1990). Pathophysiology. In: Respiratory Medicine (Ed.Brewis RAL, Gibson GJ and Geddes DM). pp507-519 Balliere Tindall, London.

PRIDE NB and MACKLEM PT. (1986). Lung mechanics in disease. In: Handbook of Physiology Section 3. The respiratory system (Ed Fishman AP). Volume 3 Part II pp659-692 Williams and Wilkins Company, Baltimore.

QUANJER PH. (1983). Standardised lung function testing. Bull. Eur. Physiopathol. Respir;**19**(suppl 5):45-51.

RAMPULLA C, BAIOCCHI S, DACOSTO E and AMBROSINI N. (1992). Dyspnoea on exercise; Pathophysiologic mechanisms. Chest;**101** (suppl):248s-252s.

RAMSBOTTOM R,BREWER J and WILLIAMS C. (1988). A progressive shuttle run test to estimate maximal oxygen uptake. Brit. J. Sports Med;**19**:207-209.

REID L. (1960). Measurements of the bronchial mucous gland layer: A diagnostic yardstick in chronic bronchitis. Thorax;**15**:132.

ROCHESTER DF, ARORA NS, BRAUN NMT and GOLDBERG SK. (1979). The respiratory muscles in chronic obstructive airways disease COPD. Bull. Europ. Physiopath. Resp;**15**:951-975.

ROCHESTER DF. (1984). The respiratory muscles in COPD. Chest;**85**:6,suppl 47-50.

ROCHESTER DF. (1991). Effects of COPD on the respiratory muscles. In: Chronic obstructive pulmonary disease. (Ed. Cherniack NS).pp134-157 W B Saunders, Philadelphia.

ROGERS TK and HOWARD P. (1992). Pulmonary haemodynamics and physical training in patients with chronic obstructive pulmonary disease. Chest;**101**:289s-292s.

SAUNIER C, GIMINEZ M and HARTEMANN D. (1979). Blood glycolysis during muscular exercise in patients with chronic lung disease and hypoxemia. Bull. Europ. Physiopath. Resp;**15**:291-302.

SCHIFFMAN PL. (1991). Acid-base disorders in COPD. In; Chronic obstructive pulmonary disease (Ed. Cherniak NS). pp181-183. W B Saunders, Philadelphia.

SCOTT SM. (1989). A progressive walking test for the evaluation of functional capacity in patients with chronic airflow limitation. M.Sc project, Loughborough University.

SEAN NC, STULBARG MS, DOHERTY JJ, GOLD WM et al. (1989). Exercise induced bronchodilation in patients with severe COPD. Am. Rev. Respir. Dis;**129**(suppl):581-583.

SEVERA E, GIMINEZ M, MOHAN-KUMAR T, CANDINA R et al. (1983). Oxygen uptake at maximal exercises in chronic airflow obstruction. Bull. Europ. Physiopath. Resp;**19**:553-556.

SHAH AC, BABB TG, MOTTRAM CD, VIGGIANO et al. (1992). Lactate threshold in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**145**:581a.

SHARP JT, LITH PV, NUCHPRAYOON CV et al. (1968). The thorax in chronic obstructive lung disease. Am. J. Med;**44**:39-46.

SIEGEL S. Nonparametric statistics. (1956). McGraw Hill, New York.

SILVERMAN M, BARRY J, HELLERSTEIN H, JANOS J and KELSEN S. (1988). Variability of the perceived sense of effort in breathing during exercise in patients with chronic obstructive pulmonary disease. Am. Rev. Respir. Dis;**137**:206-209.

SIMPSON K, KILLIAN K, McCARTNEY N, STUBBING DG et al. (1992). Randomised controlled trial of weight lifting in patients with chronic airflow limitation. Thorax;**47**:70-75.

SINCLAIR DJM and INGRAM CG. (1977). Controlled trial of supervised exercise training in chronic bronchitis. BMJ;**i**:519-521.

SKINNER JS and McLELLAN TH. (1980). The transition from aerobic to anaerobic metabolism. Research Quarterly for Ex. and Sport;**51**:234-248.

SNELL PG and MITCHELL JH. (1984). The role of maximal oxygen uptake in exercise performance. Clin. Chest Med.**5**:51-61 (Ed Loke J) W B Saunders, Philadelphia.

