INTERRELATIONSHIPS OF DEFORMITY, IMPAIRMENT, DISABILITY AND HANDICAP IN ADOLESCENT IDIOPATHIC THORACIC SCOLIOSIS

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Abstract

Pulmonary impairment and a reduced working capacity are recognized consequences of advanced spinal deformity. In idiopathic scoliosis, the severity of pulmonary impairment is thought to be directly related to the angle of lateral spinal curvature. In turn, the angle of spinal curvature and associated pulmonary impairment are believed to account for reductions in working capacity. Breathlessness is assumed to be the handicapping symptom which limits the ability of these subjects to perform work. There is an implied predictable and sequential relationship between the degree of spinal deformity, severity of pulmonary impairment, extent of disability, and handicap from breathlessness in this condition.

The purpose of this thesis was to quantify spinal **deformity** (nature and extent), pulmonary **impairment** (mechanical and gas exchanging properties), **disability** (working capacity) and **handicap** (exertional symptoms) in a large group of subjects with idiopathic scoliosis, so that the relationships between these elements could be determined. It was anticipated that these relationships would be more variable (weaker) than is commonly implied. A further aim therefore, was to identify additional factors which contribute to pulmonary impairment, disability

and exertional symptoms in these subjects. The influences of respiratory muscle, peripheral muscle and cardiac factors on these relationships were considered to be potentially important.

Seventy nine subjects (M:F 13:66; age 21 (SD 10.1)) with mild-moderate idiopathic thoracic scoliosis (Cobb angle 45° (SD 18.4)) were studied.

Pulmonary impairment in the group as a whole was moderate, with the vital capacity being reduced to 79% of predicted (SD 13.6). Angle of scoliosis was one of four features of the spinal deformity which contributed to pulmonary impairment; longer curves (number of vertebrae), higher curve position and loss of the normal thoracic kyphosis also had an additive influence.

Disability was significant, with exercise capacity being reduced to 86% (SD 17.4) of predicted; nature and extent of spinal deformity was unrelated to disability. Similarly, there was no direct relationship between pulmonary impairment and the extent of disability.

Application of a psychophysical symptom rating scale showed that both the intensity of breathlessness and leg effort were increased during exercise, but most subjects stopped exercising due to leg effort rather than breathlessness. This finding focused attention on the relationship of disability to peripheral muscle factors.

Leg muscle volume and lean body mass were closely related to maximum working capacity. The relationship of leg muscle volume to maximum oxygen consumption was similar to that previously reported in normal subjects; this suggests that reduced muscle bulk, rather than qualitative muscular differences, is a particularly important contributor to disability. Once between subject differences in muscularity were taken into account, an additional influence of pulmonary impairment on disability was evident.

A higher heart rate response during exercise was also found in more disabled subjects, suggesting that cardiac performance may also influence work capacity in this group.

The belief that angle of scoliosis is responsible for pulmonary impairment which in turn causes disability, is a misleading oversimplification. Additional factors relating to the spinal deformity, and to physiological impairments of other than the respiratory system, have a profound influence on these relationships, and may be the dominant contributors to pulmonary impairment, disability and handicap in idiopathic scoliosis.

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%X	Percent sign preceding a symbol indicates percentage of predicted normal value.
X/Y%	Percent sign following a symbol indicates a ratio function with the ratio expressed as a percentage.
$X_{50\%}$	Subscript 50% indicates that variable X was measured at 50% of predicted normal work capacity
BP	Blood pressure (mmHg)
Br	Breathlessness (10 point Borg scale)
Dia	Diastolic
DL_{CO}	Diffusing capacity of the lung for carbon monoxide (single breath) (ml/min/mmHg)
f	respiratory frequency (breath/min)
FEV_1	Forced expired volume in one second (l)
FRC	Functional residual capacity (l)
HR	Heart rate (beat/min)
LE	Leg effort (10 point Borg scale)
KCO	Diffusing capacity for CO per unit alveolar volume (ie. DL_{CO}/VA) (ml/min/mmHg/l)
max	Maximum

MEP	Maximum expiratory pressure (occluded airway at TLC) (cmH_2O)
MIP	Maximum inspiratory pressure (occluded airway at FRC) (cmH2O)
PEF	Peak expiratory flow (l/min)
$P\bar{v}CO_2$	Mixed venous partial pressure of carbon dioxide (oxygenated) (mmHg)
R	Respiratory exchange ratio, the ratio of CO_2 output to O_2 uptake in the lungs.
RV	Residual volume (l)
SaO_2	Arterial oxygen saturation (%)
Sys	Systolic
V_A	Alveolar volume (single breath) (l)
$\dot{V}_A/\dot{Q}$	Ventilation to perfusion relationship
VC	Vital capacity (l)
$\dot{V}CO_2$	Carbon dioxide output (l/min)
$\dot{V}_E$	Expired minute ventilation (l/min)
$\dot{V}E_{Cap}$	Ventilatory capacity derived from FEV_1 and maximum inspiratory flow rate.
$\dot{V}_E/\dot{V}CO_2$	Ventilatory equivalent for carbon dioxide. The ventilation required to excrete a liter of carbon dioxide (l/l).
$\dot{V}_E/\dot{V}O_2$	Ventilatory equivalent for oxygen. The ventilation associated with a liter of oxygen uptake.
$\dot{V}_I$	Inspiratory flow rate (l/min)
$\dot{V}max_{xx}$	Maximum expiratory flow at xx% of VC (note: 100% VC = TLC; 0% VC = RV)
$\dot{V}max_{xx\%TLC}$	Maximum expiratory flow at xx% of predicted TLC

$\dot{V}O_2$	Oxygen intake (l/min)
V_T	Tidal volume (l)
W	Work (kpm)

Chapter 1

Introduction

As a number of divergent topics are addressed in this chapter, I will initially outline its layout, in the hope of avoiding subsequent confusion. The chapter is divided into four sections, of which the first three are the most substantial.

In the first section, "Concepts of deformity, impairment, disability and handicap", the meaning of these terms is discussed; particularly with regard to their interpretation and use throughout this thesis.

The second section, "Idiopathic Scoliosis", provides a review of this condition, emphasizing what is known about deformity, impairment, disability and handicap in this population.

The third section, "Interrelationships of deformity, impairment, disability and handicap", reviews previously published studies which have examined these relationships.

Finally, the fourth section, "Purpose of the thesis", is self explanatory.

1.1 Concepts of deformity, impairment, disability and handicap.

Before deformity, impairment, disability and handicap can be assessed and their interrelationships examined, a clear understanding of the meaning of each of these terms is required. The World Health Organization's classification system for impairment, disability and handicap has been adopted (World Health Organization, 1980). A brief description of this classification is outlined below, emphasizing how each term has been interpreted in this series of studies. Definitions have been shortened to increase clarity.

1.1.1 Deformity

"deviation from normal shape or form"

The normal spine is composed of 24 vertebrae, their intervertebral discs and supporting connective tissue structures, and extends from the cranium superiorly to the sacrum inferiorly. In its resting position, the normal spine is straight when viewed directly from in front (radiologically) or from behind (clinically and radiologically), that is to say, in the frontal plane. Vertebral orientation (transverse plane) is normally constant throughout the length of the spine; the spinous processes being directed posteriorly, lining up one below the other and connected to each other by the posterior longitudinal ligament. In distinction, when viewed from the side (sagittal plane), the spine is not straight but composed of a number of curves; lordotic (convex anteriorly) in the lumbar region, and kyphotic (convex

posteriorly) in the thoracic region, the combination insuring that the head lies directly above the sacrum. Deviation from this normal resting form constitutes deformity.

When deviation occurs in the frontal plane it is termed scoliosis which, in the absence of lateral vertebral body wedging as may be seen in congenital scoliosis, is invariably associated with some degree of vertebral body rotation, with or without changes of antero-posterior vertebral angulation. Therefore, assessment of spinal anatomy in association with scoliosis requires characterization of the three dimensional nature of the deformity with measurements in the frontal (scoliosis), sagittal (kyphosis/lordosis) and transverse (rotational) planes. The length of the spine involved (vertebral number) and the location of the curve between the base of the skull and the sacrum, adds further to characterization of the deformity.

1.1.2 Impairment

"any loss or abnormality of psychological, physiological or anatomical structure or function".

Idiopathic scoliosis may be associated with psychological, physiological or anatomical abnormalities resulting in many different types of impairment. As the focus of these studies is the interrelationships of physiological abnormalities, spinal deformity and handicap (defined below), use of the term impairment will be

confined to description of physiological deficits relating to the cardiorespiratory system and peripheral muscles.

The concept of pulmonary impairment is well developed and has previously been defined in terms of changes in pulmonary mechanics and the capacity of the lungs to exchange gas. Mechanical changes are quantified most simply and routinely by spirometry, and gas exchanging capacity by measurement of diffusing capacity for carbon monoxide (DL_{CO}). As normal values for these measurements vary with age, sex, race and body size, the results of spirometry and DL_{CO} are usually standardized for these expected variations, being expressed as % predicted reference (normal) values. %VC predicted is the primary measure of pulmonary impairment used in these studies, as i) it has previously been established that airflow limitation is not associated with scoliosis, obviating the need for a dynamic measure of pulmonary impairment, and ii) in the past, VC has been the most widely used assessment of pulmonary function in scoliotic patients. Many other measures of pulmonary function have also been collected and analyzed in the studies of this thesis, to determine if more detailed characterization of pulmonary impairment could advance understanding of the cause of disability and handicap in these patients.

Impaired cardiac function may also contribute to disability and handicap, if support of the active peripheral muscle is deficient. Unlike the respiratory system for which there are many valuable maneuvers for assessing maximal performance

(eg. VC, PEF, MIP, MEP), maximal cardiac function is more difficult to assess as the variables of interest (eg. maximum cardiac output or perfusion pressure) are not under voluntary control. Clinical, electrocardiographic and, when indicated, echocardiographic evaluation was performed to exclude subjects with structural heart disease (eg. congenital) from these studies (Simonds et al, 1989). In the study population, differences in cardiac function, or cardiac impairment, was inferred from the heart rate and blood pressure responses at standardized work rates.

Peripheral muscle impairment was assessed by measuring the amount of muscle available to do work (eg. lean body mass and leg muscle volume) and by determining selected static muscle strengths.

