CHAPTER 1

INTRODUCTION AND AIMS

1.1 INTRODUCTION

Society is well aware of the benefits of physical activity, as exercise is consistently promoted as a way of maintaining fitness and health. Research has shown that exercise is also beneficial in those with chronic illnesses like Cystic Fibrosis (CF). For children with this incurable, life-limiting illness, exercise is an important element of treatment, enhancing mucous clearance and delaying the characteristic decline in pulmonary function.

Increased awareness of these benefits highlights the need for accurate assessment of physical activity and exercise tolerance in children with CF. As well as extending current knowledge, regularly measuring activity emphasises it's importance to families, and allows clinicians to suggest areas for improvement.

Physical activity is assessed by accelerometry and questionnaires. Accelerometers are worn by the patient and automatically record activity and intensity based on limb movements. Various activity questionnaires are currently used to assess general activity levels as well as intensity of activity and energy expenditure. Exercise tests measure exercise tolerance (based on the rate of oxygen consumption, $\dot{V}O_{2peak}$) and exercise capacity. The most common tests involve treadmill and cycle ergometer protocols; step tests and walking tests are often used for fieldwork.

Since 1994, the Respiratory Laboratory at the Royal Children's Hospital (RCH) has conducted annual treadmill-based tests of aerobic fitness ($\dot{V}O_{2peak}$) in CF clinic patients (Roberts, 2001). The tests are part of each patient's annual assessment and include completion of the Cystic Fibrosis Physical Activity Questionnaire (CF-PA).

The CF-PA consists of two sections. The first assesses general well-being and morbidity over the past month and the second, an activity diary, quantifies all activity over the past week, including activities such as housework and gardening, as well as regular sports. It requires patients to indicate the days of participation and the total minutes, allowing calculation of total activity. Energy expenditure is estimated by assigning intensity values (METs) to each activity. Activity intensities are classified as multiples of 1 MET (the equivalent of sitting quietly) or as the ratio of the specific metabolic rate associated with the activity, divided by the resting metabolic rate (Ainsworth et al, 1992).

The activity diary section of the CF-PA has not been validated against objective measurements of physical activity, such as heart rate monitor data or accelerometers, meaning results cannot be confidently interpreted. It was the primary aim of this study to validate the CF-PA, by comparing questionnaire scores with data recorded by an accelerometer over 7 days. Comparisons were also made with two commonly used questionnaires, the Modifiable Activity Questionnaire for Adolescents (MAQ) (Aaron et al, 1995) and Physical Activity Questionnaire for Children (PAC-Q) (Kowalski et al, 1997).

Including a treadmill-based exercise test, anthropometry and spirometry in the methodology of this study allowed further investigation of relationships between physical activity, lung function, BMI and aerobic fitness. Of particular interest following a recent study by Nixon et al (2000), was participation in vigorous activity and the effect of this on fitness and lung function.

1.2 AIMS

This study aimed to:

1) Validate the CF-PA in terms of general, weekend and vigorous activity
2) Compare three questionnaires (CF-PA, MAQ, PAC-Q) to determine which was the most effective for estimation of children's activity levels
3) Use accelerometer, exercise test and spirometry measurements to investigate relationships between physical activity, intensity, pulmonary function and aerobic fitness

CHAPTER 2

BACKGROUND INFORMATION & LITERATURE REVIEW

2.1 INTRODUCTION

Knowledge of the benefits of exercise, particularly in children with CF, has prompted extensive research in the areas of exercise testing and assessment of physical activity.

Literature relating to exercise during health and disease will be reviewed, focusing on exercise tolerance, limitations to and benefits of exercise, exercise testing, and assessment of physical activity in the CF population.

2.2 EXERCISE IN HEALTH

2.2.1 GENERAL BENEFITS OF EXERCISE

Regular physical activity benefits men and women of all ages. The World Health Organisation recommends clinicians encourage all patients to participate in a regular activity programme that suits their health status and lifestyle (Sundberg and Jansson, 1998).

Exercise has positive effects on various body systems. There is evidence to indicate that high levels of activity and aerobic fitness are associated with favourable blood lipid and lipoprotein profiles (Armstrong and Welsman, 1997) and that exercise has hypotensive benefits with only three twenty-minute sessions per week (Lesniak and Dubbert, 2001). Blood pressure reduction may explain Sundberg and Jansson's (1998) finding that exercise reduces the risk of premature death and the incurrence or death from ischaemic heart disease. In agreement with Lesniak and Dubbert, they found that the benefits of exercise were attainable with only moderate physical activity, a dose-dependent relationship existing between physical activity and health benefits.

There are specific benefits of exercise for children and adolescents, and some relationships seen in adults are not as well established in younger people. For example, there is no convincing evidence that activity is related to improved lipid profiles in children. In addition, although hypotensive effects of exercise have been noted in children with hypertension, significant improvements when blood pressure is normal have not been observed (Armstrong and Welsman, 1997).

Increased physical activity is associated with decreased body fat and increased muscle mass in children and adolescents, and is also beneficial in the management of diabetes mellitus. Research has shown that in conjunction with dietary modification and insulin administration, exercise enhances insulin sensitivity, thus reducing the dependence on exogenous insulin and improving the lipid profile (Armstrong and Welsman, 1997).

By enhancing bone mineral density, childhood exercise also reduces the risk of developing osteoporosis in adult life, which is partially attributed to age-related decline in physical activity and subsequent loss of bone mass (Cotran et al, 1999).

Finally, physical activity has positive effects on young people's psychological well-being. It is associated with improvements in self-esteem, and reductions in stress, anxiety and depression. Higher academic achievements have also been observed (Armstrong and Welsman, 1997).

2.2.2 NORMAL PHYSIOLOGIC RESPONSE TO EXERCISE

The most commonly used expressions of exercise tolerance are rate of oxygen consumption ($\dot{V}O_{2peak}$) or peak aerobic power, and peak work capacity (Wmax). Oxygen consumption reflects the supply of oxygen by the cardiorespiratory system and its uptake by working muscles (Webb and Dodd, 1995).

The physiological changes associated with exercise such as a 5-fold increase in cardiac output (CO) and 12-fold increase in minute ventilation ($\dot{V}_E$)(Godfrey and Mearns, 1971) act to increase supply of oxygen to exercising muscles. The pulmonary system increases ventilation to provide oxygen to the bloodstream; the cardiovascular system delivers the oxygenated blood to the muscles.

When exercise begins, $\dot{V}_E$ rises almost immediately to meet oxygen demands of the muscles. This is achieved by increases in tidal volume (V_T) and breathing frequency (f_b). V_T reaches 50% to 60% of the vital capacity (VC), then increases in ventilation are accounted for by f_b (Orenstein, 1991).

Exercise becomes limited by breathlessness and muscle fatigue, which occur when muscle metabolism enters the anaerobic phase and lactic acid accumulates due to inadequate oxygen supply (Webb and Dodd, 1995).

For the pulmonary response to be useful, the cardiovascular system must increase CO and pulmonary blood flow to match the increased ventilation with increased perfusion (Orenstein, 1993).

2.2.3 EXERCISE TOLERANCE

According to Orenstein (1993), exercise tolerance in normal subjects depends on various systemic factors. Pulmonary and non-pulmonary problems can interfere with the process of providing oxygenated blood to exercising muscles. Anaemia may lower oxygen-carrying-capacity of the blood, an inefficient cardiovascular system may fail to deliver blood to appropriate muscles, or the muscles may not appropriately process the oxygen for contraction (Orenstein, 1993).

In health, exercise capacity is constrained by circulatory rather than ventilatory limits. Once the limits of stroke volume, cardiac frequency and oxygen delivery are met, muscles fatigue (Webb and Dodd, 1995). Despite immense demands on the respiratory system, it has a huge reserve capacity, seldom limiting exercise. However, children with respiratory ailments such as CF may be restricted by pulmonary factors (Orenstein, 1993).

2.3 CYSTIC FIBROSIS

2.3.1 INTRODUCTION TO CYSTIC FIBROSIS

CF, an incurable and life-limiting condition (Robinson, 2001), is the most important genetic paediatric disorder (Cotran et al, 1999) and the commonest cause of chronic suppurative lung disease in Caucasian children (Olinsky, 1996).

It is characterized by abnormally viscous mucous secretions, which obstruct organ passages resulting in multisystemic clinical manifestations such as recurrent pulmonary infections, pancreatic insufficiency, intestinal obstruction, malnutrition, hepatic cirrhosis, steatorrhoea and male infertility. These may appear any time from before birth to adulthood (Cotran et al, 1999).

2.3.2 INCIDENCE

Incidence varies in the literature, but highlights how relatively common CF is. Cotran et al (1999) reported it as being 1 in 1500 to 1 in 4000 live births, while Nixon et al (2000) documented it as 1 in 3300 live births. Closer to home, Olinsky (1996) suggested an incidence in Australia of approximately 1 in 2500 live births.

It is the most common lethal genetic disease affecting white populations (Cotran et al, 1999) and extremely rare in non-Caucasian populations with only occasional reports in Asian and Africans.

2.3.3 GENETICS

CF is an inherited autosomal recessive trait, meaning that two copies of the defective gene are needed to cause disease. The CF gene is on the long arm of Chromosome 7. It codes for the Cystic Fibrosis Transmembrane

Regulator (CFTR) protein, a chloride channel that normally allows passage of chloride ions through the cell membrane (Crystal, 1995).

2.3.4 CLINICAL MANIFESTATIONS

The CFTR protein is highly concentrated on the apical membrane surface of epithelial cells of the respiratory tract, gastrointestinal tract and sweat glands. When dysfunctional, chloride transport abnormalities cause increased sweat chloride concentration. In the airways, decreased chloride secretion leads to increased sodium and water reabsorption causing dehydrated mucous, defective mucociliary action and mucous plugging of airways (Cotran et al, 1999).

The pancreas and lungs are primarily affected (Davis et al, 1996). In the pancreas, thick mucous prevents digestive enzymes from reaching the small intestine, impairing digestion of dietary fat and protein and causing malnutrition. According to Olinsky (1996), malabsorption is eventually present in 85-90% of patients. In the lungs, airway obstruction and stasis of mucous encourage bacterial infection and subsequent bronchiolitis, bronchitis, bronchiectasis, and eventually fibrosis and irreversible loss of pulmonary function (Nixon et al, 2000).

2.3.5 PROGNOSIS

The lifespan of CF patients has dramatically improved. 30% born during the 1940s lived to 12 months and only 10% to 10 years (Olinsky, 1996). In 1971, less than 50% of patients reached 20. (Godfrey and Mearns, 1971). Nowadays, major clinics report survival rates of at least 70-80% at 20. Life expectancy has advanced well into adult life (Robinson, 2001), the median age of survival now being in the early 30s (Olinsky, 1996).