SPIRO SG, HAHN HL, EDWARDS RHT and PRIDE NB. (1975). An analysis of the physiological strain of sub-maximal exercise in patients with chronic obstructive bronchitis. Thorax;**30**:415-425.

SPIRO SG. (1977). Exercise testing in clinical medicine. Br. J. Dis. Chest;**71**:145-172.

SPIRO SG and ROBERTS CM. (1991). Lung function testing. Medicine International;**88**:3661-3668.

SRIDHAR G, CLEMENS RE, ZINTEL TA and GALLAGHER. (1993). Dead space loading and exercise limitation in moderate chronic obstructive pulmonary disease (COPD). Am. Rev. Respir. Dis;**147**:189a.

STENSEL DJ, HARDMAN AE, BROOKE-WAVELL K, JONES PRM et al. (1992). The influence of brisk walking on endurance fitness in previously sedentary, middle aged men. J.Physiol; **446**:123p.

STUBBING DG, PENGELLY LD, MORSE JL and JONES NL. (1980). Pulmonary mechanic during exercise in subjects with chronic airflow limitation. J. Appl. Physiol;**49**:511-515.

SUE DY, WASSERMAN K, MORRICCA RB and CASABURI R. (1988). metabolic acidosis during exercise with chronic obstructive pulmonary disease. Chest;**94**:931-38.

SUTTON PP, LOPEZ-VIDIERO MT, PAVIA D, NEWMAN SP et al (1985). Assessment of percussion, vibratory shaking and breathing exercises in chest physiotherapy. Eur. J. Respir. Dis;**66**:147-152.

SWEER L AND ZWILLICH CW. (1990). Dyspnoea in the patient with chronic obstructive pulmonary disease etiology and management. Clin. Chest Med. **11**:363-374 (Ed Hodgkins JE) W B Saunders, Philadelphia.

SWERTS PMJ, MOSTERT R and WOUTERS EFM. (1990). Comparison of corridor and treadmill walking in patients with severe chronic obstructive pulmonary disease. Physical Therapy;**70**:439-442.

SWINBURN CR, WAKEFIELD JM and JONES PW. (1984). Relationship between ventilation and breathlessness during exercise in chronic obstructive airways disease is not altered by prevention of hypoxaemia. Clin. Sci;**67**:515-519.

SWINBURN CR, WAKEFIELD JM and JONES PW. (1985). Performance, ventilation and oxygen consumption in three different types of exercise tests in patients with chronic obstructive lung disease. Thorax;**40**:581-586.

THURLBECK WM. (1990)a. Pathology of chronic airflow limitation. Chest;**97**:2,suppl 6-10.

THURLBECK WM.(1990)b. Pathophysiology of chronic obstructive pulmonary disease. Clin. chest med. **11**:389-404 (Ed Hodgkins JE) W B Saunders, Philadelphia.

THURLBECK WM. (1991)a. Pathology of chronic airflow limitation. Medicine International;**89**:3715-3721.

THURLBECK WM. (1991)b. Pathology of chronic airflow limitation. In: Chronic obstructive pulmonary disease. 4th ed. (Ed. Cherniak NS). pp104-121. W B Saunders, Philadelphia.

TOBIN MJ, PEREZ W, GUENTHER SM, LODATEO RF and DANTZER DR. (1987). Does rib cage-abdominal paradox signify respiratory muscle fatigue? J. Appl. Physiol;**63**:851-860.

WAGNER PD. (1992). Ventilation-perfusion matching during exercise. Chest;**101**:192s-198s.

WANNER A. (1990). The role of mucus in chronic obstructive pulmonary disease. Chest;**97**:2 suppl 11-15.

WASSERMAN K, VAN KESSEL AL and BURTON GG. (1967). Interaction of physiological mechanisms during exercise. J. Appl. Physiol;**21**:71-85.

WASSERMAN K and WHIPP BJ. (1975). Exercise physiology in health and disease. Am. Rev. Respir. Dis;**112**:219-249.

WASSERMAN K, HANSEN JE, SUE DY and WHIPP BJ. (1987). Principles of exercise testing and interpretation. Lea & Febiger, Philadelphia.