1.1.3 Disability

"any restriction or lack of ability (resulting from impairment) to perform an activity in the manner or within the range considered normal for a human being"

According to this definition, disability represents a reduced ability or capacity to perform activities compared to normal subjects. Quantification of disability therefore requires measurement of both the capacity of the individual being studied and knowledge of the expected normal capacity for that person in the absence of impairment. In the context of assessment of cardiorespiratory function, exercise testing is ideally suited for quantification of disability. The

mechanical work performed can be accurately measured, as can the metabolic consequences of the activity - oxygen consumption ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$). Work capacity therefore reflects the integration of cardiac (circulatory), respiratory (gas exchange) and neuromuscular (contractile machinery) apparatus. Reference values, standardized for differences in age, sex and body size, are well defined and allow an individual's work capacity to be expressed as a percentage of predicted values (Jones et al, 1985; Jones and Killian, 1987). Measurement of maximal power output (rate of performing work) during a standardized incremental exercise test (Jones, 1988) (chapter 2.2.5) has been the method used to quantify disability in these studies. The cardiorespiratory response to exercise may also yield insights about the physiological mechanisms underlying differences in disability and handicap.

1.1.4 Handicap

"disadvantage for a given individual resulting from an impairment or disability, that limits or prevents fulfillment of a role that is normal (depending on age, sex, social and cultural factors) for that individual".

This definition of handicap reflects the limitations imposed by a given impairment or disability on an individual's life style. As such, the severity of handicap is partly determined by an individual's recreational and occupational demands, in addition to the severity of the underlying impairment and disability.

As the demands of an individual's life style are difficult to quantify and may change markedly with circumstance (eg. parenthood, change of occupation), under this broad definition, handicap is difficult to quantify.

In the context of cardiopulmonary performance, impairment manifests itself to patients as unpleasant symptoms of an intensity greater than expected for a given level of activity. If individuals are only prepared to exert themselves until symptoms reach a critical level of discomfort, it is apparent that with advancing impairment this symptom level will be reached at ever reducing work rates; work capacity falls and disability increases. Subjects are therefore handicapped by excessive symptoms.

Previous studies have established that breathlessness and muscular effort (leg effort when cycling) usually limit muscular activity in normal subjects (Killian et al, 1992a; Killian et al, 1992b). In the presence of additional pathological processes (eg. coronary artery disease or arthritis) other symptoms (eg. chest pain or joint discomfort) may limit activity, but this is unlikely to occur in patients with idiopathic scoliosis.

Using psychophysical techniques, the intensity of symptoms during exercise can be measured (see psychophysics (appendix 2) and muscular symptoms (appendix 3). As the rate of work performance has a major influence on the intensity of associated symptoms (Kearon et al, 1991a; Kearon et al, 1991b), symptom intensities have to be interpreted in the light of power output. In these

studies, we have chosen to define handicap in terms of "excessive muscular effort or breathlessness experienced during the performance of a standardized task". The standardized task was an incremental exercise test on a cycle ergometer to a symptom limited maximal power output.

Using this somewhat curtailed definition, handicap can be quantified in terms of scaled symptom intensities at work rates standardized to expected normal work capacity. The contribution of different factors, including features of deformity and impairment, to handicap (excessive symptoms) can then be assessed. By measuring symptom intensities at different relative work rates (eg. 25%, 50%, 75% of predicted exercise capacity), indirect estimates of symptom intensities that would be associated with different recreational and occupational activities may be obtained (eg. walking, manual labor).

1.2 Idiopathic scoliosis

1.2.1 What is adolescent idiopathic thoracic scoliosis?

The normal spine is straight when viewed directly from behind; any lateral curvature is termed a **scoliosis**. Isolated lateral spinal curvatures rarely occur without rotation or antero-posterior angulation of the spine, but as these features are less obvious than the scoliosis on frontal radiographs, they are often overlooked. Although strictly, scoliosis only refers to one element of this complex

three dimensional distortion, in common usage "scoliosis" has become an umbrella term for all spinal deformities which include lateral curvature.

A cause for scoliosis can only be determined in 10-20% of cases (Nordwall, 1973), in whom neuromuscular, structural skeletal and connective tissue abnormalities are most commonly implicated. In the majority, no predisposing condition is evident; these cases are termed **idiopathic**.

Classification is further subdivided by age at onset of the scoliosis, those cases presenting close to or during puberty being termed **adolescent**; and by position of the curve, those cases whose apex is a thoracic vertebra being termed **thoracic** (traditionally, apex at the 12th vertebra is classified as thoracolumbar, but not in this thesis).

Therefore, **adolescent idiopathic thoracic scoliosis**, refers to all cases of spinal deformity which include scoliosis as a component, developing close to or during puberty, for which no underlying cause is known, and whose apex is a thoracic vertebra. This group constitutes the majority of cases of spinal deformity.

1.2.2 Epidemiology

No precise figure is available for the prevalence of idiopathic scoliosis, the findings of different studies varying widely (DeSmet, 1985a). The reason for differences in reported prevalence is probably largely due to methodological

differences between studies (Leaver et al, 1982), although true differences in prevalence between populations also occur (Segil, 1974; Lonstein and Carlson, 1984). Methodological issues which may influence prevalence estimates include differences in (i) referral patterns, (ii) methods of case examination, and (iii) the criteria used to decide on the presence of a significant scoliosis (Leaver et al, 1982).

DeSmet reviewed the epidemiology of scoliosis (DeSmet, 1985a), analyzing studies on the basis of the method of screening, extent of deformity, age, sex and country of origin of the populations screened. Studies using the forward bending

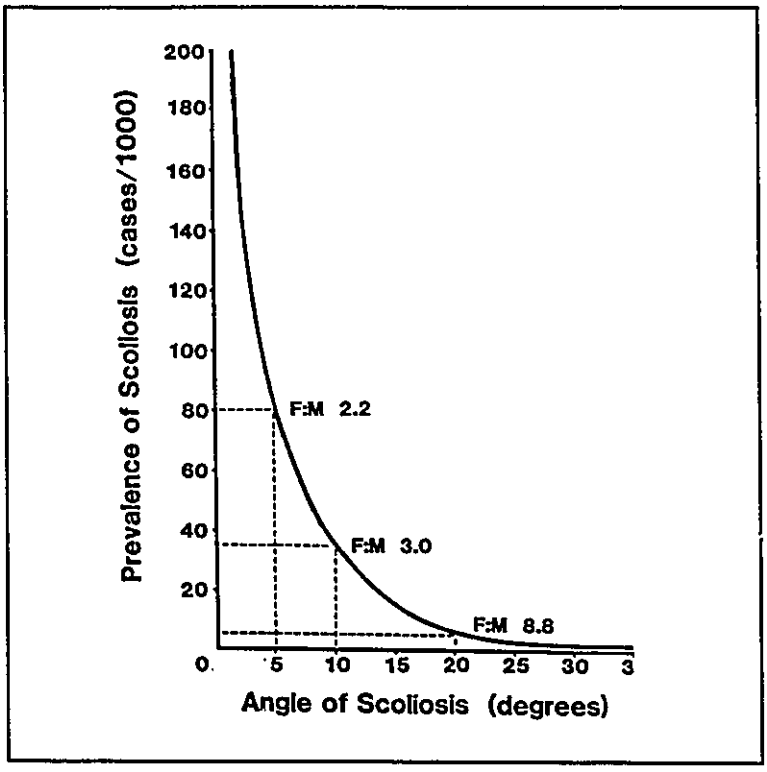


Figure 1.1 Prevalence and sex distribution of idiopathic scoliosis according to severity.

test as the screening method, reported prevalence rates which varied more than a hundred fold, from 0.07 - 8.5%. The average prevalence rate for the twelve studies which used that method of screening test was 2.1% (SE 0.66%). In DeSmet's review, the average prevalence for radiologically confirmed curves of $\geq$ 5 degrees was 7.7% (SE 1.83%, 10 studies); for curves $\geq$ 10 degrees was 3.4% (SE 0.68%, 15 studies); and for curves of $\geq$ 20 degrees was 0.43% (SE 0.036%, 7 studies). Female to male ratio (F:M) also increased with severity of the scoliosis. The average F:M ratio for curves $\geq$ 5 degrees was 2.2; for curves of $\geq$ 10 degrees was 3.0; and for curves $\geq$ 20 degrees was 8.8 (figure 1.1). Finally, there is also a higher familial incidence of scoliosis (Wynne-Davies, 1968; Cowell et al, 1972; Rogala et al, 1978).

1.2.3 Pathogenesis

By definition, the cause of spinal deformity is unknown in this condition; idiopathic scoliosis is a diagnosis of exclusion. Current evidence suggests that no single factor will be identified as being responsible for this condition; probably a combination of factors culminate in scoliosis in a given individual. The relative importance of these factors is likely to differ among subjects.

Many different pathogenic factors have been proposed, including mechanical factors with skeletal growth rate abnormalities (Willner, 1974; Willner, 1975a; Skogland and Miller, 1981; Lawton et al, 1983; Dickson et al, 1984;

Dickson, 1985; Smith and Dickson, 1986), central (Sahlstrand et al, 1978; Yamada et al, 1984; Herman et al, 1985; Wyatt et al, 1986), and peripheral (Chiu et al, 1989) nervous system defects, primary abnormalities of muscle (Wong et al, 1977; Yarom et al, 1982; Zetterberg et al, 1983; Ford et al, 1984) and connective tissue defects (Pedrini et al, 1973; Oegema et al, 1983). As previous reviewers of this topic have noted (Ponseti, 1976; Nachemson and Sahlstrand, 1977; Harrington, 1977; Rinsky and Gamble, 1988; Byrd, 1988), the supporting evidence for each of these theories lacks consistency, and firm conclusions cannot be reached. Part of the difficulty with establishing the pathogenic mechanism for this condition is that studies have usually been performed on subjects with established or advanced scoliosis, so that if abnormalities are detected, it is difficult to determine if they are primary or have occurred secondary to long-standing deformity. Acknowledging these difficulties, there is little doubt that genetic, growth and mechanical factors influence the onset and rate of progression of deformity. How these factors interact with each other, and with other factors such as neuromuscular or connective tissue disturbances is speculative.