2.3.6 MANAGEMENT OF CF

Treatment aims to avert irreversible changes and is accomplished by clearing mucopurulent secretions and preventing or combating infection (Olinsky, 1996). This is accomplished with antibiotics, physiotherapy, physical activity and aerosol inhalants that break up mucous.

Management of gastrointestinal symptoms and prevention of malnutrition involves enzyme supplementation (Olinsky, 1996).

Gene therapy is a future treatment under investigation (Crystal, 1995. Flotte, 2002. Davies et al, 2001), possibly providing hope of a cure.

2.4 LIMITATIONS OF EXERCISE TOLERANCE IN CYSTIC FIBROSIS

2.4.1 INTRODUCTION

CF patients have decreased aerobic power and exercise tolerance, defined by reduced $\dot{V}O_{2peak}$ (Freeman et al, 1993. Boas, 1997). Some studies have shown that there is a further anaerobic limitation (Ashish et al, 1998. Boas et al, 1996).

Most patients with mild CF have normal exercise tolerance (Orenstein, 1993), but this eventually declines with disease progression (Cerny and Armitage, 1989. Godfrey and Mearns, 1971. Moorcroft et al, 1997. Freeman et al, 1993).

Godfrey and Mearns (1971) grouped 41 CF patients into categories of mild, moderate and severe disease based on clinical and radiological findings. In what was the first study to perform sophisticated exercise testing of CF patients, they used progressive cycle ergometer testing to assess exercise tolerance. One major finding was that the sicker the group, the lower the exercise tolerance, indicated by high correlation (r=0.71) between Maximal Voluntary Ventilation (MVV) and Work Capacity (W_{max}). The methodology was comprehensive, using both steady state and progressive exercise tests. The study sample was representative with a wide range of ages (6-21 years), balanced gender and encompassing the entire spectrum of disease, although there was no mention of the participation rate. Absence of controls was acceptable as the study focused on CF only.

Orenstein and Nixon (1991) supported this finding, assigning 110 CF patients to 3 groups based on FEV_1 and discovering that the patients with the best pulmonary function had the best exercise tolerance. Pearson correlation revealed a highly significant relationship between $\dot{V}O_{2peak}$ and FEV_1 (r=0.47, P<0.0001). They also examined this relationship in terms of male and female differences, finding that females had lower exercise tolerance overall, regardless of pulmonary function.

Cerny and Armitage (1989) suggested reasons for exercise capacity reduction with disease progression, hypothesizing that in mild disease, normal exercise capacity is maintained because normal pulmonary reserves in gas exchange exist. This reserve capacity is progressively reduced until pulmonary factors become the primary limitation.

A study comparing maximum exercise capacity and endurance exercise capacity (duration of exercise at 80% of patient's $\dot{V}O_2max$) in matched CF patients and controls, found that lung function was positively correlated with maximum oxygen uptake (r=0.83, P<0.001) and work load (r=0.79, P<0.001) (Freeman et al, 1993). This was in agreement with the previous studies, indicating that exercise capacity is well preserved in mild disease, but reduced in severe disease.

Moorcroft et al (1997) also found that patients with mild disease could maintain $\dot{V}O_{2peak}$ *despite* declining lung function. $\dot{V}O_{2peak}$ was not reduced because $\dot{V}_{E\ peak}$ was unaffected. They hypothesised that nutrition may have also contributed to maintenance of fitness.

This supported a study by Lands et al (1992), which using step-wise linear regression with $\dot{V}O_{2max}$ as the independent variable, found that exercise tolerance was best accounted for by a combination of FEV_1 and the 30-second sprint work performed by subjects. The sprint-work indicated the importance of nutrition, as it would have been reduced if malnutrition caused loss of muscle mass. These findings confirmed that the two main factors influencing exercise tolerance in CF were pulmonary function and nutritional status.

2.4.2 PULMONARY LIMITATION TO EXERCISE IN CF

In contrast to healthy individuals, the primary exercise limitation in CF is pulmonary rather than cardiac (Boas, 1997. Cerny et al, 1982), as indicated by high ventilations during exercise without peak heart rates (Hjeltnes et al, 1984. Lands et al, 1992).

The most published finding of studies in this area is the increased dead space in patients (V_D), which causes the dramatically increased ventilations.

This pattern emerged in the study by Godrey and Mearns (1971), which grouped CF patients according to lung function, Group 3 representing the most severe disease. V_D was enlarged in all but 1 of their 41 patients, in whom it was 122% of predicted. Very significant enlargements were seen, with over twice the expected value in all but 7 children. Even in the fittest children, the mean value for V_D was 226% of predicted. The enlarged V_D correlated with clinical grade as indicated by a significant negative correlation between FEV_1 and V_D (r=- 0.56), especially between groups 2 and 3. The authors hypothesised that this was because parenchymal damage (demonstrated by increased V_D) wouldn't occur until recurrent pulmonary infections and airway damage had caused a certain degree of airway obstruction. V_D was also related to mechanical evidence of airways obstruction indicated by the FEV_1 (r=0.54. regression coefficient= -1.09) so that the higher the V_D, the lower the FEV_1 (Godfrey and Mearns, 1971).

Although this study is old, its findings have been consistently supported. Cerny et al (1982) made the same claim when they compared cardiorespiratory adaptations of exercise between 21 CF patients and 17 controls. The patients were grouped on the basis of their FEV_1. After exercise, they observed consistently higher ventilations in the 4 CF groups, even in the patients with no resting pulmonary dysfunction.

More recently, it was suggested that an increased ventilatory equivalent for oxygen during rest and exercise, together with an increased residual volume was indicative of enlarged dead space (Stanghelle et al, 1992).

Although hyperventilation is intended to compensate for enlarged V_D, studies have shown that it limits exercise in severe disease (Freeman et al, 1993. Webb and Dodd, 1995). These studies showed that CF patients with mild to moderate disease could exercise to almost the same degree as healthy individuals. Patients with more severe disease (FEV_1 <30%) have less capacity to increase V_T, meaning that high ventilation maintenance during exercise depends on increased breathing frequency. This mechanism creates excessive work for the respiratory muscles leading to fatigue and premature exercise termination, and aggravates hyperinflation of the lungs (Webb and Dodd, 1995).

Regnis et al (1991) observed a similar pattern of breathing. Hyperinflation during exercise was caused by a strategy of increasing breathing frequency rather than tidal volume, which mimimises resistive work.

They also studied detrimental effects of hyperinflation brought about by another compensatory mechanism- the maintenance of End-Expiratory Lung Volume (EELV), which is important in determining an appropriate ventilatory response to exercise. In health, the EELV decreases during exercise, optimising diaphragm length and increasing abdominal wall recoil to aid inspiration. CF patients normally have increased EELV during exercise. This compensatory mechanism aims to reduce the expiratory flow limitation characteristic of CF, but resulting hyperinflation increases work for the respiratory muscles, leading to early fatigue and exercise termination (Regnis et al, 1991).

Regnis et al (1991) studied the regulation of EELV in 22 CF patients to see if responses related to the degree of pulmonary impairment. They divided patients into two groups based on whether they decreased (Subgroup A) or increased (Subgroup B) their EELV during a progressive cycle ergometer test. Subgroup A had considerably better resting lung function and saturations, and significantly higher W_{max} and $\dot{V}O_{2peak}$. Subgroup B in comparison had very severe lung disease, limited W_{max} and desaturation during exercise. Increasing breathing frequency was their sole mechanism to improve ventilation.

This supports the claim of Webb and Dodd (1995) and Freeman et al (1993) that ventilation limits exercise in severe disease. It also backs up Orenstein's (1993) suggestion that many CF patients have normal exercise tolerance, and the many authors who have found that it declines with disease progression (Cerny and Armitage, 1989. Godfrey and Mearns, 1971. Moorcroft et al, 1997. Freeman et al, 1993).

Mostly, increased ventilation is sufficient to maintain blood oxygen levels, but desaturation may occur in severe disease (Webb and Dodd, 1995). Henke and Orenstein (1984) studied oxygen saturation during exercise in CF patients and found that saturation was uncommon across the spectrum of disease severity (only 13 out of 91 patients changed SaO_2 by 5% or more), but larger degrees were more likely to occur in patients whose FEV_1 was less than 50% of their VC. Resting $\dot{V}O_2$ was a less-predictable factor for desaturation (Henke and Orenstein, 1984). Other proposed predictors of exercise-induced desaturation are an FEV_1 less than or equal to 60% predicted (Marcotte et al, 1986) and an FEV_1 less than 35% predicted (Lebecque et al, 1987).

Henke and Orenstein (1984) concluded that most patients could tolerate even maximal exercise without significant desaturation, but those with FEV_1 less than 50% of VC needed supervised exercise testing with ear oximetry before undertaking an exercise program.

Alternatively, Marcus et al (1992) suggested CF patients with advanced disease would benefit from breathing supplemental oxygen during exercise. They found that this resulted in longer exercise, higher $\dot{V}O_{2max}$, higher O_2 pulse and less arterial desaturation.

2.4.3 NUTRITION AS A LIMITATION TO EXERCISE

Nutritional status is closely related to exercise tolerance in CF (Coates et al, 1980. Marcotte et al, 1986). Poor digestion and malabsorption are characteristic features and if unmanaged, lead to loss of body fat followed by loss of muscle, which has specific consequences for exercise depending on the site of muscle loss. Loss from legs will affect treadmill/cycle ergometer performance; respiratory muscle loss will impair breathing mechanics (Boucher et al, 1997). According to Lands et al (1992), muscle loss does not affect performance of remaining muscle.

Boucher et al's (1997) study found that in patients with significant lung disease (FEV_1<75%), activity level was related to nutritional status rather than lung function. Improving nutrition may therefore be a way of preventing activity decline and improving quality of life.

Unlike Boucher et al (1997), Moorcroft et al (1997) found that nutritional status was related to lung function, but the correlation was not strong (r=0.19). Their results also demonstrated that BMI could be improved despite a declining lung function if better nutritional management outweighed any adverse influence that a lower FEV_1 might have had on weight.

Aerobic *and* anaerobic parameters of exercise are limited in CF, but nutrition is the major determinant of anaerobic capacity. This relationship works both ways; anaerobic training exercises such as weightlifting achieve significant improvements in body weight and muscle strength (Ashish et al, 1998).

Research has also investigated supplemental nutritional programs and their effect on exercise tolerance. Skeie et al (1987) examined the effect of long-term home parenteral nutrition, including IV fat emulsion and found that participants gained weight and improved their ability to participate in daily activities. The extremely small sample size (only 2 patients) indicated a pilot study, prompting further research.

Hanning et al, (1993) examined the effects of dietary supplementation on skeletal muscle strength by randomly assigning patients to receive or not receive noninvasive nutritional supplementation. Skeletal muscle strength correlated significantly (r=0.76) with growth, indicating that it may be a functional index of changes in nutritional status.