WASSERMAN K. (1984). The anaerobic threshold measurement to evaluate exercise performance. Am. Rev. Respir. Dis;**129**:35-40.

WASSERMAN K, SUE DY, CASABURI R and MORRICA RB. (1989). Selection criteria for exercise training in pulmonary rehabilitation. Eur. Respir. J;**2**:604s-610s.

WASSERMAN K and KOIKE A. (1992). Is the anaerobic threshold truely anaerobic? Chest;**101**:211s-218s.

WEIR DC, FREEMAN W, ROBERTS KT, STABLEFORTH DE and BURGE PS. (1991). Comparison of measure of quality of life inpatients with cystic fibrosis (CF) and chronic airflow obstruction (CAO). Thorax;**46**:228p.

WEST JB. (1987). Pulmonary pathophysiology- the essentials (3rd ed) williams and Wilkins, Baltimore.

WHIPP BJ.(1983) Exercise hyperventilation in patients with McArdles disease (letter). J. Appl. Physiol;**55**:1638-1639.

WHIPP BJ, WARD SA and WASSERMAN K. (1984). Ventilatory response to exercise and their control in man. Am. Rev. Respir. Dis;**129**(suppl):s17-s20.

WHIPP BJ and WASSERMAN K. (1988). Respiratory physiology in exercise. In: Textbook of respiratory medicine. (Ed Murray JF & Nadel JA) pp167-195. W B Saunders, Philadelphia.

WHIPP BJ and PARDY RL. (1986). Breathing during exercise. In: Handbook of Physiology Section 3. The respiratory system (Ed Fishman AP). Volume 3 Part II pp605-629 Williams and Wilkins Company, Baltimore.

WHIPP BJ and WARD SA. (1991). Coupling of ventilation to pulmonary gas exchange during exercise. In: Exercise pulmonary physiology and pathophysiology (Lung biology in health and disease series/52).(Ed Whipp BJ & Wasserman K)

pp271-308. Marcel dekker inc., New York.

WILMORE JH. (1984). Acute and chronic physiological response to exercise. In: Exercise in cardiovascular health and disease.(ed.Amsterdam EA, Wilmore JH and DeMaria MD). pp53-69 York medical books.

WOLKOVE N, DAJCZMAN BSN, COLACONE A and KREISMAN H. (1989). The functional relationship between pulmonary function and dyspnoea in obstructive lung disease. Chest;**96**:6 1247-1251.

WRIGHT JL, LAWSON LM, PARE PD, KENNEDY S, WIGGS B and HOGG JC. (1984). The detection of small airways disease. Am. Rev. Respir. Dis;**129**:989-994.

YOUNES M (1991). Determinants of thoracic excursions during exercise. In: Exercise pulmonary physiology and pathophysiology (Lung biology in health and disease series/52).(Ed Whipp BJ & Wasserman K). pp1-65. Marcel Dekker inc., New York.

ZuWALLACK RL, PATEL K, REARDON JZ, CLARK BA et al. (1991). Predictors of improvement in the 12-minute walking distance following a six-week pulmonary rehabilitation program. Chest;**99**:805-808.

APPENDICES

APPENDIX A

THE SHUTTLE WALKING TEST

INSTRUCTIONS TO THE OPERATOR/PATIENT

Before you start the progressive shuttle walking test it is important to check that your cassette player is running at the right speed and that the tape has not stretched. To help you with this we have put two accurately timed bleeps 60 seconds apart on the tape. Check the timing now.

TIMED MINUTE

The object of the progressive shuttle walking test is to walk for as long as possible to and fro, along the 10m course, keeping to the speed indicated by the bleeps on the cassette. You will hear these bleeps at regular intervals. You should walk at a steady pace aiming to turn around the cone at one end of the course when you hear the first bleep and at the other end when you hear the next.

At first your walking speed will be very slow but you will need to speed up at the end of each minute. Your aim should be to follow the set rhythm for as long as you can , each single bleep signals the end of a shuttle and each triple bleep signals an increase in walking speed.

You should stop walking only when you become too breathless to maintain the required speed or can no longer keep up with the set pace.

The test is maximal and progressive. In other words it is easy at the start and harder at the end. The walking speed for the first minute is very slow you have 20 seconds to complete each 10m shuttle, so don't go too fast.