1.2.4 Natural history

In keeping with the overall framework of this thesis, the natural history of idiopathic scoliosis will be addressed under the headings of deformity (curve progression), impairment (physiological disturbances), disability (work status), and handicap (symptoms). Although published reports often do not fall neatly into one

of these categories, it is hoped that by imposing this framework, clarity will be enhanced. In addition, mortality rate in idiopathic scoliosis will be considered.

Before embarking on this review, it is valuable to first consider difficulties which natural history studies of idiopathic scoliosis may encounter. This is important as failure to address these issues may weaken the conclusions of individual studies, and may help to account for differences in findings between studies.

Ideally, at the start of a natural history study, an "inception cohort" should be assembled at an early and uniform stage of deformity, such as a community screening program, to ensure that the full spectrum of idiopathic scoliosis (good and poor prognostic groups) is represented (Department of Epidemiology and Biostatistics, 1981). If this is not feasible, as a minimum, the method of case referral should be clear. Subjects should then be followed prospectively with care to avoid, or at least account for, losses to follow up. As knowledge of prognostic factors may influence outcome measurements, blind assessment with application of objective outcome criteria is desirable during follow up.

These goals are difficult to achieve with idiopathic scoliosis. Adequate follow up is difficult to achieve, as this requires monitoring for many decades, and the transition from childhood to adulthood is often accompanied by geographical relocations (Collis and Ponseti, 1969). Although some outcomes such as curve progression, pulmonary impairment and mortality can be clearly defined, others

of equal importance, such as psychological consequences, disability and handicap, are more difficult to quantify. In practice, most studies of the natural history of this condition originate from centers specializing in scoliosis management, and their findings may have limited generalizability. Some reports are further complicated by including cases of secondary (Nachemson, 1968) and early onset (congenital or infantile) (Branthwaite, 1986) scoliosis which have a poorer prognosis. As it would now be considered unethical to withhold treatment from subjects with progressive deformity, recent reports of untreated series are likely to represent atypical populations (Ponseti and Friedman, 1950; Collis and Ponseti, 1969; Weinstein et al, 1981; Picault et al, 1986) and extrapolation of their findings to idiopathic scoliosis in general may not be valid.

Acknowledging that the ideal approach based on an inception cohort is rarely feasible in chronic conditions such as idiopathic scoliosis, an alternative strategy is to develop a coherent concept of the natural from cross sectional studies which summarize a variety of clinical experiences.

1.2.4.1 Natural history of deformity (curve progression)

The angle of scoliosis is the only measure of spinal deformity which has been followed prospectively (Ponseti and Friedman, 1950; Collis and Ponseti, 1969; Brooks et al, 1975; Rogala et al, 1978; Weinstein et al, 1981; Weinstein and Ponseti, 1983; Lonstein and Carlson, 1984; Picault et al, 1986; Bunnell, 1986;

Pehrsson et al, 1991). In those studies which achieved a high percentage follow up (Brooks et al, 1975; Rogala et al, 1978; Lonstein and Carlson, 1984; Bunnell, 1986; Pehrsson et al, 1991), the likelihood of curve progression (variably defined, both between and within (Bunnell, 1986) studies) differed widely, from as little as 5.2% (Brooks et al, 1975) to as much as 37% (Bunnell, 1986). These differences in frequency of progression can largely be accounted for by differences in age, sex, severity of deformity, variability of criteria defining progression, method of assembly and duration of follow up of the study populations.

A number of factors emerge as prognostically important for curve progression. Female preponderance increases with curve severity, reflecting a greater propensity for progression of deformity in girls. One study (Bunnell, 1986) suggested that this gender related risk of progression may equalize in curves greater than 30 degrees. Progression is more common for younger children (Brooks et al, 1975; Lonstein and Carlson, 1984; Bunnell, 1986), which probably reflects a positive relationship between progression and the pubertal growth spurt (Duval-Beaupere, 1971). Similarly, the risk of progression falls with advancing skeletal maturity (Lonstein and Carlson, 1984; Bunnell, 1986). The larger the curve at time of detection, the more likely it is to continue progressing (Rogala et al, 1978; Weinstein et al, 1981; Lonstein and Carlson, 1984; Bunnell, 1986), which may just reflect an already established faster rate of progression of these curves. These three factors (age, skeletal maturity, curve severity) are interactive. Lonstein and Carlson calculated that the risk of curve progression for a skeletally mature

child with a curve of less than 19 degrees was 1.6%, as opposed to a risk of 68% in an immature child with a curve between 20 and 30 degrees (Lonstein and Carlson, 1984). Curve position also influences progression; single lumbar curves are more stable (Lonstein and Carlson, 1984; Bunnell, 1986). No relationship was found between progression and family history of idiopathic scoliosis, associated kypho/lordosis, or height-weight ratio (Bunnell, 1986).

Late childhood and adolescence is the critical time for evolution and progression of idiopathic scoliosis, but deformity may also progress after reaching maturity (Nachemson, 1968; Collis and Ponseti, 1969; Weinstein et al, 1981; Weinstein and Ponseti, 1983; Ascani et al, 1986; Pehrsson et al, 1991). Studies from Iowa observed a mean curve progression of 15 degrees over the first twenty years following skeletal maturity in in 134 subjects with idiopathic scoliosis (Collis and Ponseti, 1969) (initial angle of scoliosis 37 degrees (Ponseti and Friedman, 1950)), with a further increase of 3.9 degrees over the next 10 year (Weinstein et al, 1981). An Italian study of 187 subjects also found that after an average follow up of 34 years post maturity, all curves had increased - on average 0.4° per year (Ascani et al, 1986). Although the data available from long term studies is less reliable, it appears that the risk of progression increases with curve size and is greater for single thoracic curves (Collis and Ponseti, 1969; Weinstein et al, 1981; Ascani et al, 1986).

1.2.4.2. Natural history of impairment (physiological progression)

Few studies have followed the course of physiological function in nonoperated idiopathic scoliosis. Those studies which have, confined their assessment to respiratory impairment (Collis and Ponseti, 1969; Weinstein et al, 1981; Pehrsson et al, 1991).

Studies from Iowa prospectively evaluated a large cohort of untreated idiopathic scoliotic patients (Ponseti and Friedman, 1950) after at least twenty (Collis and Ponseti, 1969) and thirty (Weinstein et al, 1981) years of observation. Of the initial 444 cases of idiopathic scoliosis who were assessed, 50 underwent early spinal fusion and 36 were of congenital or juvenile onset; the remaining 358 cases making up the study cohort. Cohort assembly was not described but probably consisted of referrals to an orthopaedic service rather than "all comers" from a screening program. The authors stated that they practiced a conservative approach to management, that many cases received physiotherapy and brace management, and that subjects with minimal curves were excluded from the study. Seventy six per cent of cases involved the thoracic spine: cervicothoracic, 1%; thoracic, 22%; thoracolumbar, 16%; combined thoracic and lumbar, 37%. Twenty four percent were lumbar. Mean curve magnitude at stabilization (start of the long-term observation period) was 37 degrees.

Twenty four years later, of the initial 358 patients, 106 returned for review and had spirometry performed. Vital capacity in these subjects averaged 87 %

predicted (approximated from data provided). Forty three of 80 (54%) of curves involving the thoracic spine had a VC of less than 85 %predicted. Prediction of reference VC was based on "deformed" height which would have lead to overestimation of % predicted values, due to the loss of height which is known to occur with scoliosis (Hepper et al, 1964; Bjure et al, 1968; Johnson and Westgate, 1970; Linderholm and Lindgren, 1978; Kumano and Tsuyama, 1982; Helms et al, 1986). Unfortunately, progression of pulmonary impairment during this twenty four year period could not be assessed as pulmonary function was not measured at the onset of the study.

After a further ten years (Weinstein et al, 1981), 76 subjects of the original cohort again returned for assessment and in 69 of these, spirometry was measured. Vital capacity averaged 90 % predicted. Twenty seven of 49 (55%) curves involving the thoracic spine had a VC less than 85 %predicted. One patient with a thoracic curve died of cor pulmonale in the intervening ten years.

Because a high proportion of patients was unavailable for follow up assessment of pulmonary function, these findings need to be interpreted with caution. These studies suggested that progression to severe pulmonary impairment is largely confined to single thoracic curves.

A Swedish group recently reported a 20 year follow up study of pulmonary function in unfused idiopathic scoliosis (Pehrsson et al, 1991). Spirometry was obtained on 20 of 25 survivors who qualified for assessment. During the follow up

period, seven of the original 45 patients has fusions performed, eight died (two of respiratory failure), three had been misclassified as idiopathic, two were lost to follow up and five either refused or were unable to perform spirometry. Scoliosis angle was 79° (SD 49) in 1968 and 86° (SD 46) in 1988. On average VC was 64 %predicted in 1988, and decreased 0.4 l over the 20 years, which was equivalent to that expected due to aging. Six of the original cohort developed respiratory failure (two died, four surviving: Po_2 44-58 mmHg, Pco_2 48-65 mmHg); their VC had been 1.3 l (34 %predicted) in 1968.

Branthwaite's (1986) retrospective survey of cardiorespiratory consequences of idiopathic scoliosis is difficult to evaluate due to the presence of i) a large proportion of pre "adolescent" onset cases, ii) frequent unrelated cardiorespiratory disease and iii) incomplete data in these subjects who attended the Brompton Hospital. A trend to greater pulmonary impairment was noted in the 5^{th} and 6^{th} decades, largely confined to subjects with an age of onset less than 5 years.

Although there are few longitudinal studies of the natural history of cardiorespiratory function in idiopathic scoliosis, a large number of cross sectional studies yield a clear picture of the physiological sequence which occurs with progressive impairment in this condition.