2.4.4 MUSCLE FUNCTION AS A LIMITATION TO EXERCISE

De Meer et al (1999) found that in children with CF, muscle force was decreased and associated with diminished maximal workload, even in the absence of diminished pulmonary or nutritional status.

Abnormalities in muscle function were also noted by De Meer et al (1995). They investigated the possible role of diminished efficiency of mitochondrial oxidative phosphorylation and found that in CF, the oxidative work performance of skeletal muscle was reduced. They proposed that this might have been related to secondary pathological changes in the muscle.

Lands et al (1993) did not find any abnormality in muscle function. Rather, they found increased respiratory strength related to the increased work of breathing in CF. They also observed decreased leg strength in patients compared to controls, which they attributed to a smaller mass as a consequence of mild malnutrition rather than the quality and function of the remaining muscle.

2.5 EXERCISE TESTING IN CHILDREN WITH CYSTIC FIBROSIS

2.5.1 INTRODUCTION TO EXERCISE TESTING

Since Godfrey and Mearns (1971) published their finding of decreased exercise tolerance with progression of disease, exercise testing has been the subject of extensive investigation.

In 1992, Nixon et al sought to determine the prognostic value of exercise testing in addition to known factors associated with poor survival such as female sex, impaired pulmonary function, older age, malnutrition and colonization of the respiratory tract by *Burkholderia Cepacia*. 109 CF patients had pulmonary and exercise testing in the 1970s and were followed up in 8 years to determine the factors that were associated with subsequent mortality. Patients with the highest levels of aerobic fitness ($\dot{V}O_{2peak} \geq 82\%$ predicted) had a 55% greater rate of survival than those with the lowest levels of fitness ($\dot{V}O_{2peak} \leq 58\%$ predicted). An extremely important finding supporting exercise testing in CF children is that after adjusting for other risk factors, patients with higher aerobic fitness were over three times as likely to survive than patients with lower fitness levels.

A more recent study in the adult CF population further supported the prognostic value of exercise testing. (Moorcroft et al, 1997). Although FEV_1 was found to be the main predictor of mortality, $\dot{V}O_{2peak}$, W_{max} and $\dot{V}_{Epeak}$ also correlated with long-term survival.

2.5.2 TYPES OF EXERCISE TESTS

Various tests are used to assess exercise tolerance, with different types specific to the area of interest (Orenstein, 1998). Examples include the 3-minute step test (Balfour-Lynn et al, 1998), 6-minute walk test (Nixon et al, 1996. Gulmans et al, 1996. Chetta et al, 2001), and the gold standard treadmill and cycle ergometer tests.

The step tests have the advantage of portability, therefore are useful for field work, but treadmill and cycle ergometer tests are most commonly used in CF clinics (Rowland TW, 1993). This is because they can test maximum workload sustainable or the amount of energy that can be brought in and processed, as well as ventilatory and cardiac responses to progressively increasing workloads (Orenstein, 1998).

The advantage of the cycle ergometer is that it is quieter and less expensive and space consuming than a treadmill. The treadmill however, elicits greater levels of $\dot{V}O_{2peak}$ and peak heart rate. A poorly motivated child may exercise longer on it because unlike the cycle ergometer where children can stop pedaling and terminate tests before attaining maximal exercise, the treadmill doesn't require maintenance of a specific pedaling rate (Rowland, 1993).

2.5.3 EXERCISE TEST PROTOCOLS

Specific protocols are also used for specific purposes. The Bruce and Balke treadmill protocols are popular in CF exercise laboratories and clinics (Rowland, 1993).

The Bruce protocol involves progressive increases in slope and speed. However, the work increments are unequal, and although chosen to represent levels of light, moderate and maximal exercise stress, are not suitable for children.

The Balke protocol is more suitable for children, providing a constant speed with a 2% increase in grade each minute. It was modified in this study to produce one-minute intervals of 1%.

2.6 BENEFITS OF EXERCISE FOR CF PATIENTS

2.6.1 INTRODUCTION

Aerobic fitness is associated with better prognosis in healthy populations and CF patients (Nixon et al, 1992) and other than being colonized with *Burkholderia Cepacia*, is the strongest correlate with long-term survival (Orenstein, 1998). It is extremely important to encourage physical activity in CF patients so they can benefit from improvements in mucociliary clearance, $\dot{V}O_{2peak}$, exercise tolerance, ventilation, pulmonary function, muscle strength and endurance, and self-esteem.

2.6.2 BENEFITS OF EXERCISE AND EXERCISE PROGRAMS

Mucociliary clearance is extremely important to prevent airway obstruction and infection. It is normally achieved with a twice-daily course of physiotherapy, but compliance with this regime is poor (Bilton et al, 1992). After Zach et al (1982) suggested that chest physiotherapy could be partially replaced by exercise, Bilton et al investigated the impact of exercise, physiotherapy and combinations of the two on sputum expectoration. Although exercise alone was less productive than physiotherapy, a combination of the two with exercise being performed first, was preferred by patients.

Improved sense of well-being is another benefit of exercise. Schneiderman et al (2000) randomly assigned 72 CF patients to an exercise group (minimum 20 minutes exercise, 3x weekly) or a control group (normal physical activity). Pulmonary function declined more slowly in the exercise group, and patients reported positive attitudes towards the program, improved self-esteem and feelings of competence. Similar results were found in an outpatient exercise-training program (Gulmans et al, 1999).

Most importantly, exercise programs have consistently achieved positive changes in physiological parameters. Improvements have been seen in exercise tolerance and VO_{2peak} (Tuzin et al, 1998. Orenstein et al,

1981. Gulmans et al, 1999. Weitz De Jong et al, 1994. Selvadurai et al, 2002), W_{max} (Weitz De Jong et al, 1994. Tuzin et al, 1998) VC and pulmonary function (Heijerman et al, 1992), oxygen pulse (Heijerman et al, 1992. Weitz De Jong et al, 1994) muscle endurance strength (Orenstein et al, 1981.Gulmans et al, 1999), and ventilation (Tuzin et al, 1998). Improvement in activities of daily living also emphasized the influence of physical fitness on quality of life.

Heijerman et al (1992) made the important finding that in addition to a three week, twice-daily exercise program improving lung function in 10 CF patients, those with severe disease maintained these benefits and cardiopulmonary fitness was preserved one year after programme completion. Follow-up revealed further extraordinary improvements after the programme; the possibility of heart-lung transplantation had being abandoned in all patients.

Benefits can be attained regardless of the kind of exercise undertaken, providing participants are compliant. Selvadurai et al (2002) recommend a combination of aerobic and resistance training.

2.7 PHYSICAL ACTIVITY IN CHILDREN WITH CF

Male CF patients have higher exercise tolerance than females, even when resting pulmonary functions are equal (Orenstein et al, 1991). Evidence is accumulating that this may be due to reduced physical activity levels in girls (Olinsky 1996. Hussey et al, 2001. Armstrong and Welsman, 1997).

Nixon et al (2000) made the important discovery that CF children do not participate in less activity than their peers. Rather, they spend less time in vigorous activities, even when nutritional status and pulmonary function are adequate. They used Kriska's Modifiable Activity Questionnaire (MAQ) (Aaron et al, 1995) to record activity levels and intensity, and investigated whether this difference in vigorous activity was related to aerobic fitness and disease status. They found that in patients with lower lung function, hours of vigorous activity correlated with pulmonary function and aerobic fitness. This raises the need for further research not only into the measurement of physical activity, but specifically the assessment of vigorous activity in order to support this new finding.

CF patients' attitudes towards exercise are positive (Stanghelle et al, 1988). However, a study by Boas et al (1999) indicated that parents perceive more barriers to physical activity than benefits. Only half of this group were aware of the benefits of exercise in CF, therefore education may help encourage increased activity in CF children.

2.8 MEASURING PHYSICAL ACTIVITY IN CHILDREN WITH CF

2.8.1 QUESTIONNAIRES

Activity questionnaires are a simple and effective means of assessing physical activity.

The MAC-Q developed by Kriska was validated in 1995 (Aaron et al, 1995) and has been used in several studies since (Nixon et al, 2001. Hussey et al, 2001). It focuses on leisure-time activity for the past twelve months. A comprehensive table records the activities, as well as the months per year, days per week and minutes per day for each.

The Physical Activity Questionnaire for Children (PAC- Q) was found by Crocker et al (1997) to have a strong correlation with physical activity. This was supported by Kowalski et al (1997), who compared it to a motion sensor, activity recall interview, step-test of fitness and self-administered physical activity questionnaire. It is a ten-part questionnaire focusing on physical activity in spare time (e.g. before/after school, at recess, weekends etc) over the past week. Questions relate to both frequency and intensity of activity. An example is *"In the last 7 days, on how many evenings did you do sports, dance or played games in which you were very active."* One question allows participants to indicate whether anything prevented them from doing activities in that week.

Activity questionnaires are not without fault. They may not be entirely valid due to the overestimation of activity levels by children and parents alike (Janz et al 1995). In recall questionnaires, activities may also not be remembered accurately.

For questionnaires that assess activity intensity, each activity is assigned an intensity value (Ainsworth et al, 1992). All activities are assigned intensity units expressed as METs, based on their rate of energy expenditure.

2.8.2 ACCELEROMETERS

The CSA monitor has been validated in children with CF using heart rate and $\dot{V}O_{2\,peak}$ (Janz, 1995).

It is small (6.6x4.x1.5 cm), lightweight (70 gm), powered by a 0.5 volt AA lithium battery (Janz, 1995) and is worn on a belt just above the right hipbone.

It measures movement in a single vertical axis (displacement of the hip during activity causes upwards and downwards movements) and generates a signal proportional to the force acting on it. These signals are digitized and compiled over a predefined time period called the *epoch.* After each epoch, the movement count is stored in a memory that can hold twelve weeks worth of data (Janz, 1995). The monitor data is readily downloaded onto computer.

2.9 CONCLUSION AND HYPOTHESES

Review of the literature emphasizes the importance of exercise testing and assessment of physical activity in children with CF.

As a result of previous research, it is hypothesised that:

1) The questionnaire scores will correlate weakly with physical activity data recorded by the accelerometer, but will not be significant enough for validation
2) Patients with higher levels of vigorous activity will have higher pulmonary function and aerobic fitness.
3) Patients with higher levels of general activity will have higher pulmonary function and fitness.

CHAPTER 3

METHODOLOGY

3.1 LOCATION OF STUDY AND ETHICS APPROVAL

The study was conducted in the Respiratory Laboratory and Cystic Fibrosis Outpatient Clinic at the Royal Children's Hospital (RCH) Melbourne, Australia.