The test will start in 15 seconds so line up at the start now.

Level 1 starts with a triple bleep after the 4 second countdown.

10M SHUTTLE TEST

APPENDIX B.

BORG BREATHLESSNESS SCORE

0	NOTHING AT ALL	
0.5	VERY, VERY SLIGHT	(JUST NOTICEABLE)
1	VERY SLIGHT	
2	SLIGHT	
3	MODERATE	
4	SOMEWHAT SEVERE	
5	SEVERE	
6		
7	VERY SEVERE	
8		
9	VERY, VERY SEVERE (ALMOST MAXIMAL)	
10	MAXIMAL	

APPENDIX B.

BORG PERCEIVED EXERTION SCALE

6		
7	-	VERY, VERY LIGHT
8		
9	-	VERY LIGHT
10		
11	-	FAIRLY LIGHT
12		
13	-	SOMEWHAT HARD
14		
15	-	HARD
16		
17	-	VERY HARD
18		
19	-	VERY, VERY HARD
20		

APPENDIX C.
CHRONIC RESPIRATORY DISEASE QUESTIONNAIRE

First Administration, 7 Point Scale

INTERVIEWER FORM

This questionnaire is designed to find out how you have been feeling during the last two weeks. You will be asked about how short of breath you have been, how tired you have been feeling and how your mood has been.

1. I would like you to think of the activities that you have done during the last two weeks that have made you feel short of breath. These should be activities which you do frequently and which are important in your day-to-day life. Please list as many activities as you can that you have done during the last 2 weeks that have made you feel short of breath.

(CIRCLE THE NUMBER ON THE ANSWER SHEET LIST ADJACENT TO EACH ACTIVITY MENTIONED. IF AN ACTIVITY MENTIONED IS NOT ON THE LIST, WRITE IT IN, IN THE RESPONDENT'S OWN WORDS, IN THE SPACE PROVIDED).

Can you think of any other activities you have done during the last 2 weeks that have made you feel short of breath?

(RECORD ADDITIONAL ITEMS)

2. I will now read a list of activities which make some people with lung problems feel short of breath. I will pause after each item long enough for you to tell me if you have felt short of breath during that activity during the last 2 weeks. If you haven't done that activity during the last 2 weeks, just say "No". The activities are:

(READ ITEMS, OMITTING THOSE WHICH RESPONDENT HAS VOLUNTEERED SPONTANEOUSLY. PAUSE AFTER EACH ITEM TO GIVE RESPONDENT A CHANCE TO INDICATE WHETHER HE/SHE HAS BEEN SHORT OF BREATH WHILE PERFORMING THAT ACTIVITY DURING THE LAST WEEK. CIRCLE THE NUMBER ADJACENT TO APPROPRIATE ITEMS ON ANSWER SHEET).

1. BEING ANGRY OR UPSET
2. HAVING A BATH OR SHOWER
3. BENDING
4. CARRYING, SUCH AS CARRYING GROCERIES
5. DRESSING
6. EATING
7. GOING FOR A WALK
8. DOING YOUR HOUSEWORK

9. HURRYING
10. MAKING A BED
11. MOPPING OR SCRUBBING THE FLOOR
12. MOVING FURNITURE
13. PLAYING WITH CHILDREN OR GRANDCHILDREN
14. PLAYING SPORTS
15. REACHING OVER YOUR HEAD
16. RUNNING, SUCH AS FOR A BUS
17. SHOPPING
18. WHILE TRYING TO SLEEP
19. TALKING
20. VACUUMING
21. WALKING AROUND YOUR OWN HOME
22. WALKING UPHILL
23. WALKING UPSTAIRS
24. WALKING WITH OTHERS ON LEVEL GROUND
25. PREPARING MEALS

3a) Of the items which you have listed, which is the most important to you in your day-to-day life? I will read through the items, and when I am finished, I would like you to tell me which is the most important.

(READ THROUGH ALL ITEMS SPONTANEOUSLY VOLUNTEERED AND THOSE FROM THE LIST WHICH PATIENT MENTIONED)

Which of these items is most important to you in your day-to-day life?