Initially, a non obstructive ventilatory defect with reductions in total lung capacity (TLC) and vital capacity (VC) develops (Caro and DuBois, 1961; Gazioglu et al, 1968; Bjure et al, 1969; Bjure et al, 1970; Weber et al, 1975; Kafer, 1975;

Lindh and Bjure, 1975; Jones et al, 1981; Cooper et al, 1984; Aaro and Ohlund, 1984; Muirhead and Conner, 1985; Smyth et al, 1986; Kennedy et al, 1987; Gagnon et al, 1989). The forced expiratory volume in one second (FEV_1) falls in parallel with the VC, the FEV_1/VC ratio remaining normal (Bergofsky et al, 1959; Gazioglu et al, 1968; Bjure et al, 1969; Bjure et al, 1970; Weber et al, 1975; Olgati et al, 1982; Aaro and Ohlund, 1984; Muirhead and Conner, 1985; Kennedy et al, 1987; Gagnon et al, 1989). Functional residual capacity (FRC) falls in parallel with TLC and VC, reductions in residual volume occurring to a lesser degree (Bergofsky et al, 1959; Caro and DuBois, 1961; Bjure et al, 1970), if at all (Gazioglu et al, 1968; Weber et al, 1975; Kafer, 1975; Olgati et al, 1982; Aaro and Ohlund, 1984; Cooper et al, 1984; Muirhead and Conner, 1985; Gagnon et al, 1989).

Despite reductions in lung volumes, in the early stages of pulmonary impairment, distribution of ventilation remains grossly normal (Bergofsky et al, 1959; Caro and DuBois, 1961; Shannon et al, 1970; Littler et al, 1972; Weber et al, 1975; Olgati et al, 1982; Cooper et al, 1984), although uneven distribution, associated with airway closure at volumes above FRC, may occur with more advanced deformity (Bjure et al, 1970). The pattern of breathing adopted tends to be one of low tidal volumes (V_T) and high breathing frequencies (f) (Caro and DuBois, 1961; Smyth et al, 1968; DiRocco et al, 1983; Ramonatxo et al, 1988), alveolar ventilation being maintained by increases in minute ventilation ($\dot{V}_E$) (Bergofsky et al, 1959; Kafer, 1976). Subtle disturbances of ventilation to perfusion ($\dot{V}_A/\dot{Q}$) ratios may lead to minor reductions in arterial partial pressure of oxygen

(Po_2), but significant arterial oxygen desaturation rarely occurs in the absence of severe reductions in lung volumes (Shannon et al, 1970; Weber et al, 1975; Kafer, 1976; Gagnon et al, 1989).

With progressive loss of lung volume, pulmonary arterial blood flow loses its normal vertical gradient of distribution (West and Dollery, 1960), with the upper zones becoming equally as well perfused as the bases (Dollery et al, 1965; Shannon et al, 1970; Littler et al, 1972). At this stage pulmonary arterial pressure may be normal at rest but rise precipitously during exercise, when the already largely recruited pulmonary vascular bed is required to accommodate increases in cardiac output (Bergofsky et al, 1959; Shneerson, 1978).

Reductions in lung volumes and ventilatory capacity may progress. This progression is thought to be due to a combination of i) direct effects of the spinal and rib cage deformities, ii) stiffening of the chest wall (Bergofsky et al, 1959; Caro and DuBois, 1961; Ting and Lyons, 1963; Kafer, 1975) and lungs (Bergofsky et al, 1959; Cook et al, 1960; Caro and DuBois, 1961; Ting and Lyons, 1963; Cooper et al, 1984), iii) uncoupling of the inspiratory muscles (Cooper et al, 1984) and (iv) additional chest wall deformations during the act of breathing. Eventually, particularly with advancing age (Kafer, 1976), alveolar ventilation may become compromised; alveolar and arterial partial pressure of carbon dioxide (Pco_2) increase and alveolar Po_2 decreases (Bergofsky et al, 1959; Kafer, 1976). Low alveolar oxygen tensions, coupled with the development of $\dot{V}A/\dot{Q}$ disturbances

(Bergofsky et al, 1959; Westgate, 1968; Shannon et al, 1970), lead to progressive arterial hypoxemia which further contributes to increases in pulmonary arteriolar resistance. Pulmonary hypertension becomes established at rest (Bergofsky et al, 1959) and may eventually lead to cor pulmonale and premature death.

The findings of these cross sectional studies may have been heavily influenced by the selection criteria for the study subjects, which are likely to have been biased towards greater cardiorespiratory dysfunction. Consequently, the frequency and time course with which these changes occur remains uncertain, although the sequence of physiological changes is likely to be correct.

1.2.4.3 Natural history of disability (work capacity)

Disability associated with idiopathic scoliosis has been assessed in terms of i) ability to meet the demands of employment, or ii) formal exercise tests which measure maximal work capacity or oxygen consumption.

Nilsonne and Lundgren found that 47% of long term nonoperated survivors (mean age 62 yrs) with scoliosis were unable to work (Nilsonne and Lundgren, 1968). In a younger population (mean age 48 yrs), Nachemson reported inability to work in 22% of idiopathic scoliotics (Nachemson, 1968). Given that both studies reported an increased mortality rate, this data from survivors yields an underestimate of disability. In contrast, the long term follow up studies from Iowa, concluded that there was little reduction in work and recreational capacity (Collis

and Ponseti, 1969; Weinstein et al, 1981). It appears that inability to work was also uncommon in the Italian study (Ascani et al, 1986).

Leech et al's study (1985), which measured work capacity in very mild scoliotics (mean Cobb angle, ~10°) using a modified incremental exercise test, found no reduction in work capacity compared to controls. Shneerson (1980) reported a 15.5% reduction in $\dot{V}O_{2\,max}$ (predicted from deformed height, ~32% reduction if predicted from arm span) in 20 adolescents who had been selected for surgery (mean Cobb, 62°). Bjure et al (1969) found a maximal oxygen uptake of 30 ml/kg in 9 subjects with a mean Cobb angle of 87°, judged to be ~75% of predicted. Three further studies, with mean Cobb angles of 33° (Chong et al, 1981), 28° (DiRocco et al, 1983) and 22° (DiRocco and Vaccaro, 1988) also found reductions in maximal oxygen consumption, but did not express these reductions as %predicted. Smyth et al (1986) reported $\dot{V}O_{2\,max}$ in idiopathic scoliotic subjects with a mean Cobb angle of 17° but, due to the exclusion of data from 8/44 subjects judged to have exercised sub maximally, their findings can not be compared with normals. In a later study from the same institution (Kesten et al, 1991), 15 adults with mean age of 33 yrs and Cobb angle of 47° were found to have a significant reduction of $\dot{V}O_{2\,max}$ of 31.6 ml/kg which was ~84% of control values.

1.2.4.4 Natural history of handicap (progression of symptoms)

Back pain, breathlessness and psychological disturbances secondary to the cosmetic effects of spinal deformity, are generally considered to be the main symptoms associated with idiopathic scoliosis. Again, there are few longitudinal studies of the natural history of symptoms in scoliosis. A number of cross-sectional studies have noted the frequency of different symptoms, but there is little detailed data, and scaling of symptom magnitudes has rarely been performed.

1.2.4.4.1 Back pain

Nilsonne found that 90% of long-term survivors with idiopathic scoliosis were aware of back symptoms (Nilsonne and Lundgren, 1968). In contrast, the Iowa group reported that after an average of 24 years follow up, only 16% (Collis and Ponseti, 1969), and after a further ten years of follow up, only 12% (Weinstein et al, 1981) of respondents experienced back pain sufficient to restrict activities or recreation. In the later study, back symptoms were similar to an age and sex matched control population attending a dermatology clinic. The Italian study reported back pain in 61% of their patients, which was considered similar to the normal population (Ascani et al, 1986).

Two additional long-term follow up studies reported back pain in 40% (Nachemson, 1968) and 62% (Fowles et al, 1978) of their study populations, but

many cases of non idiopathic scoliosis were included in both studies and lack of controls makes interpretation difficult.

In summary, back pain is common in adult idiopathic scoliosis, but probably no more so than in the general population. Back pain appears to be uncommon in younger subjects with idiopathic scoliosis.

1.2.4.3.2 Breathlessness

Although the association of breathlessness with idiopathic scoliosis has been noted in many reports (Bergofsky et al, 1959; Mankin et al, 1964; Dollery et al, 1965; Collis and Ponseti, 1969; Bjure et al, 1970; Kafer, 1975; Weinstein et al, 1981; Branthwaite, 1986; Ascani et al, 1986; Pehrsson et al, 1991), few have attempted to quantify the frequency of its occurrence or its severity.

Bjure (1970) studied the interrelationship between deformity, pulmonary impairment and breathlessness in 50 untreated idiopathic scoliotic subjects, some of whom were congenital. Twenty seven of these subjects were drawn from a previous long term follow up study of greater than 30 years duration (Nachemson, 1968); the remaining 23, all under 30 years of age, had recently been admitted for orthopaedic management. More than half (26/50) complained of breathlessness associated with activities ranging from "walking fast or up a hill" (10/26) to "dressing or similar activities" (3/26). Twenty years later, 14 of these subjects

completed the same questionnaire; the number who complained of breathlessness increased from 5 to 8 during this interval (Pehrsson et al, 1991).

In the Iowa studies, after a minimum of twenty years follow up, 30 of 195 respondents (15%) complained of "shortness of breath which occasionally limited their activity", but only five of these (2%) complained of "dyspnoea after walking two blocks or climbing one flight of stairs" (Collis and Ponseti, 1969). Ten years later, 47 of 161 (29%) experienced the milder category of breathlessness and 4/161 (2.5%) experienced "severe breathlessness" after two blocks or one flight of stairs. The Italian study reported cardiorespiratory symptoms in 22% of patients. Although breathlessness was a common symptom in Branthwaite's retrospective survey (Branthwaite, 1986), for the reasons previously noted, these findings are difficult to interpret. Branthwaite concluded that disabling breathlessness was rare in older unfused adolescent idiopathic scoliotics.

In contrast to long term studies of older populations, in a younger population (9-20 yrs) of 33 subjects with mostly mild to moderate idiopathic scoliosis (Ferguson angle (Ferguson, 1930) < 50 degrees in 31 cases) , only four subjects were noted to have mild (3 cases) or moderate (1 case) dyspnoea on exertion. Similarly, respiratory symptoms were no more frequent in a follow up study of 125 youths (mean age 17 yrs) with stabilized mild scoliosis (maximum Cobb 46 degrees, $\leq$ 15 degrees in 83%) than in a control population (Leech et al, 1985).

In response to a mailed questionnaire, 44/115 subjects with idiopathic scoliosis (many of congenital, infantile or juvenile onset) complained of breathlessness (Scadding and Zorab, 1969). As discussed later, frequency of breathlessness was related to angle of scoliosis.