Ethics Approval was granted on the 13/7/2001, by the Royal Children's Hospital Ethics in Research Committee. The study was assigned the reference number **EHRC 21080A.**

3.2 RECRUITMENT OF PARTICIPANTS

3.2.1 SELECTION CRITERIA

Participants were required to be between seven and eighteen years old, with a definitive diagnosis of CF based on a sweat test or genetic test. An exercise test must have been completed in the past year or immediately before the study.

Only local patients were approached as the monitors needed to be returned to the hospital and were unsuitable for postage.

3.2.2 RECRUITMENT PROCEDURE

Patients were recruited from the Respiratory Laboratory and the CF Outpatient's Clinic, depending on whether they had completed an exercise test in the previous 12 months.

Outpatient clinic appointments were reviewed weekly. Patients with appointments and due for an annual exercise test were telephoned. The exercise test was explained and a booking made for the day of their appointment.

Before the test, parents and patients were informed about the study and shown activity monitors. If interested, an information statement (Appendix A) with further details was provided to parents to read during the test.

If patients agreed to participate, the monitor was set to begin counting approximately half an hour later and fitted to them before they left the hospital. They were provided with 3 questionnaires (see 3.3.7) to complete after removal of the monitor in seven days. An activity monitor information statement (Appendix B) and a copy of the consent form (Appendix C) were given.

Patients not due for exercise tests but booked in for outpatient appointments were recruited from this clinic. They were met in the waiting room and informed of the study in the same manner. Pre-set activity monitors were fitted, and the relevant forms handed out. The data from their most recent exercise test was retrieved for use in the study.

A third group of 11 patients did not wear monitors but agreed to complete the 3 questionnaires.

3.2.3 SAMPLE SIZES

The sample for the entire study (that is, to answer all proposed questions) included those who wore monitors and/or had exercise tests and /or completed the questionnaires. n= 52 (M=28 F=24)

The study was divided into 3 main parts. Due to the variation in questionnaire response rates and monitor success among patients, each part used different sample sizes.

PART 1: CF-PA VALIDATION:

44 patients were given monitors. Two patients removed them early due to discomfort, one monitor was lost and another did not work properly. Another participant wore the monitor for a week but did not complete the questionnaires (although their data was useful for examining relationships between activity, fitness and lung function) and one set of questionnaires was completed incorrectly. Excluding those 5 withdrawn patients, n= 39 (M=18 F= 21).

PART 2: COMPARISON OF QUESTIONNAIRES:

Response rates to each questionnaire, and therefore each comparison varied, but the overall sample included the 39 patients who wore monitors and answered questionnaires correctly, and the 11 patients who answered the questionnaires only (n= 50)

PART 3: ANALYSIS OF RELATIONSHIPS BETWEEN FITNESS, ACTIVITY, LUNG FUNCTION AND BMI.

Numbers varied according to the relationship being investigated, but the overall sample included those who wore monitors successfully and had exercise tests. (n= 41)

3.3 EQUIPMENT AND INSTRUMENTATION

3.3.1 LUNG FUNCTION TESTING- THE MASTERLAB SYSTEM

Lung function tests were performed prior to every exercise test using the MasterLab System, built by *Jaeger*, which included a body plethysmograph with built in spirometer.

The testing was carried out in accordance with the Australian Thoracic Society recommendations (ATS, 1995).

The lung function test examined two parameters of breathing capacity- flow and volume. Patients sat in the body plethysmograph box wearing a noseclip, with their mouth over the mouthpiece. After several normal breaths, they performed a maximal inspiration, followed by maximal expiration. This was repeated at least twice. In order to measure lung volumes and airways resistance, the door of the box was closed. The patient continued to breathe normally through the mouthpiece, while shutters transiently blocked off the air they were breathing. A printed report was generated upon completion of the test (Appendix D).

The MasterLab system was calibrated daily following entry of ambient conditions. Calibration was performed automatically by the computer, and manually using a 3-litre syringe which when pumped, created inspiratory and expiratory flow-volume loops.

3.3.2 HEART RATE MONITOR

All patients wore a Polar Vantage NV heart rate monitor during the exercise test, which was strapped, around their chests above the xiphoid process of the sternum (Bate, 2001). A damp strip of paper toweling placed between the strap and skin improved conductance.

A digital watch on the treadmill displayed the recorded heart rate.

3.3.3 SATURATION MONITOR

Participants' blood oxygen saturation levels were monitored throughout the exercise test, using an Oltimeda pulse oximeter connected to the left middle finger. Saturations (including resting) were manually recorded at one-minute intervals.

3.3.4 THE OXYCON METABOLIC ASSESSMENT SYSTEM

The Oxycon Metabolic Assessment System measured aerobic fitness. It consisted of the following:

- Triple V volume transducer- this device, connected to the mouthpiece, measured the minute ventilation. An end tidal line inserted near the mouthpiece allowed continuous monitoring of CO_2 and O_2 concentrations of inspired and expired air.
- Computer program- this took measurements from the transducer and used them to display graphs of oxygen consumption, ventilation, heart rate and respiratory exchange ratio in the context of the predicted values for each patient' age and height.

  Printed tables gave 10 second recordings of the following:

  - Ventilation $\dot{V}_E$ (L/Min)
  - Rate of Oxygen consumption $\dot{V}O_{2peak}$ (ml/(kg.min))
  - Heart rate HR-ox bpm
  - Respiratory Exchange Ratio (RER) or Respiratory Quotient (RQ) ($\dot{V}CO_2/\dot{V}O_2$)
  - Oxygen Equivalent ($\dot{V}_E/\dot{V}O_2$) -Total volume of air breathed compared with the amount of O_2 consumed (Rowland, 1993).
  - Carbon Dioxide Equivalent ($\dot{V}_E/\dot{V}CO_2$) – Total volume of air breathed compared to amount of CO_2 blown off (Rowland, 1993).
  - End Tidal Partial Pressure Oxygen PET O_2 kPa
  - End Tidal Partial Pressure Carbon Dioxide $PETCO_2$ kPa
  - Oxygen Saturation SaO_2 (%)
  - Breathing Frequency BF/min
  - Dyspneoic Index DY- a measure of breathlessness ($\dot{V}_E/FEV_1$ x 35)

The Oxycon system was calibrated daily

1) Automatically, using a gas analyzer system while connected to a gas cylinder with known concentrations of O_2 and CO_2.
2) Manually, using a 2-Litre syringe connected to the transducer to create flow-volumes loops.

3.3.5 MEASURING $\dot{V}O_{2peak}$- THE TREADMILL TEST

Metabolic data recorded during the test was used to examine relationships between fitness, physical activity lung function and BMI.

$\dot{V}O_{2peak,}$ defined as the maximum rate of O_2 consumption averaged over the last 30 seconds of exercise (Rowland, 1993), was assessed via indirect calorimetry using the Oxycon Metabolic Analysis System.

The treadmill test procedure is explained in detail in Section 3.4.2

3.3.6 THE COMPUTER SCIENCE APPLICATIONS (CSA) ACCELEROMETER

The CSA monitor (described in section 2.8.2) was worn by participants for 7 consecutive days. They were instructed to remove it only for water activities and sleep. After removal, the monitor was returned to the hospital and the information downloaded.

3.3.7 ACTIVITY QUESTIONNAIRES

1. CYSTIC FIBROSIS PHYSICAL ACTIVITY QUESTIONNAIRE (CF-PA) (APPENDIX E)

SCORING:

A scoring system was proposed by Gutierrez-Schwanhauser (2001).

The diary was arranged into categories of activities. Subjects selected categories that included activities they had participated in and specified the duration of participation. If a particular activity within a group was specified, its individual MET value was assigned; otherwise, an average MET value for the entire category was used. When multiple activities were specified per category, their MET values were averaged (Appendix F).

The minutes spent in those activities were multiplied by the assigned MET values, giving the number of METs per week for that category. Each category was summed, giving an overall total of METs for the week.

Information about the time spent in activities such as walking to/from school, climbing stairs and recess/lunchtime also contributed to the final score.

Finally, a figure was extracted to represent activity intensity by including sports in the weekly total, while excluding categories like housework, gardening and playing.

2. MODIFIABLE ACTIVITY QUESTIONNAIRE FOR ADOLESCENTS (MAQ) (APPENDIX G)

SCORING:

The activity diary was scored by assigning MET values to each nominated activity. Using the calculations below, each activity was expressed in hours per week averaged over the past year, or in terms of METs per hour per week (Aaron and Kriska, 1995).

For each activity:

(*Number of months) x (days/week) x (4.3 weeks/month) x (minutes per day) ÷ (52 week/year)* = hours per week averaged over past year

Then:

(Hours/week) x (MET value) = MET/hour/week

3. PHYSICAL ACTIVITY QUESTIONNAIRE FOR CHILDREN (PAC-Q) (APPENDIX H)

SCORING:

Questions were scaled from 1-5, with higher scores indicating more activity (Kowalski et al, 1997). The scores were summed, and the mean value of the nine questions calculated. This questionnaire did not estimate energy expenditure.

3.4 STUDY PROTOCOL

3.4.1 PRE-EXERCISE TEST PROCEDURE

A standard procedure was strictly followed prior to each test.

Anthropometric measurements of height and weight were recorded. These were entered into the MasterLab and Oxycon systems to calculate predicted values for the spirometry, and predicted ranges for the exercise data, specific to each patient's age group.

A lung function test was performed, and Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC), and Maximal Mid-Expiratory Flow (MMEF) were obtained from the flow/volume loops. Functional Residual Capacity (FRC), Total Lung Capacity (TLC), Vital Capacity (VC) and Residual Volume (RV) were determined by plethysmography. The most important of these measurements was the FEV_1 - the volume exhaled in the first second of expiration- an important measure of the extent and type of lung disease (West, 1974).

The test supervisor used the measurements of lung function, the patients' age and their previous exercise test data to choose an appropriate treadmill speed.

After completion of the lung function test, the patient was connected to the heart rate and saturation monitors.

At this point, they moved onto the treadmill, and were put on the mouthpiece. Final spirometry was performed, with 2 maximal inspirations followed by maximal expirations.

Finally, the patient performed some leg stretches to prevent discomfort during and after the test. The test procedure was fully explained, resting oxygen saturation and heart rate were recorded and the test was ready to commence.

3.4.2 THE TREADMILL TEST

The protocol used for the treadmill test was in accordance with the Modified Balke Protocol for paediatric exercise testing (Rowland, 1993).

For the first 2 minutes, patients walked at a fixed speed with the treadmill at zero elevation. After 2 minutes, the treadmill was raised to an elevation of 4%, with the speed kept constant. Each minute thereafter, treadmill elevation increased by increments of 1%. The speed was usually kept constant. However, if the patients' heart rate and Respiratory Exchange Ratio were not rising, speed was increased. Patients were encouraged to jog and the speed adjusted accordingly.