(LIST ITEM ON RESPONSE SHEET)

b) Of the remaining items, which is the most important to you in your day-to-day life? I will read through the items, and when I am finished, I would like you to tell me which is the most important.

(READ THROUGH REMAINING ITEMS)

Which of these items is most important to you in your day-to-day life?

(LIST ITEM ON RESPONSE SHEET)

c) Of the remaining items, which is most important to you in your day-to-day life?

(LIST ITEM ON RESPONSE SHEET)

d) Of the remaining items, which is most important to you in your day-to-day life?

(LIST ITEM ON RESPONSE SHEET)

e) Of the remaining items, which is most important to you in your day-to-day life?

(LIST ITEM ON RESPONSE SHEET)

(FOR ALL SUBSEQUENT QUESTIONS, ENSURE RESPONDENT HAS APPROPRIATE RESPONSE CARD IN FRONT OF THEM BEFORE STARTING THE QUESTION)

4. I would now like you to describe how much shortness of breath you have experienced during the last 2 weeks while doing the 5 most important activities you have selected.

a) Please indicate how much shortness of breath you have had during the last 2 weeks while (INTERVIEWER: INSERT ACTIVITY LIST IN 3a) by choosing one of the following options from the card in front of you: (GREEN CARD)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

b) Please indicate how much shortness of breath you have had during the last 2 weeks while (INTERVIEWER: INSERT ACTIVITY LIST IN 3b) by choosing one of the following options from the card in front of you: (GREEN CARD)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

c) Please indicate how much shortness of breath you have had during the last 2 weeks while (INTERVIEWER: INSERT ACTIVITY LIST IN 3c) by choosing one of the following options from the card in front of you: (GREEN CARD)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

d) Please indicate how much shortness of breath you have had during the last 2 weeks while (INTERVIEWER: INSERT ACTIVITY LIST IN 3d) by choosing one of the following options from the card in front of you: (GREEN CARD)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH

3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

e) Please indicate how much shortness of breath you have had during the last 2 weeks while (INTERVIEWER: INSERT ACTIVITY LIST IN 3e) by choosing one of the following options from the card in front of you: (GREEN CARD)

1. EXTREMELY SHORT OF BREATH
2. VERY SHORT OF BREATH
3. QUITE A BIT SHORT OF BREATH
4. MODERATE SHORTNESS OF BREATH
5. SOME SHORTNESS OF BREATH
6. A LITTLE SHORTNESS OF BREATH
7. NOT AT ALL SHORT OF BREATH

5. In general, how much of the time during the last 2 weeks have you felt frustrated or impatient? Please indicate how often during the last 2 weeks you have felt frustrated or impatient by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

6. How often during the past 2 weeks did you have a feeling of fear or panic when you had difficulty getting your breath? please indicate how often you had a feeling of fear or panic when you had difficulty getting your breath by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

7. What about fatigue? How tired have you felt over the last 2 weeks? Please indicate how tired you have felt over the last 2 weeks by choosing one of the following options from the card in front of you: (ORANGE CARD)

1. EXTREMELY TIRED
2. VERY TIRED
3. QUITE A BIT OF TIREDNESS

4. MODERATELY TIRED
5. SOMEWHAT TIRED
6. A LITTLE TIRED
7. NOT AT ALL TIRED

8. How often during the last 2 weeks have you felt embarrassed by your coughing or heavy breathing? Please indicate how much of the time you felt embarrassed by your coughing or heavy breathing by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

9. In the last 2 weeks, how much of the time did you feel very confident and sure that you could deal with your illness? Please indicate how much of the time you felt very confident and sure that you could deal with your illness by choosing one of the following options from the card in front of you: (YELLOW CARD)

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

10. How much energy have you had in the last 2 weeks? Please indicate how much energy you have had by choosing one of the following options from the card in front of you: (PINK CARD)

1. NO ENERGY AT ALL
2. A LITTLE ENERGY
3. SOME ENERGY
4. MODERATELY ENERGETIC
5. QUITE A BIT OF ENERGY
6. VERY ENERGETIC
7. FULL OF ENERGY

11. In general, how much of the time did you feel upset, worried or depressed during the last 2 weeks? Please indicate how much of the time you felt upset, worried or depressed during the past 2 weeks by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME

2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

12. How often during the last 2 weeks did you feel you had complete control of your breathing problems? Please indicate how often you felt you had complete control of your breathing problems by choosing one of the following options from the card in front of you: (YELLOW CARD)

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

13. How much of the time during the last 2 weeks did you feel relaxed and free of tension? Please indicate how much of the time you felt relaxed and free of tension by choosing one of the following options from the card in front of you: (YELLOW CARD)

1. NONE OF THE TIME
2. A LITTLE OF THE TIME
3. SOME OF THE TIME
4. A GOOD BIT OF THE TIME
5. MOST OF THE TIME
6. ALMOST ALL OF THE TIME
7. ALL OF THE TIME

14. How often during the last 2 weeks have you felt low in energy? Please indicate how often during the last 2 weeks you have felt low in energy by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

15. In general, how often during the last 2 weeks have you felt discouraged or down in the dumps? Please indicate how often during the last 2 weeks you felt discouraged or down in the dumps by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME

2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

16. How often during the last 2 weeks have you felt worn our or sluggish? Please indicate how much of the time you felt worn out or sluggish by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

17. How happy, satisfied or pleased have you been with your personal life during the last 2 weeks? Please indicate how happy, satisfied or please you have been by choosing one of the following options from the card in front of you: (GREY CARD)

1. VERY DISSATISFIED, UNHAPPY MOST OF THE TIME
2. GENERALLY DISSATISFIED, UNHAPPY
3. SOMEWHAT DISSATISFIED, UNHAPPY
4. GENERALLY SATISFIED, PLEASED
5. HAPPY MOST OF THE TIME
6. VERY HAPPY MOST OF THE TIME
7. EXTREMELY HAPPY, COULD NOT HAVE BEEN MORE SATISFIED OR PLEASED

18. How often during the last two weeks did you feel upset or scared when you had difficulty getting your breath? Please indicate how often during the last 2 weeks you felt upset or scared when you had difficulty getting your breath by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

19. In general, how often during the last 2 weeks have you felt restless, tense or uptight? Please indicate how oten you have felt restless, tense or uptight by choosing one of the following options from the card in front of you: (BLUE CARD)

1. ALL OF THE TIME
2. MOST OF THE TIME
3. A GOOD BIT OF THE TIME
4. SOME OF THE TIME
5. A LITTLE OF THE TIME
6. HARDLY ANY OF THE TIME
7. NONE OF THE TIME

APPENDIX D.

CALIBRATION PROCEDURES

D.i. Gas analysers

The equipment was calibrated immediately prior to expired air analysis and if necessary re-calibrated every hour. The Taylor Servomex oxygen analyser and the Lira Infra-red carbon dioxide were both calibrated initially with oxygen free nitrogen (a null gas) and then with a gas mixture of a known concentration.

D.ii The Oxylog

The oxygen analysers of the Oxylog was calibrated at the start of each individual study to zero pO_2. Oxygen free nitrogen was passed over the two sampling tubes until a stable zero reading is obtained. Prior to each use of the Oxylog the oxygen sensors were calibrated to atmospheric PO_2 at barometric pressure.

APPENDIX E.

GAS ANALYSIS

E.i The determination of the oxygen and carbon dioxide content, volume and temperature of the expired air :- the Douglas bag.

The collection of expired air was well mixed immediately prior to analysis. A small sample of air was extracted from the Douglas bag via a sample tube connected to a Hy-flow pump (Metcalf Industries Ltd.). The rate of sampling was measured by a gap flow meter. The expired air was directed into the carbon dioxide analyser for 120 seconds, during this time the rate of flow was recorded. After 120 seconds the flow was directed to the O_2 analyser for 60 seconds. During which time the deflection of the CO_2 meter needle was recorded and the flow rate to the O_2 noted. At the end of the 60 seconds the flow was stopped and the digital display was recorded once stabilised.

The volume of remaining expired air in the Douglas bag was measured by evacuation through a dry gas meter. The total volume of ventilation required the addition of this volume to the volume of air passed through the gas analysers. The temperature was measured as the expired air passed over a thermistor placed in the outlet tube of the dry gas meter.