In summary, complaints of breathlessness appear to be uncommon in young idiopathic scoliotic subjects with milder deformity, but may become prominent with advancing age. The absence of studies which have scaled the severity of breathlessness under standardized conditions (eg. known ventilatory demands) in both idiopathic scoliotic and control populations, make it difficult to assess the relative prevalence and severity of this symptom.

1.2.4.3.3 Psychological disturbances

After a minimum of twenty years of follow up, the Iowa group (Collis and Ponseti, 1969) obtained questionnaire responses from 54% of an initial cohort of 358 subjects who had been managed non surgically. Ninety per cent of respondents were married; 54% believed that their deformity was apparent to others when they were dressed; 19% volunteered feelings of "limitation in personality functioning". None had required psychiatric treatment relating to their deformity, but two suicides (precipitating factors unknown) had occurred during the period of follow up. Comparison with a control population was not performed.

Ten years later, when 161 of the original cohort were reviewed, 21% were judged to have mild psychological reactions to their deformity (Weinstein et al, 1981). Most subjects felt less self conscious about their deformity as they got older.

Nilsonne and Lundgren reported follow up findings on 102 of an initial cohort of 113 (90%) Swedish patients, a minimum of 50 years after they had presented to an orthopaedic clinic (Nilsonne and Lundgren, 1968). Seventy six percent of traced cases had never married, suggesting major psychological sequelae for patients with idiopathic scoliosis (probably moderate to severe deformity) during the earlier part of this century.

Psychological disturbance was also reported in 19% (35/187) of untreated cases from Italy (Ascani et al, 1986) who also had a lower than normal marriage rate. Formal psychiatric and psychological evaluation of 26 female cases of severe idiopathic scoliosis (mean Cobb angle 105 degrees) uncovered poor psychological adjustment with evidence of hypersensitivity and insecurity (Bengtsson et al, 1974). Fallstrom also reported disturbances of personality development with distorted body image and dissatisfaction with medical attention received, in 195 consecutive patients treated either surgically or by brace (Fallstrom et al, 1986). In this study, despite similar severity of deformity, those patients who received bracing alone scored significantly less well. A possible negative influence of body braces on psychological status needs to be remembered when considering studies of

"untreated" scoliosis, as some form of bracing was frequently used in these patients (Ponseti and Friedman, 1950; Nilsonne and Lundgren, 1968; Collis and Ponseti, 1969; Weinstein et al, 1981).

In summary, there is persuasive evidence that idiopathic scoliosis is associated with significant psychological distress, particularly in younger female patients.

1.2.4.5 Mortality

It has long been recognized that scoliosis, including idiopathic cases, may be associated with cardiorespiratory failure and premature death (Chapman et al, 1939; Bergofsky et al, 1959; Nilsonne et al, 1968; Nachemson, 1968; Branthwaite, 1986; Ascani et al, 1986; Shneerson et al, 1978; Libby et al, 1982; Swank et al, 1982; Pehrsson et al, 1991). Therefore, unless scoliosis also confers some advantage which prolongs life expectancy (unlikely), untreated scoliosis must be associated with an increased mortality rate.

The long-term follow up study by Nilsonne and Lundgren (Nilsonne and Lundgren, 1968) reported a relative mortality rate of 2.2 in untreated idiopathic scoliosis. Mortality rate was normal until 45 years of age, but thereafter increased markedly. The authors also noted that as many of subjects who were lost to follow up (11/113) may have died when young, the true mortality rate, both overall and in younger subjects, may have been underestimated. Sixteen of the 46 reported

deaths occurred secondary to right heart failure, suggesting that spinal deformity was instrumental and not just coincidental to their demise.

A second Swedish study (Nachemson, 1968) succeeded in tracing 117 of 130 (90%) cases of scoliosis of varied aetiology, after a minimum of 30 years. Forty five per cent of their cases were classified as idiopathic, though the true proportion may have been as high as 67% if, as has been suggested (Brunk, 1951), cases attributed to rickets were in fact idiopathic in nature. The overall relative mortality rate was approximately twice normal, with the idiopathic group having the lowest mortality. Three of five deaths in idiopathic scoliotic patients were due to "kyphoscoliotic cardiomyopathy with cor pulmonale".

The Italian study also found that mortality rate was twice normal; the ten deceased patients died of cardiopulmonary complications (Ascani et al, 1986).

After a minimum of thirty years follow up, the Iowa group reported a mortality rate in untreated idiopathic scoliotic subjects which was similar to a sex and date of birth matched control population; cor pulmonale was the cause of death in only one of the 33 patients who had died. These findings are likely to be overly optimistic. Firstly, a large proportion of the original cohort who were lost to follow up (38%) may have had a higher mortality (lost due to early deaths?). Secondly, those subjects expected to have the worst prognosis were excluded from the study (53/444 (12%) had spinal fusions).

After 20 years of follow up 2/42 subjects with unfused idiopathic scoliosis had died of respiratory failure, further evidence that this condition may lead to premature death.

The follow up studies performed by Fowles et al (1978) and Branthwaite (1986) do not permit calculation of mortality rates for adolescent idiopathic cases.

1.3 Interrelationships of deformity, impairment, disability and handicap

Screening programs attempt to detect clinically important conditions at an early and frequently asymptomatic stage, so that treatments of proven benefit can be instituted early. If spinal deformity was never associated with unpleasant cosmetic effects, symptoms or functional disturbances, it would be an unimportant skeletal anomaly - an incidental radiological finding, not requiring detection or treatment. Although the natural history of this condition is uncertain, it is clear that the consequences of scoliosis are significant; symptoms and functional disturbances associated with idiopathic scoliosis may be profound and even fatal. Scoliosis screening programs aim to detect mild curves which can then be monitored for significant progression, with early intervention to arrest progressive deformity in the minority of cases where this occurs. The anticipated benefits are a reduction in the need for major spinal surgery, and long-term prevention of the symptomatic and functional disturbances already described.

Although it is appealing to suggest that:

i) the extent of respiratory impairment is directly related to, and predictable from the degree of scoliosis;

ii) the severity of symptoms (breathlessness) and disability (reduced work capacity) is directly related to, and predictable from the severity of pulmonary impairment;

these assumptions are questionable. The following sections will review the available evidence regarding the strength of the relationships between i) spinal deformity; ii) pulmonary impairment; iii) disability; and iv) handicap from symptoms in idiopathic scoliosis.

1.3.1 Relationship of pulmonary impairment to spinal deformity

1.3.1.1 Angle of scoliosis

Most studies which have examined the relationship between spinal deformity and pulmonary impairment have taken the angle of scoliosis, as their measure of deformity, and VC as their measure of pulmonary impairment. Angle of scoliosis is measured in degrees, usually from a frontal spinal radiograph by Cobb's method (see spinal deformity, 2.2.3), and VC is usually expressed as % predicted normal reference value (%VC), thereby standardizing for expected differences on

the basis of age, sex, and height of the subjects. This review will first examine the published relationships between angle of scoliosis and %VC predicted, and subsequently, the relationship between other measures of deformity and pulmonary impairment.

Nineteen studies were found in the English literature which documented the relationship between angle of scoliosis and %VC in patients with idiopathic scoliosis. Some of these studies included cases of scoliosis which were not idiopathic in nature, but as it was possible to analyze the idiopathic cases separately, they have been included in this review. The composition and findings of these studies are summarized in table 1.1 Data from one small study of physical training (Bjure et al, 1969) has not been included in this table as it was considered probable that these 11 cases were analyzed in a subsequent larger study of pulmonary impairment, from the same authors (Bjure et al, 1970). One further study (DiRocco and Vaccaro, 1988) documented Cobb angle and VC on 19 subjects, but did not express VC as % predicted. Analysis of this data found that there was no relationship between Cobb angle and VC, either directly ($p=0.3$) or after standardizing for differences in age, sex and height ($p=0.1$).

In many of these reports, description of the subjects and presentation of the results was in a different format to that shown in this table, requiring some recalculation or estimation from tables or figures. Before considering their results,

Study		n	Scoliosis (degree)		VC (%pred)	Linear Regression			
			Mean	Range	Mean	c	Slope	r^2	p
Bergofsky	1959	19	102	70-150	56	126	-0.72	0.56	<0.001
Collis	1961	37_T	~85	20-150	~75	~110	~-0.47	~0.44	<0.001
Mankin	1964	33	~33	3-95	76	87	-0.4	-	-
Gazioglu	1968	62	62	25-100	71	-	-	<0.06	NS
Makley	1968	31	67	40-133	70	~107	~-0.56	~0.33	<0.001
Westgate	1969	~12	~85	40-180	70	95	-0.33	0.66	<0.005
Bjure	1970	50	~75	~10-190	~66	98	-0.42	.74	<0.001
Kaffer	1975	51	80	35-150	61	88	-0.34	0.24	<0.001
Weber	1975	~23	72	35-118	71	100	-0.42	0.2	<0.01
Stoboy	1978	~9	66	37-130	~69	~109	-0.6	0.86	<0.001
Weinstein	1981	20_T	98	25-156	65	~106	-0.42	0.55	<0.001
"		21_C	68	32-109	95	104	-0.19	0.08	>0.1
"		26_L	55	19-138	106	-	-	-	NS
Olgiati	1982	22	66	40-160	83	103	-0.31	0.22	<0.05
Aaro	1984	33	51	20-93	~76	-	-	0.46	<0.001
Smyth	1984	44	17	<30	94	-	-	0.02	0.38
Leech	1985	125	~10	3-46	105	-	-	<0.04	NS
Muirhead	1985	51	52	20-90	82	~87	~0.19	0.03	>0.1
Kennedy	1987	13	29	12-49	84	98	-0.49	0.12	>0.1
Gagnon	1989	42	58	37-110	81	~96	~0.28	0.04	>0.1

Table 1.1 Studies documenting the relationship between angle of scoliosis and vital capacity
%VC = c + Angle of Scoliosis x Slope. Subscripts: T, thoracic; C, cervical; L, lumbar.

a number of important methodological differences between the studies which may have influenced their findings, will be considered.