The test continued for between 8 and 10 minutes. It was terminated for the following reasons

- An appropriate RER (≥1.1) or Heart Rate (> 90% predicted) were reached
- Patients desaturated > 15%
- No further increase in $\dot{V}O_{2peak}$ was seen with increased workload
- The patient felt discomfort and wished to finish

Patients were given standardized encouragement throughout the test.

3.4.2.1 SAFETY DURING THE TEST

At all times, two people were present- the most experienced to run the treadmill and supervise the patient, the other to monitor computer data, saturations and heart rate. The supervisor kept one hand behind the patients' back at all times and regularly checked that the patient felt okay.

Upon test completion, patients walked for 2 minutes at 2km/hour and 0% elevation, while metabolic parameters were recorded. They were then seated and given water, and monitored for at least 10 minutes before leaving the laboratory.

3.4.2.2 DATA COLLECTION DURING THE TEST

Heart Rate and saturations were manually recorded each minute on an exercise test-recording sheet (Appendix I).

Concentrated Inspired and Expired gases were measured continuously (breath by breath) and the results were averaged at 10-second intervals and displayed on the computer as graphs by the Oxycon system. A 3-page print out of these data (Appendix J) was used to determine the metabolic parameters described above by averaging the results over the last 30 seconds of exercise.

After the test, patients were asked to rate their perceived exertion (RPE) in terms of their legs and breathing. This rating was on a scale of 0-10, with 10 being the highest difficulty (Borg, 1982).

3.5 MONITORING PHYSICAL ACTIVITY WITH THE CSA MONITOR

The monitor was fitted to the patient before they left the hospital so that they could see how it was positioned correctly. It was placed firmly above the right hip with the notch facing upwards. The epoch was set at one minute, and activity recorded for seven consecutive days, providing a minute-by-minute chronological recording of movement for the entire week.

3.6 COMPLETION OF QUESTIONNAIRES

The questionnaires were given to the participants before they left the hospital. They were told to complete them after removal of the monitor in seven days. Until then, they were asked not to look at them nor pay extra attention to their activity during the week.

3.7 CONCLUSION OF METHODS

The monitors were downloaded onto computer and analysed using the SWAM computer package associated with the CSA system. Further analysis and statistical results were performed using a local software product (CSA Fix, Gorman, 2000) and Microsoft Excel (2000 edition), respectively.

The questionnaires were all scored according to the guidelines in section 3.3.7

The activity data and questionnaire scores were then analysed and compared with the lung function and exercise test data.

3.8 DATA AND STATISTICAL ANALYSIS

Regression was the statistical technique most commonly used. It was performed for the CF-PA validation between activity (general, weekend and intensity) and questionnaire scores, between the 3 questionnaires, and for all the relationships in Part 3 between BMI, lung function, activity and fitness.

ANOVA was used to examine differences in activity, BMI and fitness between the three lung function groups.

The "Day by Day" component of the SWAM program was used for calculation of daily, weekly and weekend average activity counts per minute. To express activity in terms of MET expenditure, Table 3.1 (Trost, 2001) and its corresponding equations were used to account for age-related differences. In general, the younger a child, the less the number of counts required for each MET. The CSA fix program used these values to establish the amount of time spent in each activity range.

Patients were divided into 3 groups based on their lung function- Group 1 ($FEV_1 \leq 75\%$ predicted), Group 2 ($76\% \leq FEV_1 \leq 94\%$) and Group 3 ($95\% \leq FEV_1$). Each relationship was analysed again in each individual group.

A p-value less than 0.05 was considered significant.

TABLE 3.1: CSA COUNT CUT-OFFS (COUNTS/MIN) FOR DEFINING EXERCISE INTENSITY IN METS, IN CHILDREN AND ADOLESCENTS (Trost, 2001)

Age (years)	3 METS	6 METS	9 METS
	Counts Required		
6	614	2972	5331
7	633	3064	5495
8	803	3311	5819
9	913	3521	6130
10	1017	3696	6374
11	1135	3908	6681
12	1263	4136	7010
13	1399	4382	7364
14	1547	4646	7745
15	1706	4932	8158
16	1880	5243	8607
17	2068	5581	9094
18	2274	5951	9627

CHAPTER 4

DEFENCE OF METHODOLOGY

4.1 DEFENCE OF SAMPLE SIZE

Previous work in the area by the respiratory laboratory at RCH has shown that in order to demonstrate differences in $\dot{V}O_{2peak}$ between groups, a sample size of at least 32 was required. This figure was based on a 5% (α) level of significance and an 80% (β) power for a mean difference in $\dot{V}O_{2peak}$ of 7ml.kg.min (± 10 SD) between groups (Gutierrez, 1996).

Limited recruitment time and exclusion of rural residents limited the available patients, but the final sample of 41 for the analysis of fitness, activity, lung function and BMI still exceeded the minimum requirement.

4.2 DEFENCE OF PATIENT SELECTION METHOD RECRUITMENT

The exclusion of rural patients was an unfortunate limitation to the recruitment of study participants, but could not be avoided as previously explained.

Other than the basic selection criteria, patients were not excluded for any other reason and most eligible patients were approached.

Approximately 80 patients were eligible to be involved. Of these, roughly 60 were approached. The others did not present for exercise tests or cancelled outpatient appointments, therefore, there was no opportunity to ask for their participation. At other times, no activity monitors were available for eligible patients, thus limiting the recruitment rate. Efforts were made to follow up these people on subsequent visits.

The study had a good participation rate for those patients approached. In terms of the disease spectrum, the sample was limited by recruiting outpatients, who were in better condition than inpatients. In addition, exercise tests may not have been appropriate for some outpatients with very poor lung functions. For these reasons, the study group may not have been entirely representative of the total CF clinic.

4.3 DEFENCE OF RESEARCH DESIGN

The study design was chosen because not only did it allow attempted validation of the questionnaire, but by including data from exercise tests, lung function tests and two additional questionnaires, the large range of data available made it possible to examine interrelations between these tests.

Dividing the sample into individual lung function groups also enabled the study to investigate relationships in a similar fashion to previous studies (Godfrey and Mearns, 1971. Orenstein and Nixon, 1991).

The study protocol mimimised participant inconvenience. All exercise tests were performed when patients were already at the hospital and monitors were fitted on the same day.

All clinical tests were done in accordance with current recommendations and guidelines. The lung function test was conducted in line with American Thoracic Society Standards and the treadmill test was based on a modified Balke protocol, a widely acceptable and safe paediatric assessment tool.

All exercise and spirometry equipment was calibrated daily, and the CSA monitor had previously been validated as an effective and accurate means of measuring physical activity (Janz, 1995).

A control group was not included for the questionnaire validation as the CF-PA only applied to CF patients.

Time restrictions for recruitment meant that a control group was also not included for analysis of relationships between fitness, activity, BMI and lung function. However, the respiratory laboratory plans to extend this study by recruiting age and sex-matched controls and comparing these relationships between healthy children, and those with CF.

CHAPTER 5

RESULTS

5.1 INTRODUCTION

Two subject samples were used. 41 subjects wore activity monitors, had exercise tests and completed the questionnaires. 39 were used to validate the CF-PA questionnaire (Part 1), and 41 were used to investigate relationships between activity, fitness, BMI and lung function (Part 3). The 11 extra subjects who completed the questionnaires were used, along with the first 41 children, to examine comparisons between the questionnaires (Part 2).

TABLE 5.1: PATIENT DEMOGRAPHICS

	Subject sample used for Part 1	**Subject sample used for Part 3**	**Subject sample used for Part 2**
Sample Size	n= 39	n= 41	n= 41+(11)= 52
Male/Female Ratio	M=18 F=21	M= 20 F= 21	M= 28 F= 24
Age	12.73 ± 3.15	12.48 ± 3.16	12.63 ± 3.16
Height (Cm)	149 ± 15.34	148.1 ± 15.11	149.43 ± 15.84
Weight (Kg)	41.99 ± 14.09	41.51 ± 13.68	42.31 ± 13.76
Body Mass Index (BMI) (Kg/m^2)	18.36 ± 2.91	18.39 ± 2.83	18.40 ± 2.66
$\dot{V}O_{2peak}$ (ml (Kg.Min))	43.25 ± 6.58	43.00 ± 6.53	43.16 ± 6.54
$\dot{V}O_{2peak}$ (% predicted)	107.54 ± 13.98	106.45 ± 14.38	104.49 ± 15.57
$\dot{V}_{E\,max}$ (L/Min)	61.66 ± 22.76	61.03 ± 22.11	63.01 ± 23.12
$\dot{V}_{E\,max}$ (% predicted)	94.66 ± 23.99	94.12 ± 23.33	92.56 ± 22.33
FVC (L)	2.47 ± 1.00	2.44 ± 0.97	2.56 ± 0.99
FVC (% predicted)	87.32 ± 16.33	88.05 ± 16.43	89.14 ± 15.66
FEV_1 (L)	1.94 ± 0.87	1.93 ± 0.84	2.00 ± 0.81
FEV_1 (% predicted)	81.24 ± 20.01	82.17 ± 20.34	83.29 ± 19.17

5.2 PART 1: CF-PA VALIDATION

Linear regression showed a weak positive relationship between CF-PA scores (METs/week) and CSA counts (average counts/minute/week) ($r = 0.26$, $p = 0.11$).

A similar correlation was observed between CF-PA scores and weekend physical activity ($r = 0.23$, $p = 0.12$). The graphs of both relationships are shown below.