E.ii The determination of oxygen content and ventilation:- Oxylog

The volume of inspired air is measured through a turbine type flow meter and is displayed digitally each minute to the nearest 1 litre. $\dot{V}O_2$ is displayed digitally having a resolution of 0.01 $l.min^{-1}$. The calculations of the equipment make the assumptions

1. The volume of inspired air is corrected to 0°C dry at the pressure of the experiment, temperature is measured with a

thermistor at the flow meter.

2. The $\dot{V}_E$ is only correct if the R value is equal to 1.

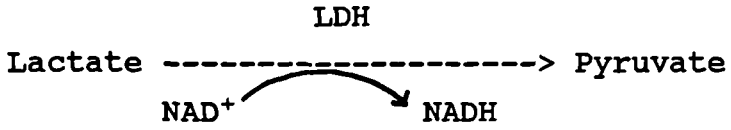
The error in oxygen consumption measurements are :-

R	% error in volume
0.7	-5.3
0.8	-3.5
0.9	-1.8
1.0	0
1.1	1.8

APPENDIX F.

BLOOD LACTATE ASSAY

Blood lactate assays were performed using the fluorometric enzymatic method described by Maughan (1982). It is dependent upon the release of NADH by the following reaction;



In the conversion of lactate to pyruvate (catalysed by LDH) the co-factor NAD^+ is reduced to NADH. NADH has a natural fluorescence which is measured as an indication of the concentration of lactate. Excess LDH and NAD^+ were used to ensure the complete conversion of all lactate present.

Fluorometric analysis of the resulting reaction mixture measures the fluorescence of NADH, which varies according to the initial lactate concentration. The actual values were established by relating each sample to a regression equation computed from a series of lactate standards of known concentration.

The process of analysis was carried out as follows:

SOLUTIONS.

a) 2.5% Perchloric acid.

b) Hydrazine buffer (1.1 mmol.l^{-1}, pH 9.4): (1.3g hydrazine sulphate, 5.0g hydrazine hydrate and 0.2g ethylenediamino tetra-acetic acid disodium salt (EDTA) in 100 ml of distilled water).

c) Reaction mixture: 2 mg NAD^+ and 10 μl LDH per ml of hydrazine buffer, prepared immediately prior to use.

STANDARDS.

Standard of 1, 2, 3, 4 and 5 mmol l^{-1} conncentration were

prepared from 1.0 M sodium L-Lactate solution for the analysis of the results presented in Chapter 7. For the samples described in Chapter 8 standards of 1, 2, 4, 6, 8 and 10 mmol.l^{-1} were prepared.

DEPROTINISATION

20 μl of blood was deproteinised by adding 200 μl of perchloric acid. It was then mixed thoroughly and stored at -20°C before analysis.

PROCEDURE

1. Samples were removed from the freezer and allowed to thaw at room temperature.
2. Once defrosted the samples were mixed thoroughly using the 'whirlimix' and the precipitate was separated by spinning in the centrifuge (Eppendorf, model 5412) for 4 minutes.
3. From each sample, in duplicate, 20 μl of supernatant was pipetted into a test tube (washed in nitric acid). A clean pipette was used for each sample.
4. A corresponding volume of each of the standard solution was pipetted into four test tubes and subjected to the same procedure.
5. 200 μl of reaction mixture was added to all the test tubes.
6. All the test tubes were mixed again, covered and left to incubate for 30 minutes.
7. After incubation 1 ml of lactate diluent 0.07 M HCl was added to halt the reaction, and the tubes mixed.
8. The samples were read against the blanks and standards with a fluorimeter (Perkin Elmer 1000M).
9. The lactate concentration was established from the regression equation of the standards using a BBC micro-computer with software developed in the department (Loughborough).

The r value of the regression equations for the standard

solutions was >0.99 for each of the 4 batches.

DETERMINATION OF THE COEFFICIENT OF VARIATION

Four repeated measures were made on five standard solutions for the determination of the coefficient of variation for the assay.

Standard	mean	C of V
1 $mmol.l^{-1}$	61.0	4.2%
2 $mmol.l^{-1}$	85.7	0.5%
3 $mmol.l^{-1}$	107.0	0.6%
4 $mmol.l^{-1}$	127.1	1.5%
5 $mmol.l^{-1}$	165.7	0.1%