There were marked differences between the study populations. Five of the reports, describe findings in subjects who had been selected for surgical stabilization of their spines (Gazioglu et al, 1968; Makley et al, 1968; Westgate and Moe, 1969; Stoyboy, 1978; Olgati et al, 1982). Deformity in these patients, in addition to being more advanced, may have been associated with greater respiratory impairment or symptomatic consequences than is usual in idiopathic scoliosis in general, thereby encouraging selection for surgical management. The converse may have been true for the non surgically managed patient populations (Collis and Ponseti, 1969; Weinstein et al, 1981). Subject selection in many of the other studies may also have been biased towards the more severely impaired and symptomatic, as they reflect the experience of centers which specialize in the management of scoliosis or respiratory diseases (Bergofsky et al, 1959; Mankin et al, 1964; Bjure et al, 1970; Weber et al, 1975; Kafer, 1975; Aaro and Ohlund, 1984; Muirhead and Conner, 1985; Gagnon et al, 1989), not necessarily a representative cross-section of idiopathic scoliotic patients in general. Leech et al's study (1985) of cardiorespiratory function in patients who had been discharged from follow up, following detection by a screening program, avoids this referral bias but is confined to a very mildly deformed good prognostic group.

Other important differences between the study populations relate to the pattern and severity of deformity studied. Collis and Ponseti (1969) and Weinstein et al (1981) analyzed different curve locations separately, while other authors (when stated) confined themselves to thoracic curves, with or without exclusion of combined (Muirhead and Conner, 1985) or thoracolumbar (Muirhead and Conner, 1985; Gagnon et al, 1989) curves. An unspecified number of Bjure's subjects with idiopathic scoliosis (Bjure et al, 1970) were of congenital onset which may have influenced the findings of this study.

Methods of predicting reference values, for expression of impairment as percent of predicted VC, also differed widely between studies. These methods included body surface area (Mankin et al, 1964; Westgate and Moe, 1969); deformed height (Bergofsky et al, 1959; Collis and Ponseti, 1969; Westgate and Moe, 1969; Makley et al, 1968; Leech et al, 1985); various estimates of non-deformed height (Gazioglu et al, 1968; Bjure et al, 1970; Weber et al, 1975; Olgati et al, 1982; Aaro and Ohlund, 1984; Smyth et al, 1984b; Muirhead and Conner, 1985; Kennedy et al, 1987; Gagnon et al, 1989); age and sex alone (Kafer, 1975); or not stated (Stoyboy, 1978; Weinstein et al, 1981). The angle of scoliosis was measured by Cobb's method except in two of the earlier studies (Mankin et al, 1964; Collis and Ponseti, 1969) which used Ferguson's method.

As can be seen from table 1.1, there is little doubt that a statistically significant inverse relationship exists between the severity of thoracic scoliosis and

VC, 13/20 studies confirming this finding. Failure to find a significant relationship in two of the studies may have been due to the mild extent and narrow range of deformity in these reports (Smyth et al, 1984b; Leech et al, 1985). Lack of a significant association in another study (Kennedy et al, 1987), which found the slope of the relationship between Cobb angle and %VC to be similar to many of the larger positive studies, is probably due to inadequate statistical power with a small number of subjects. In addition, although the long term follow up studies from Iowa (Collis and Ponseti, 1969; Weinstein et al, 1981) found a convincing relationship for their thoracic curves, this was not so for combined, thoracolumbar or lumbar curves.

The slope describing the relationship between %VC and Cobb angle had a mean of -0.38 %VC per degree (SE 0.05), indicating that on average, a ten degree increase in scoliosis is associated with a fall in VC of approximately 4% of normal VC. For this calculation, a slope of 0 was assigned to three of the negative studies (Gazioglu et al, 1968; Smyth et al, 1984b; Leech et al, 1985); a single study was excluded due to a lack of data concerning slope (Aaro and Ohlund, 1984); and the second Iowa follow up study (Weinstein et al, 1981) was excluded as most of the patients were accounted for in the earlier study (Collis and Ponseti, 1969). Data from one further study (Bjure et al, 1969) was not processed, as these patients are probably part of a larger study from the same authors (Bjure et al, 1970).

The intercept value for the linear regression equation (%VC when scoliosis is zero) should be 100% if there is a straight line relationship between the angle of scoliosis and %VC, and if the equations used to calculate %VC were appropriate. The mean value for the 14 studies in which an intercept was available was 100.7 (SE 2.96) which is in good agreement with the expected value. Intercept differences between studies may in part be due to differences in the prediction equation used.

Although there is a significant relationship between pulmonary impairment and angle of scoliosis, the predictive strength of this relationship (reflected by r^2 and the SD of the residuals) was low; r^2, which indicates the proportion of the variability of one measure which can be accounted for by variability in the other, was 0.3 (SD 0.28) for the 16 studies in which it could be estimated (thoracic and combined curves assessed separately (Weinstein et al, 1981)). In other words, only 30% of the variability in VC %predicted could be accounted for on the basis of differences in the severity of scoliosis. Due to incomplete information, it was not possible to assess the SD of residuals around the predicted relationships.

In summary, this review confirms that there is a statistically significant relationship between pulmonary impairment and scoliosis; on average, %VC decreases ~0.4 per degree of scoliosis. It was also found that the relationship is variable; angle of scoliosis is a poor predictor of pulmonary function in individual cases.

As might be expected, similar quantitative relationships exist between the severity of scoliosis and reductions in other lung volumes, particularly TLC and FRC, and less consistently, RV (Bjure et al, 1970; Weber et al, 1975; Kafer, 1975; Olgati et al, 1982).

1.3.1.2 Other features of spinal deformity

A smaller number of studies have examined the relationship of pulmonary impairment to features of deformity other than the angle of scoliosis.

Bergofsky et al (1959) noted that in their group of severely deformed patients, pulmonary impairment increased with the angle of kyphosis, in addition to the angle of scoliosis. This finding is in disagreement with other investigators who have reported greater than expected pulmonary impairment when scoliosis is associated with hypokyphosis (reduction of the normal thoracic kyphosis) or lordosis (Nash and Kevins, 1974; Winter et al, 1975; Aaro and Ohlund, 1984), a finding which has been attributed to an associated reduction in antero-posterior chest diameter.

Muirhead found a trend towards greater impairment with hypokyphosis, but the difference in pulmonary function between curves greater and less than 20 degrees kyphosis was not significant (Muirhead and Conner, 1985).

Vertebral column and rib cage rotation have also been associated with pulmonary impairment (Mankin et al, 1964; Aaro and Ohlund, 1984), although generally these measures of deformity have been less predictive of pulmonary impairment than the angle of scoliosis.

Curve position and pattern may also influence impairment; single thoracic curves have the most deleterious influence, single lumbar curves probably have little if any effect, while combined double curves and thoracolumbar curves have an intermediate impact on pulmonary function (Collis and Ponseti, 1969; Weinstein et al, 1981). Three studies failed to find an association between the position of the thoracic curves and severity of pulmonary impairment (Bergofsky et al, 1959; Mankin et al, 1964; Aaro and Ohlund, 1984). In addition, Bergofsky et al noted that curve length and direction did not appear to influence severity of impairment.

The relationship of deformity to measures of pulmonary impairment other than lung volumes has been addressed. Three studies (Westgate and Moe, 1969; Kafer, 1976; Weinstein et al, 1981) found a negative correlation between Cobb angle and Po_2, though this was not confirmed by Weber (Weber et al, 1975). In Kaffer's study (1976), Po_2 was more closely related to lung volume than to the angle of deformity. In a separate report, Kaffer (1975) also found an inverse relationship between Cobb angle or VC and total respiratory resistance, particularly the chest wall component.

1.3.2 Relationship of disability to spinal deformity and pulmonary impairment

Studies documenting the relationship of disability to either spinal deformity or pulmonary impairment, are sparse.

Chong et al (1981) reported a significant negative correlation between percentile performance on a Bruce protocol exercise test and Cobb angle, and "a definite trend" between $\dot{V}O_{2\,MAX}$ and the angle of scoliosis.

There was no relationship between these variables in DiRocco et al's (1983) study of 14 subjects who had a reduced $\dot{V}O_{2\,max}$. In a later study of nineteen subjects (Cobb angle, 12-40°) using more intense exercise, DiRocco and Vaccaro (1988) again found a reduction in $\dot{V}O_{2\,max}$, particularly with curves greater than 25°. Using regression analysis on the data provided in that study, there was a weak relationship between $\dot{V}O_{2\,max}$/kg/min and Cobb angle ($p=0.014$), but the relationship between $\dot{V}O_{2\,max}$ and Cobb angle was not significant ($p=0.2$) after standardizing for differences in age, sex and height. VC and $\dot{V}O_{2\,max}$ were also unrelated after standardizing for age, sex and height.

There was no relationship between $\dot{V}O_{2\,max}$ and angle of scoliosis in Leech et al's (1985) study of very mild scoliotic youths, but exercise capacity was judged to be normal in this group.

Bjure et al (1969) did not comment on the relationship between Cobb angle and maximal oxygen consumption, but noted that there was no correlation between $\dot{V}O_{2\,MAX}$ and reduction of VC in this small study.

Although various aspects of the cardiorespiratory response to exercise have been reported in a number of additional studies, data relating exercise capacity to extent of deformity or pulmonary impairment were not included (Mankin et al, 1964; Stoyboy, 1978; Shneerson and Madgwick, 1979; Shneerson, 1980; Smyth et al, 1986; Kumano and Miyashita, 1986).

In summary, in the absence of studies of adequate size, the relationship of disability to either spinal deformity or pulmonary impairment is uncertain. The evidence which is available suggests that at best, these relationships are weak.

1.3.3 Relationship of handicap (symptoms) to spinal deformity and pulmonary impairment

Few studies have addressed the relationship of symptoms to either deformity or pulmonary impairment. The data which are available will be reviewed under the headings of the symptoms studied.

1.3.3.1 Pain

Evidence suggests that there is little relationship between back pain and either the severity or location of the curve (Nachemson, 1968; Collis and Ponseti, 1969; Ascani et al, 1986).