FIGURE 5.1: CF-PA SCORES VS AVERAGE ACTIVITY COUNTS/MIN/WEEK

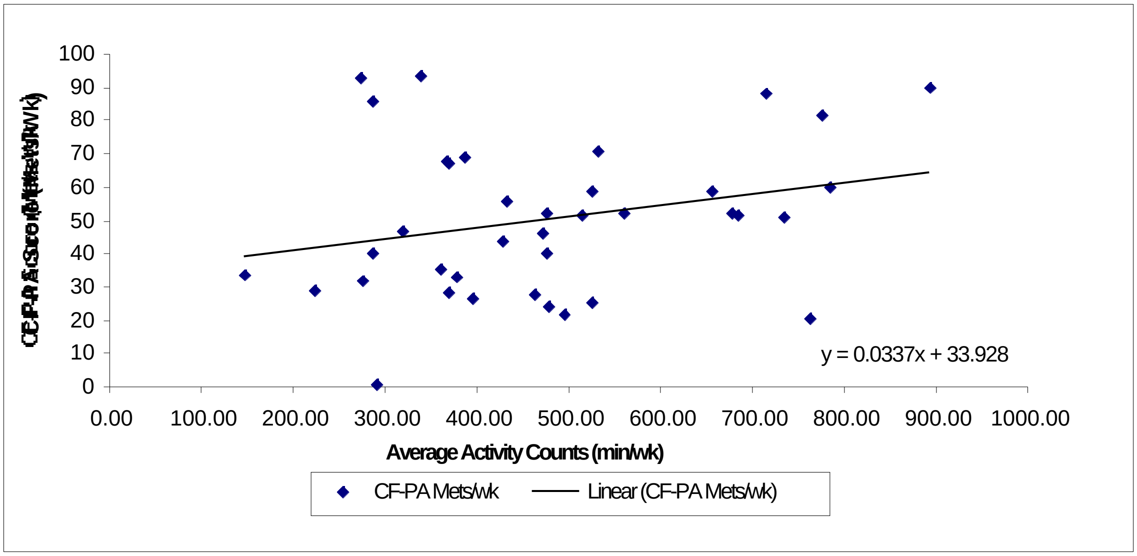
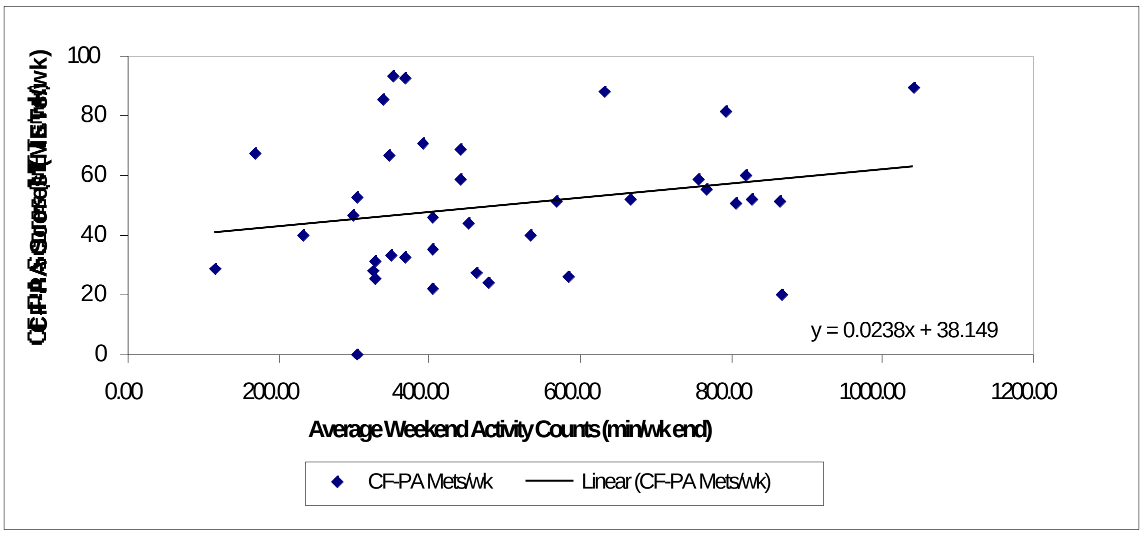


FIGURE 5.2: CF-PA SCORES VS AVERAGE WEEKEND ACTIVITY COUNTS/MIN



The intensity score derived from the questionnaire was also compared with the time spent in specific ranges of activity intensity. As shown in Table 5.2, no significant relationships existed. The largest correlation (though still very small) was seen in the activity range between 6 and 9 METs, reflecting the average MET value for all activities included in the intensity score, which was 6.44.

TABLE 5.2: CF-PA INTENSITY SCORES VS TIME SPENT IN RANGES OF ACTIVITY INTENSITY- (Correlation coefficients and p-values)

	Activity Intensity Ranges (METs)		
	3<X<6	**6<X<9**	**9<X**
CF-PA Intensity Score	**r= 0.044** **p= 0.7**	**r= 0.09** **p= 0.57**	**r= 0.05** **p= 0.76**

5.3 PART 2: COMPARISONS BETWEEN QUESTIONNAIRES

As well as the additional 11 children included, sample sizes varied for the comparisons of specific questionnaires (Table 5.3). This was because each questionnaire had different rates of completion. For example, the MAQ was aimed at adolescents, so some of the younger children did not complete it. Other children filled out questionnaires incorrectly and had to be excluded.

Of the three questionnaires, the CF-PA correlated best with the CSA counts (r= 0.26, p= 0.11).

No significant relationships were found between the CSA monitor counts and the MAQ (r= 0.02, p= 0.9) or the PAC-Q (r= 0.1, p= 0.58). There was a correlation, although just significant, between the CF-PA and MAQ (r= 0.33, p= 0.05), which were compared because they both allowed estimation of energy expenditure.

TABLE 5.3: COMPARISON OF QUESTIONNAIRES:

	CSA COUNTS	**CF-PA SCORES**
CF-PA SCORES	**n=41** **r= 0.26 p= 0.11**	**N/A**
MAQ SCORES	**n= 28** **r= 0.02 p= 0.86**	**N= 34** **r= 0.33 p= 0.05**
PAC-Q SCORES	**n=36** **r=0.1 p= 0.58**	**N/A**

5.4 PART 3: RELATIONSHIPS BETWEEN ACTIVITY, INTENSITY, LUNG FUNCTION AND BMI

5.4.1 RELATIONSHIP BETWEEN $\dot{V}O_{2peak}$ AND FEV_1

Regression was carried out between $\dot{V}O_{2peak}$ and FEV_1 (r=0.38, p= 0.14) (Table 5.4). Investigation of the same relationship in the individual lung function groups produced even weaker relationships. However, ANOVA between lung function groups showed that low a $\dot{V}O_{2peak}$ corresponded to low lung function (Table 5.5).

5.4.2 RELATIONSHIP BETWEEN FEV_1 AND BMI

The relationship between FEV_1 and BMI for the entire subject sample was also examined (r= 0.22, p= 0.16). Correlations were quite similar for lung function Groups 1 and 2, but more than twice as strong in Group 3, raising the possibility that BMI is more influential on FEV_1 in children with higher lung functions (Table 5.4). ANOVA carried out between the lung function groups with respect to BMI also showed that Group 1 ($FEV_1 \leq 75\%$ predicted) had a significantly lower BMI than groups 2 ($76\% \leq FEV_1 \leq 94\%$) and 3 ($FEV_1 \geq 95\%$) (Table 5.5).

5.4.3 RELATIONSHIP BETWEEN $\dot{V}O_{2peak}$ AND BMI

Regression was carried out between $\dot{V}O_{2peak}$ and BMI for the entire sample (r= 0.17, p= 0.28) and each lung function group (Table 5.4). The strongest correlation was seen in Group 1 (r= 0.61, p= 0.02), demonstrating a significant influence of BMI on $\dot{V}O_{2peak}$ in those with more severe lung disease.

TABLE 5.4: REGRESSIONS BETWEEN $\dot{V}O_{2peak}$, FEV_1 AND BMI

	FEV_1	**BMI**
Entire Sample		
$\dot{V}O_{2peak}$	r= 0.38 (p= 0.14)	r= 0.17 (p= 0.28)
BMI	r= 0.22 (p= 0.16)	N/A
Group 1 (FEV_1 ≤ 75% predicted)		
$\dot{V}O_{2peak}$	r= 0.27 (p= 0.33)	r= 0.61 (p= 0.02)
BMI	r= 0.22 (p= 0.41)	N/A
Group 2 (76% ≤ FEV_1 ≤ 94%)		
$\dot{V}O_{2peak}$	r= 0.32 (p=0.27)	r= 0.08 (p= 0.8)
BMI	r= 0.30 (p= 0.29)	N/A
Group 3 (95% ≤ FEV_1)		
$\dot{V}O_{2peak}$	r= 0.32 (p= 0.31)	r= 0.26 (p= 0.31)
BMI	r= 0.53 (p= 0.08)	N/A

TABLE 5.5: ANOVA: AVERAGE VALUES OF $\dot{V}O_{2peak}$, BMI AND ACTIVITY FOR EACH LUNG FUNCTION GROUP

	Sample Size	**$\dot{V}O_2$**	**BMI**	**Average Weekly Activity Counts**
GROUP 1 **FEV_1≤ 75%**	n= 15	40.38	17.75	*517.5
GROUP 2 **76% ≤ FEV_1 ≥ 94 %**	n= 14	43.29	18.68	409.07
GROUP 3 **95% ≤ FEV_1**	n= 12	45.96	18.94	513.99
		p= 0.06	p= 0.51	p= 0.18

**The sample size was 14: One subject's activity monitor did not work, however, their exercise data could be used for the analysis of $\dot{V}O_{2peak}$ and BMI.*

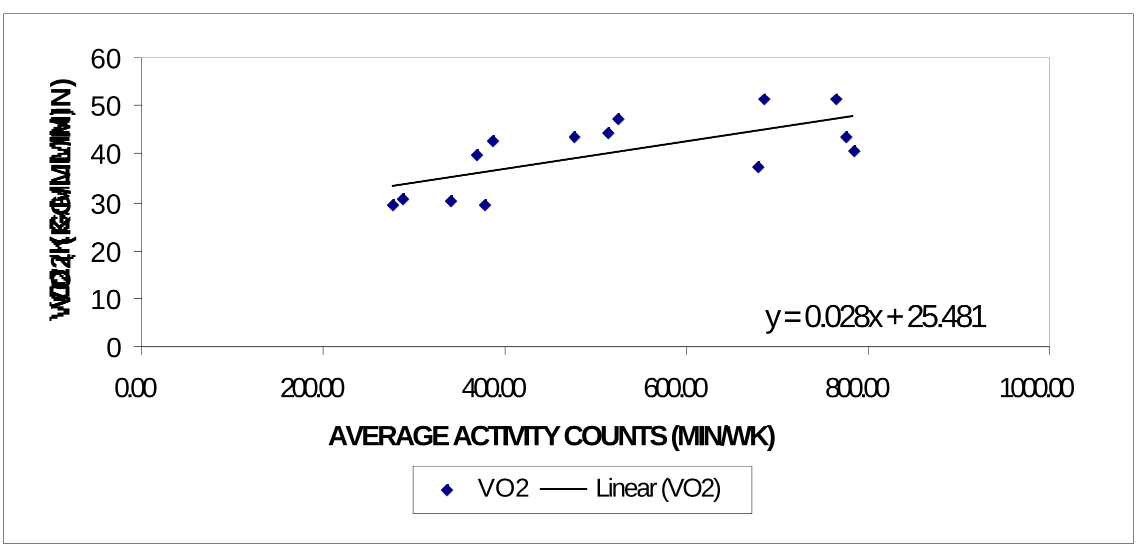
5.4.4 RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND $\dot{V}O_{2peak}$ AND FEV_1

$\dot{V}O_{2peak}$ was also compared with general and weekend physical activity. ANOVA for each lung function group showed that there was no significant difference in their amounts of activity (Table 5.5), but regression between $\dot{V}O_{2peak}$ and activity within each group revealed an important relationship (Table 5.6). In the group with the lowest lung function, $\dot{V}O_{2peak}$ was strongly correlated with activity (r= 0.68, p= 0.007) (Figure 5.3). The correlation between FEV_1 and activity was negligible in terms of the entire sample (r= 0.04, p= 0.8) but once again, a stronger relationship was observed in Group 1 (r= 0.44, p= 0.8).