1.3.3.2 Psychological disturbance

Despite progression of scoliosis, the Iowa group reported a lower prevalence of psychological disturbance (relating to appearance) at 30 years compared to 20 years follow up (Collis and Ponseti, 1969; Weinstein et al, 1981). Double major curves are considered less cosmetically obvious than single thoracic curves (Collis and Ponseti, 1969; Weinstein et al, 1981; Ascani et al, 1986), and were also found to be associated with a lesser degree of psychological disturbance in a Swedish study (Bengtsson et al, 1974). Psychological adjustment deteriorated with increasing deformity (Bengtsson et al, 1974; Ascani et al, 1986) and with impairment of VC and early age of onset (Bengtsson et al, 1974). Fallstrom found that subjects who received bracing therapy were less satisfied with treatment than those who had a surgical stabilization performed, but that the angle of curvature or size of the rib hump did not correlate with the subjects psychological assessment (Fallstrom et al, 1986). It appears therefore that the psychological consequences of idiopathic scoliosis depend at least as much on

age, age of onset, sex, personal circumstances or treatment modality as they do on pattern or severity of the deformity.

1.3.3.3 Breathlessness

Bergofsky et al (1959) compared three groups of patients with scoliosis (mostly idiopathic) who had been selected according to severity of cardiorespiratory impairment (asymptomatic, dyspnoea on moderate exertion, right heart failure). Spinal deformity, reduced lung volumes, gas exchange abnormalities and pulmonary hypertension were associated within these categories.

Bjure et al (1970) measured breathlessness on a five point category scale according to the level of activity required to provoke "dyspnoea", and examined its relationship to the extent of deformity and pulmonary impairment. Breathlessness increased with both the angle of scoliosis and the age of the patient. Thoracolumbar curves were associated with breathlessness less frequently and of a milder category than higher thoracic curves. Despite a marked correlation between deformity and pulmonary impairment, lung volumes were not significantly correlated with breathlessness.

Scadding and Zorab (1969) found a progressive increase in the frequency of breathlessness as angle of scoliosis increased. In response to mailed questionnaires to 115 cases of idiopathic adolescent scoliosis, approximately 18%

of subjects with curves of less than 30 degrees complained of breathlessness, with an increase to ~60% in those with curves greater than 90 degrees.

In the Italian study, cardiopulmonary symptoms were also more common in single thoracic curves of greater than 40° (Ascani et al, 1986).

Both long term studies from Iowa (Collis and Ponseti, 1969; Weinstein et al, 1981) found that breathlessness was associated with pattern and severity of scoliosis, and severity of pulmonary impairment. Patients with thoracic curves were twice as likely to complain of breathlessness (14/37, 38%) as were double, thoracolumbar and single lumbar curves combined (12/69, 17%). Overall, there was a fair correlation between breathlessness and pulmonary function; of the 106 patients assessed, 26 complained of breathlessness, 20 of whom had a low VC (sensitivity 77%). The converse was not true, a low VC did not always imply that subjects would be breathless; of the 48 patients with a low VC, only 20 (42%) complained of breathlessness (specificity 65%). Breathlessness correlated with severity of scoliosis in subjects with single thoracic curves, in whom there was a close relationship between deformity and pulmonary impairment, but not in subjects with the other curve patterns, in whom deformity and impairment were not significantly related.

Follow up 10 years later revealed similar results, patients with single thoracic curves having the most severe pulmonary impairment and breathlessness - mild in 16 and severe in 8 of 59 cases. Mild breathlessness was also noted by 16 of

42 (38%) double, 3 of 19 (16%) thoracolumbar, and 4 of 41 (10%) lumbar curves. Of the 23 patients who complained of breathlessness and had pulmonary function assessed, only 15 (65%) had an abnormal VC and conversely, of the 28 patients from all groups with a low VC, only 16 (58%) complained of shortness of breath.

Similarly, Mankin et al (1964) found that although 17 of their 33 patients had a significant reduction of pulmonary volumes, only four complained of breathlessness and in only one of these was it severe. They went on to emphasize the "apparent dissociation between subjective symptoms and objective evidence of pulmonary deficits in patients of this age (9-20 yrs) with scoliosis".

In summary, these studies have shown that breathlessness is loosely but inconsistently related to the severity of spinal deformity and impairment of pulmonary function in idiopathic scoliosis. Breathlessness appears to be further aggravated by advancing age. The reason for inconsistency in these relationships, and evaluation of exercise related symptoms other than breathlessness, has largely not been addressed.

1.4 Purpose of thesis

The well recognized association of spinal deformity with pulmonary impairment has focused attention on the respiratory system in subjects with scoliosis. Current concepts support a predictable relationship between spinal deformity and pulmonary impairment (outlined in figure 1.2). The angle of scoliosis

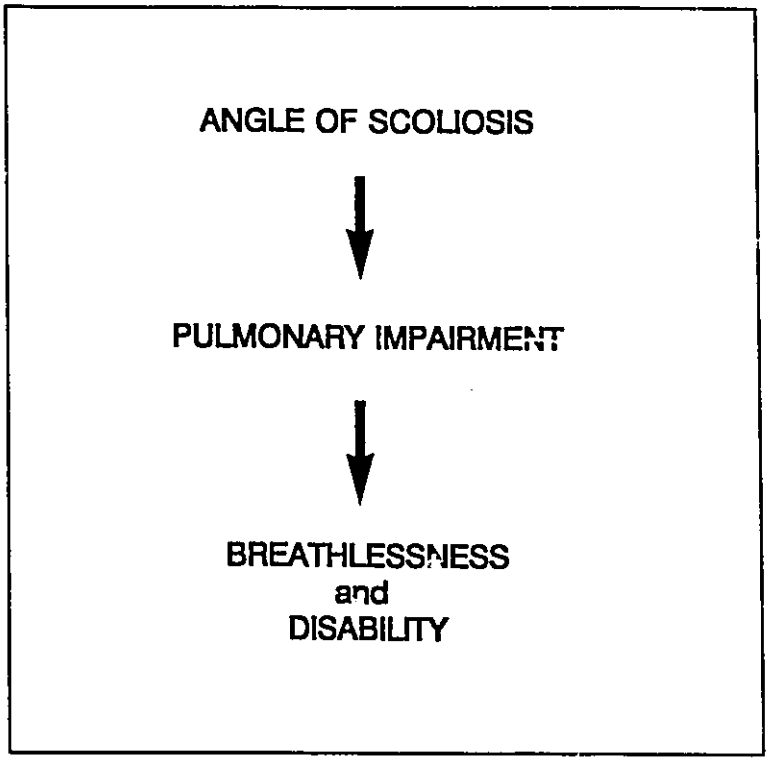


Figure 1.2 Sequential relationship of deformity, impairment, disability and handicap.

is generally thought to adequately characterize deformity for the purpose of examining this relationship. Consequently, in clinical practice pulmonary impairment is often inferred from the Cobb angle alone.

In the absence of a large Cobb angle and marked pulmonary impairment (measured or inferred), disability is not expected in idiopathic scoliosis, and is rarely formally assessed. As pulmonary impairment is considered the fundamental physiological abnormality in these patients, breathlessness is assumed to be the dominant symptom causing disability and handicap. This belief appears to be founded more on preconception than on convincing evidence. As previously

outlined, few studies have attempted to measure symptoms in this population. Those that have, support that breathlessness is increased but have rarely remarked on feelings of muscular effort or fatigue, suggesting that these symptoms may not have been considered.

The purpose of this thesis is to examine the interrelationships of spinal deformity, physiological impairment, disability and handicap. By defining these components in the specific manner which has been outlined, each can be quantified and an analysis of their interrelationships becomes feasible. Although our interpretation of these terms has limitations, we believe that this approach can advance understanding and should be more fruitful than utilizing a purely qualitative description of impairment, disability and handicap, which precludes such an analysis.

In addition, the modifying influence of peripheral muscle, cardiovascular and other factors (eg. age at onset, duration, smoking history, concomitant disease) on these relationships will be assessed. From such analyses, the validity of the pathophysiological sequence outlined in figure 1.2 can be tested. Improved understanding of these relationships would have important implications for patient management.

Chapter 2

Methods

2.1 Subjects

All current attenders and new referrals with adolescent idiopathic thoracic scoliosis, who were seen at the orthopaedic scoliosis clinic at McMaster University Medical Center over a 36 month period (March 1986 - March 1989), were studied. Referrals were mainly from other physicians; a school screening program is not in operation in this region. There were 79 subjects in all, 13 males and 66 females (see description of findings, 3.1). Assessments were also performed on eight subjects with scoliosis who were later excluded due to the presence of neuromuscular (six) and congenital heart disease (two). Three further subjects with spinal deformity were excluded as they had pure kyphosis without a scoliotic component.

Assessments of lean body mass, peripheral muscle volume and strength were not performed in the early part of the study (first 55 subjects) as their role in the evaluation of disability and handicap was not considered at the outset. After deciding that these measurements were potentially important, attempts were made

to recall the first 55 subjects. Tracing was from clinic and family doctor records, patients being contacted both by mail and by phone. Thirty six subjects returned; nine could not be contacted and 10 subjects, though contacted, were not prepared to return (eg. geographical considerations).

Comparison of the 36 subjects who returned for assessment of their peripheral musculature with the 19 who did not, failed to reveal significant differences between the two groups, except that we were less successful in getting males to return for testing (table 2.1).

	RETURNED n = 36	DID NOT RETURN n = 19	p
Sex	M = 4 F = 32	M = 5 F = 14	0.01
Age (yr)	22 (12.0)	23 (7.9)	0.8
Height (cm)	164 (9.0)	165 (9.8)	0.6
Weight (kg)	57 (9.3)	60 (11.9)	0.4
Spinal Fusion	5/36	2/19	>0.2
Cobb Angle	44 (18.5)	43 (15.4)	0.9
%VC	78 (15.3)	80 (15.2)	0.6
%Wcap	86 (16.6)	84 (16.6)	0.8
Br_{50} (Borg)	1.6 (1.76)	1.9 (1.56)	0.5
Leg_{50} (Borg)	2.1 (2.03)	2.3 (1.75)	0.6

Table 2.1 Comparison of subjects who did and did not return for muscle measurements. Mean (SD).

This suggests that those patients who returned were unlikely to differ systematically from those who did not and that failure to obtain full anthropometric

measurements on all 79 subjects was unlikely to introduce bias in subsequent analyses.

Seven subjects had previously had spinal fusions. As spinal fusion may i) change the relationship between features of deformity and physiological variables, and ii) make radiological assessment of deformity difficult, these patients were excluded from all analysis concerning deformity. They were included in analysis unrelated to deformity (eg. relationship of pulmonary impairment to exercise capacity).