TABLE 5.6: REGRESSIONS BETWEEN ACTIVITY AND BOTH FEV_I AND $\dot{V}O_{2peak}$

	FEV_1	**$\dot{V}O_{2peak}$**
Entire Sample		
Activity Counts	r= 0.04 (p= 0.8)	r= 0.37 (p= 0.02)
Group 1 ($FEV_1 \leq 75\%$ predicted)		
Activity Counts	r= 0.44 (p= 0.12)	r= 0.68 (p= 0.007)
Group 2 ($76\% \leq FEV_1 \leq 94\%$)		
Activity Counts	r= 0.23 (p= 0.43)	r= 0.21 (p= 0.48)
Group 3 ($95\% \leq FEV_1$)		
Activity Counts	r= 0.05 (p= 0.89)	r= 0.26 (p= 0.42)

FIGURE 5.3: $\dot{V}O_{2peak}$ VS AVERAGE ACTIVITY COUNTS/MINUTE/WEEK IN GROUP 1



5.4.5 RELATIONSHIP BETWEEN INTENSITY OF ACTIVITY AND BOTH $\dot{V}O_{2peak}$ AND FEV_1

$\dot{V}O_{2peak}$ and FEV_1 were also compared with the amount of time spent in specific ranges of activity intensity. Correlations, although positive, were only very small and accompanied by insignificant p-values. ANOVA for each lung function group with respect to the amount of time spent in general and vigorous activity did not show that those with lower lung function were doing less general or intense activity (Table 5.7). In fact, Group 1 had spent the most time in the activity range above 9 METs.

TABLE 5.7: ANOVA: TIME SPENT IN INTENSE ACTIVITY FOR EACH LUNG FUNCTION GROUP

	Time spent in intensity range (X) (METs) Minutes/week		
	$3<X<6$	**$6<X<9$**	**$9<X$**
GROUP 1 **$FEV_1 \leq 75\%$**	651.21	57.64	21.71
GROUP 2 **$76\% \leq FEV_1 \geq 94\ \%$**	497.36	37	8.71
GROUP 3 **$95\% \leq FEV_1$**	781.67	91.17	15.33

Despite there being no apparent trend between activity intensity and lung function in the table above, regression of FEV_1 against intensity of activity for each group revealed an important relationship. In the group with the lowest lung function, FEV_1 was strongly linked to the amount of time spent in intense activity, particularly in the range above 9 METs ($r=0.71$, $p= 0.005$) (Figure 5.4). Although always positive, the same relationship was not as strong in the higher lung function groups (Table 5.8).

Correlations between $\dot{V}O_{2peak}$ and intensity of activity were not as high, but once again, the highest figures were seen in Group 1 in the activity range above 9 METs ($r= 0.44$, $p=0.11$).

FIGURE 5.4: LUNG FUNCTION VS ACTIVITY > 9 METS IN THOSE WITH THE LOWEST LUNG FUNCTION

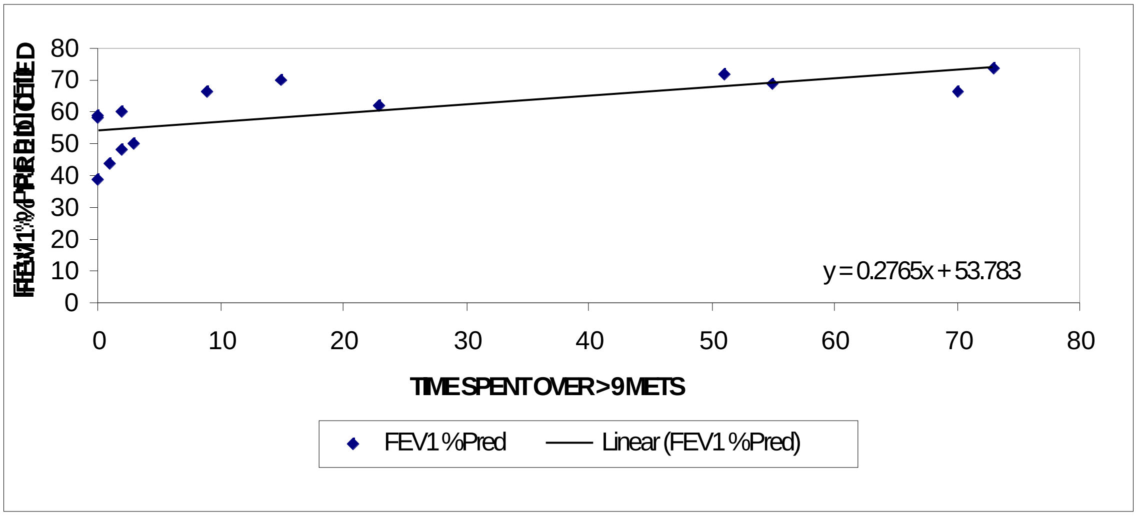


TABLE 5.8: REGRESSION BETWEEN ACTIVITY INTENSITY AND $\dot{V}O_{2peak}$ AND FEV_1

	ACTIVITY INTENSITY RANGES (METs)		
	3<X<6	**6<X<9**	**9<X**
Group 1 (FEV_1≤ 75%)			
FEV_1	r=0.55 (p=0.04)	r= 0.56 (p= 0.04)	r= 0.71 (p= 0.005)
$\dot{V}O_2$	r= 0.11 (p= 0.7)	r= 0.21 (p= 0.47)	r= 0.44 (p= 0.11)
Group 2 (76% ≤ FEV_1 ≥ 94 %)			
FEV_1	r=0.14 (p= 0.63)	r= 0.11 (p= 0.7)	r= 0.44 (p= 0.11)
$\dot{V}O_2$	r= 0.03 (p= 0.93)	r= 0.06 (p= 0.85)	r= 0.02 (p= 0.95)
Group 3 (95% ≤ FEV_1)			
FEV_1	r= 0.07 (p= 0.84)	r= 0.18 (p= 0.58)	r= 0.2 (p= 0.54)
$\dot{V}O_2$	r=0.08 (p= 0.81)	r= 0.32 (p= 0.32)	r= 0.29 (p= 0.37)

5.5 SUMMARY OF RESULTS

The most significant findings that emerged were:

- The CF-PA Questionnaire could not be validated, though it estimated activity better than the MAQ and PAC-Q
- In children with $FEV_1 \leq 75\%$ predicted: BMI and physical activity were strongly related to aerobic fitness, and activity above 9 METS correlated highly with lung function.
- In the entire population, fitness and activity, particularly weekend activity, were related.

CHAPTER 6

DISCUSSION

6.1 *PART 1: CF-PA VALIDATION*

Small correlations between CF-PA scores and all aspects of activity (general, weekend, intensity) recorded by the CSA monitor made questionnaire validation impossible. Numerous explanations may have accounted for the discrepancies between the questionnaire scores and monitor counts, with inadequacies specific to both measures of activity.

6.1.1 THE QUESTIONNAIRE

The questionnaire spans 4 pages. Its completion was time consuming and the activity diary (and focus of the study) on the last page might therefore have been completed with less thought. The fact that children and parents usually completed it together may also have resulted in twice as many inaccuracies. Parents, being unaware of what happens during school, might underestimate activity and research suggests that children overestimate their activity levels (Janz et al, 1995), have difficulty distinguishing between sport and physical activity (Wendell et al, 1997), when younger than 11, lack the cognitive skills to accurately assess activity (Booth, 2000) and can only recall 55 to 65% of their daily activities (Rowlands et al, 1997).

The questionnaire may have exacerbated these recall problems as it required accurate memory of not only the activities participated in, but also the total minutes.

Marking of the questionnaire, being very subjective, was also problematic. The marking scheme developed by Gutierrez-Schwanhauser (2001) does not eliminate inconsistencies. In particular, assigning MET values to activities was difficult. Ainsworth et al's classifications (1992) are extremely specific. The value for swimming for example, depends on factors such as the stroke and speed. In contrast, the CF-PA questionnaire was very general. Subjects did not provide any specific details about their activity so assumptions were made, leading to inaccuracy and inconsistency.

The activity diary structure was also not ideal. Most subjects only selected broad categories of activity, rather than those activities specific to them. These categories were not even grouped according to similar MET values, therefore assigning average values produced further inaccuracies in the final scores. Some subjects specified activities within categories, thus the average of these activities were used. The inconsistency of this scoring method was reflected in the overall scores.

Finally, the questionnaire was not structured to assess activity intensity, therefore, appropriate activities to include in the intensity score were estimated.

6.1.2 THE CSA ACTIVITY MONITOR

In addition to questionnaire-based problems, many inaccuracies may have been due to the activity monitors. For various reasons, the scores may have appeared less than the true activity levels.

When monitor data was downloaded onto computer, a value of zero was displayed when subjects were inactive *and* when the monitor was not being worn, making it impossible to establish the exact amount of time that the monitors were worn each day. The researchers decided to assume that values of zero during the day would be classed as inactive periods. Including these zeros may have subsequently lowered the daily averages for some subjects.

Swimming is a commonly reported form of exercise in CF children, so true activity levels were not accurately reflected when monitors were removed for all water activities. In addition, some children removed them during sports due to discomfort. It was also a problem when children forgot to wear the monitors for whole orhalf days, as all activity during those times was not recorded.

Finally, the CSA counts were confounded by age. According to Trost (2001), younger children require less counts to expend one MET. The questionnaire scoring system, although in terms of METs, did not account for these age-related differences.

6.2 *PART 2: COMPARISON OF QUESTIONNAIRES*

Of the three questionnaires, the CF-PA correlated best with activity counts. The weak relationship between the MAQ and activity monitors was surprising as this questionnaire had been previously validated and used in many studies. This discrepancy suggested that perhaps the CSA monitor did not accurately assess physical activity.

6.3 PART 3: INVESTIGATION OF RELATIONSHIPS BETWEEN PHYSICAL ACTIVITY, INTENSITY, BMI AND LUNG FUNCTION

6.3.1 RELATIONSHIP BETWEEN $\dot{V}O_{2peak}$ AND FEV_1

Small positive correlations were seen between $\dot{V}O_{2peak}$ and FEV_1 (r=0.38, p= 0.14) in the entire sample. This relationship was not stronger when examined separately in the three lung function groups. Although the correlations were weak and accompanied by high p-values, they represented the well-established finding that exercise tolerance declines with disease progression (Cerny and Armitage, 1989. Godfrey and Mearns, 1971. Moorcroft et al, 1997. Freeman et al, 1993). In addition, ANOVA between lung function groups showed that $\dot{V}O_{2\,peak}$ decreased along with FEV_1; the highest $\dot{V}O_{2peak}$ seen in Group 3, and the lowest in Group 1. One possible explanation for this decline in fitness is that as lung disease becomes more extensive with CF progression, the respiratory system is unable to maintain adequately the extremely high ventilation rate required during exercise to compensate for the characteristic increased dead space.

6.3.2 RELATIONSHIP BETWEEN FEV_1 AND BMI

Although consistently positive, the relationship between FEV_1 and BMI was not strong for the entire group or the individual lung function groups. ANOVA carried out between lung function groups with respect to BMI also showed that Group 1 ($FEV_1 \leq 75\%$ predicted) had a significantly lower BMI than groups 2 ($76\% \leq FEV_1 \leq 94\%$) and 3 ($FEV_1 \geq 95\%$). This trend reflected the contribution of nutrition to FEV_1 (Moorcroft et al, 1997). As malnutrition is characterised by loss of muscle following loss of fat, the relationship may be explained by the influence of nutrition on the strength of respiratory muscles, and the subsequent performance in lung function tests (Boucher et al, 1997).

6.3.3 RELATIONSHIP BETWEEN $\dot{V}O_{2peak}$ AND BMI

As for FEV_1, a weak positive correlation was seen between $\dot{V}O_{2peak}$ and BMI for the whole subject sample (r= 0.17. p=0.28). However, the same regression performed in the lowest lung function group found the relationship to be much stronger and highly significant (r= 0.61, p= 0.02). Correlations were less for the higher lung function groups. This finding supported Boucher et al (1997) in their suggestion that in patients with severe disease, activity is related to nutritional status rather than lung function. Although our comparison was made with fitness, rather than activity, comparisons with Boucher et al's study can be made based on another significant finding discussed in section 6.3.4

6.3.4 RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND $\dot{V}O_{2\,peak}$

In the same group of children, $\dot{V}O_{2peak}$ correlated highly with activity (r= 0.68, p= 0.007). The relationship was significant, but not as strong for the entire subject sample. Weekend activity seemed to make a significant contribution to the overall physical activity, especially in influencing $\dot{V}O_{2\,peak}$.

Unlike in adults, where there is a strong relationships between physical activity and $\dot{V}O_{2peak}$, the same relationship is conflicting in children (Armstrong and Welsman, 1997). Some studies have observed high $\dot{V}O_{2peak}$ scores in children with high activity levels, while others found that children with different levels of activity did not differ in their aerobic fitness. Another suggestion was that children do not participate in activity of enough intensity and duration to bring about significant changes in fitness (Armstrong and Welsman, 1997).

Caution is encouraged in the interpretation of results, with consideration of the difficulties associated with measuring both physical activity and $\dot{V}O_{2peak}$. Because of these difficulties, previous studies have had small sample sizes, short periods of activity monitoring, and have made predictions of aerobic fitness based on submaximal data or field tests. By conducting maximal exercise tests within a laboratory, and assessing activity for seven days, the present study attempted to overcome these shortcomings. However, the previously discussed problems associated with activity assessment through questionnaires and monitors remained, possibly influencing the final results.

Factors other than physical activity must also be considered as possible reasons for heightened $\dot{V}O_{2peak}$ in some children. It is well-established that pulmonary function can influence $\dot{V}O_{2peak}$ and it is therefore possible that children with higher lung function and higher fitness are more likely to spend their leisure-time participating in physical activity (Armstrong and Welsman, 1997). Consideration should also be given to the genetic component of $\dot{V}O_{2peak}$. Selvadurai et al (2002) found that subjects with mutations causing defective CFTR production or processing had significantly lower aerobic capacity than those with mutations conferring defective regulation of the CFTR.

6.3.5 RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND FEV_1

Correlations were not as strong between physical activity and lung function ($r = 0.04$, $p = 0.8$) although once again, the relationship was stronger in the lowest lung function group ($r = 0.44$, $p = 0.12$). This positive but weak trend reflected the conflicting findings of studies that have focused on the effects of exercise programs. Although some have found FEV_1 to improve with increased activity (Heijerman et al, 1992.), most others have found that lung function is unchanged despite noticeable improvements in $\dot{V}O_{2peak}$ (Gulmans et al, 1999. Orenstein et al, 1981. Blau et al, 2002).

The improvement in exercise tolerance seen with increased physical activity is thus not likely to be due to changes in pulmonary function. A more acceptable explanation might be that physical activity improves strength and endurance of the respiratory muscles, allowing longer maintenance of high ventilations. Another possibility is increased efficiency of the cardiovascular system to supply blood to exercising muscles.

6.3.6 RELATIONSHIP BETWEEN INTENSITY OF ACTIVITY AND BOTH FEV_1 AND $\dot{V}O_{2peak}$

Further significant findings were made when $\dot{V}O_{2peak}$ and FEV_1 were compared with intensity of activity. Once again, important correlations emerged when the relationships were examined within lung function groups, rather than in terms of the entire sample.

ANOVA showed that the amount of activity in all lung function groups was similar. From Nixon et al's study (2000), it was expected that those with lower lung functions would be spending less time in intense activities, but this was not the case for all intensity ranges.

When lung function groups were examined separately, relationships became clearer. In all groups, there were positive correlations between both FEV_1 and $\dot{V}O_{2peak}$ and level of vigorous activity. This was especially evident in Group 1, where FEV_1 significantly correlated with activity over 9 METs ($r = 0.71$, $p = 0.005$). For the same intensity level in the same group, a correlation with $\dot{V}O_{2peak}$ was also seen, though it was not as significant ($r = 0.44$, $p = 0.11$). In Groups 1 and 2, vigorous activity had more influence on FEV_1 than $\dot{V}O_{2peak}$, whereas in Group 3, the correlations with $\dot{V}O_{2peak}$ were slightly higher.

These findings supported Nixon et al's suggestion that the amount of time CF children spend in vigorous activity influences their lung function and aerobic fitness. They also highlight the need for encouragement of increased participation in vigorous activities as a way of improving fitness and delaying decline in lung function, particularly in those with more severe lung disease.

6.4 LIMITATIONS OF THE STUDY

A limitation of the study was the elimination of rural patients. Despite this, the target sample size was still met and statistical power achieved. In addition, by only recruiting outpatients, the sample was limited to the healthier portion of the CF population. However, a range of disease spectrum was included, with FEV_1 values ranging from 39-120% predicted.

Another issue that may have confounded results was the time of year children wore the activity monitors. Although this had no effect on validation of the CF-PA questionnaire, it may have influenced the analysis of relationships relating to physical activity levels (e.g. Fitness and lung function vs physical activity). Children who wore the monitors during school holidays may have had higher activity counts than children who wore them during school time. In addition, their regular activity levels may not have been accurately represented. Finally, wearing the monitor during the summer holidays, and removing it for water activities may have produced activity levels lower than normal, and lower than other children. In actual fact, it is more likely that summer holiday activity would be much higher due to free time and warm weather.

The effect of all of this on the final results was that perhaps the correlations between physical activity and fitness/lung function were actually stronger than observed.

CHAPTER 7

CONCLUSION

7.1 CONCLUSION

This study was unable to validate the CF-PA questionnaire using CSA monitors as objective measures of physical activity. Explanations for the failure of validation included issues inherent to the questionnaire itself (problems with completion, marking and structure) and to the activity monitors. Small correlations existed between monitor counts and CF-PA scores, but were accompanied by high p-values indicating statistical non-significance. However, the failure of validation does have clinical significance, highlighting the requirement for changes to be made to the questionnaire, in order for it to be able to assess accurately physical activity in the paediatric CF population and its findings be interpreted with confidence.

Recommended changes include:

- Asking patients to select specific activities rather than broad categories
- Asking for more specific details about activities to omit guesswork in the assignment of MET values
- If activity categories are kept, they should include activities with very similar MET values.
- Specific activities above a specified MET value should be stipulated for inclusion in the intensity score

An interesting finding was that the CF-PA questionnaire correlated more strongly with activity than the previously validated MAQ and PAC-Q, although this may have been related to its higher response rate. In addition, the small correlation between the CF-PA and MAQ may have reflected their similar shortcomings, with both questionnaires lacking the detail needed to accurately assign MET values.

The secondary aims of the study, to examine relationships between activity, intensity, BMI and lung function, were well achieved. Most relationships were only observed, or strengthened when examined in terms of individual lung function groups, particularly those with FEV_1 less than 75% predicted.

As expected, a positive correlation existed between physical activity (especially weekend activity) and $\dot{V}O_{2peak}$, and was strongest in the lowest lung function group. As shown in many previous studies, a trend was also seen where fitness declined in line with FEV_1. Together, these findings indicate that encouragement of activity may be particularly beneficial for children with severe lung disease, by improving or maintaining fitness and thus delaying further decline in pulmonary function.

Another significant finding in the group with FEV_1 less than 75% predicted was that there was a very strong relationship between BMI and fitness, implying that in these children, focusing on optimal nutrition might positively influence fitness, and consequently, lung function.

Finally, positive correlations were seen in all groups between time spent in intense activity and both FEV_1 and $\dot{V}O_{2peak}$. The most significant relationship was once again evident in the lowest lung function group, between activity intensity and FEV_1, in the activity range above 9 METs. This patient group and activity range also had the highest correlation with $\dot{V}O_{2peak}$, though the link between intensity and lung function was significantly higher. These findings indicate that children with CF should be encouraged to increase their level of participation in vigorous activities.

In conclusion, the clinical implications of this study are that all children with CF should be encouraged to maintain adequate nutrition and improve participation in general and vigorous activity, in order to maintain fitness and prevent decline in lung function, thus improving quality of life and possibly long-term survival.

Although the findings highlight that these measures are particularly important in children with FEV_1 less than 75% predicted, participation in vigorous activity may be easier said than done for those who are significantly limited in their exercise capacity. Nonetheless, it is not impossible, as studies have shown that exercise is safe for all degrees of disease. In these cases, exercise tests would be recommended before beginning a new exercise regime, in order to assess exercise tolerance and tendency to desaturation.

7.2 INDICATIONS FOR FURTHER RESEARCH

This study is part of a larger research project. The next step is to recruit age-matched controls and examine differences between healthy children and children with CF in terms of levels of general and vigorous activity, BMI, FEV_1 and exercise tolerance. Comparisons of vigorous activity levels for healthy children and those with CF would be especially beneficial, as Nixon et al's (2000) recent findings in this area warrant further investigation.

The concept of the effect of vigorous activity on fitness and lung function is relatively new, so further research in this area would be beneficial. The relationship could also be examined between males and females.

Finally, the failure to validate the CF-PA questionnaire creates the substantial task of its redevelopment so that validation can be attempted again.

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