Subjects with idiopathic scoliosis most commonly seek medical attention during adolescence and early adulthood, accounting for the positively skewed age distribution of the study population (chapter 3.1). Furthermore, it is recognized that patients attending referral centres may also differ from the total population of such patients due to referral practices. It should be emphasized that no patients were referred primarily for cardiorespiratory assessment, which could have biased the population to be more impaired and disabled than usual. As management decisions for idiopathic scoliotic subjects are usually made on subjects similar to the study population, our findings should be generalizable to clinical settings.

In summary, the study population consisted of consecutive, generally younger, mild to moderately deformed idiopathic scoliotic referrals to an orthopaedic clinic.

2.2 Measurements

2.2.1 Anthropometry

2.2.1.1 Height

Height was measured to the nearest 1 mm using a digital reading anthropometer (Holtain Ltd., Crymmych, Pems, U.K.). Non-deformed height was calculated from arm span with adjustments according to age and sex ((Linderholm and Lindgren, 1978), appendix 1). Deformed height was not assessed as a contributing variable and was not used to predict reference standards, except in those few subjects in which it still exceeded calculated non-deformed height.

2.2.1.2 Arm span

Arm span was recorded to the nearest 0.5 cms, by measuring the distance between the tips of the middle fingers with subject's standing facing a wall. Distances were measured with the subjects sternum and arms flat against the wall, care being taken to keep the arms horizontal.

2.2.1.3 Weight

Weight was recorded to the nearest 0.5 kgs using either a beam or a spring balance scales (Health-O-Meter, Continental, Chicago, Illinois).

2.2.1.4 Lean body mass

Skin fold thickness was measured at the left triceps (mid way between the acromion and the olecranon) and left sub scapular (below the scapular angle) sites using a Harpenden skin fold thickness calipers (Edwards et al, 1955; Tanner and Whitehouse, 1955; Tanner and Whitehouse, 1957) (Holtain Ltd., Crymmych, Pems, U.K.). Measurement error at these sites is small (Edwards et al, 1955), estimated at 0.3 - 0.6 mm for a single observer, and twice that for different observers. Body density was calculated from these two skinfold thicknesses, and subsequently used to determine percent body fat using Seri's equation, as reported by Durnin and Womersley (1974). Measurement error for percent body fat is of the order of 4 units (eg. 24±4% body fat) (Durnin and Womersley, 1974, Kispert and Merrifield, 1987). Lean body mass was calculated as follows: weight x (1 - %body fat). Measurement error estimated at ~ ±12%.

2.2.2 Peripheral muscle assessment

2.2.2.1 Lean leg volume

Leg volume measurements were performed on the right leg as this was the side on which leg strength measurements were taken. Measurement of both legs were not performed as it was felt that the additional value of the data from the second leg would be small and would not justify patient inconvenience. Lean leg volume was calculated as described by Jones and Pearson (1969). Briefly, the volume of four truncated cones (two above and two below the knee) was determined from surface measurements (circumferences using a metal tape, and lengths using an adapted digital anthropometer). Anterior and posterior thigh, medial and lateral calf skin fold thicknesses were used to derive subcutaneous fat depth (Jones and Pearsons equations (McCartney, 1983)). This allowed subcutaneous fat volume to be determined, and subtracted from total leg volume to yield lean leg volume. Bone volume, which is included in this measure, was not considered separately. In distinction to Jones and Pearson's calculations, knee and foot volumes were not included as it was considered that their muscle content and contribution to work performance would be negligible. Measurement error for lean leg volumes is small (Jones and Pearson, 1969; Davies, 1972a), Pearson and Jones found an r^2 of 0.96 between total leg volume measured directly (water displacement) and by this method. Similarly, there was good agreement between leg fat volumes measured radiologically and by this method ($r^2 = 0.88$).

2.2.2.2 Knee extensor strength

The force of a maximal voluntary contraction of the knee extensors (quadriceps) was measured by the method described by Edwards et al (1977). Subjects sat upright in an adjustable straight backed chair with their knee hanging flexed at a 90 degree angle. Straps were positioned around their waist and over the active thigh, to prevent excessive movement during the maneuver. A cuff was placed around the ankle and attached horizontally (adjustable seat height) by chain to an electronic strain gauge (Lafayette 32528) with a digital read out. Subjects performed three maximal voluntary contractions at approximately one minute intervals. The greatest peak force achieved was recorded. Peak torque was calculated from the product of force and distance between mid knee joint and mid point of the ankle strap. The coefficient of variation (c.v.) for peak extensor knee torque is estimated at ~4% using this procedure (Tornvall, 1963; Edwards et al, 1977). A mean difference in strength of 6% between the right and left leg (Tornvall, 1963) and of 8.5% between the stronger and weaker leg (Edwards et al, 1977) has also been noted.

2.2.2.3 Hand grip strength

Right hand grip strength was measured using a dynamometer (Lafayette 32528HD) with a digital read out. Peak grip strength was recorded from the maximum of three efforts. Measurement error is ~5% (Tornvall, 1963).

2.2.3 Spinal deformity

Spinal deformity was assessed from spinal radiographs taken as part of the routine clinical assessment and follow up of these subjects. PA frontal radiographs were taken in a standardized manner with the aid of a positioning device (scoliosis chariot) designed to reduce measurement error (Dawson et al, 1978). A single observer, a senior orthopaedic resident (Dr S. Kirkley), who was blinded to the subjects and other features of their assessment (eg. pulmonary function and exercise capacity) read all radiographs. Additional radiographs were not taken as i) it was intended that our assessment of deformity would be applicable to usual clinical practice and ii) we wanted to avoid additional radiation exposure to the participants. For this reason, radiographs suitable for evaluation of all features of deformity were not available for all subjects (see analysis). The following assessments were made from frontal and lateral films.

2.2.3.1 Frontal spinal radiographs

2.2.3.1.1 Angle of scoliosis (Cobb angle)

The angle of scoliosis was measured according to Cobb's method (Cobb, 1948). Briefly, the angle of intersection of perpendiculars drawn from lines passing along the end plates of the most tilted superior and inferior vertebrae (DeSmet, 1985b) was measured (figure 2.1). Intra subject measurement error is estimated

at less than 5% (Sevastikoglou and Bergquist, 1969; Beekman and Hall, 1979; Oda et al, 1982; Morrissy, 1986; Carman et al, 1989).

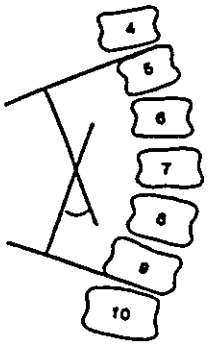
2.2.3.1.2 Length of curve

Curve length was arbitrarily defined by the number of vertebrae between the end plates used to define the Cobb angle. Although vertebrae above and below these end plates may also be part of the curve (Ferguson, 1930; Cobb, 1948), these were not included as curve length then becomes more difficult to reliably define. Measurement error is estimated at ~0.8 of a vertebra (Oda et al, 1982) or ~12% for this study.

2.2.3.1.3 Position of curve

Due to selection criteria, the apex of all curves in this study involved the thoracic vertebrae. Location of the curve was defined by the thoracic vertebra (1 - 12) which formed the apex (the apex vertebra being the most rotated one). Measurement error for selection of the apex vertebra is not known but is likely to be less than for selection of either the upper or lower vertebra when measuring Cobb angle , ~0.6 vetrebrae (Oda et al, 1982).

Frontal spinal radiograph

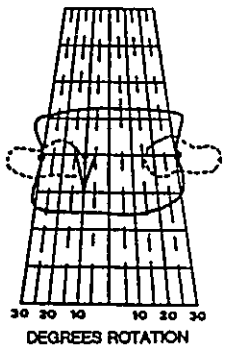


Angle of scoliosis (Cobb method)

Angle of intersection of perpendiculars from the end plates of the most tilted superior and inferior vertebrae.
40 degrees in this example.

Length of curve

Number of vertebrae between the end plates defining the Cobb angle.
5 vertebrae in this example.



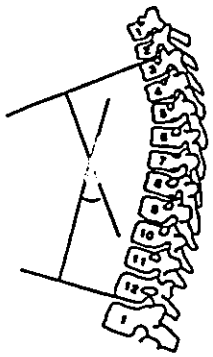
Position of curve

Defined by the thoracic vertebra (1-12) at the apex of the scoliotic curve (most rotated).
T_7 in this example.

Rotation

Rotation of the apex vertebra, assessed from deviation of the base of the spinous process from the midline, using Bunnell's method.
10 degrees in this example.

Lateral spinal radiograph



Angle of kyphosis (Cobb method)

Angle of intersection of perpenciculars from the upper endplate of T_3 to the lower endplate of T_{12}.
35 degrees in this example

Figure 2.1 Radiological assessment of deformity

2.2.3.1.3 Rotation

The extent of rotation of the spinal column accompanying scoliosis varies along the length of the curve (Deacon and Dickson, 1985; Dickson, 1987). Rotation is minimal or absent at the curve margins and maximal at the apex. Traditionally, rotation is quantified according to the apex vertebra, but the optimal method is debated (Cobb, 1948; Nash and Moe, 1969; Mehta, 1973; Benson et al, 1976; Aaro and Dahlborn, 1981; Drerup, 1985; Perdriolle and Vidal, 1985; Stokes et al, 1986; Russell et al, 1990). Bunnell's method was employed in this study as identification of the radiological landmarks used with this method is more reliable than with other methods (Russell et al, 1990). Having identified the apex vertebra, a wedge shaped transparent template is superimposed so that the lateral margins of the template and vertebra overlap (Bunnell, personal communication, figure 2.1). The angle of rotation is read directly from the template according to deviation of the base of the spinous process from the midline. Angle of rotation calculated with this method was found to differ by 3° (SD 4°) from actual rotation measured directly (isolated vertebra) (Russell et al, 1990). In scoliotic spines, precision may be reduced due to poorer radiographic definition and vertebral body distortions (Nash and Moe, 1969; Russell et al, 1990).

2.2.3.2 Lateral spinal radiographs

2.2.3.2.1 Angle of kyphosis / lordosis (Cobb method)

The normal thoracic spine is convex posteriorly with a kyphosis of between 20 and 60° (Bradford et al, 1974; Stagnara et al, 1982; Propst-Proctor and Bleck, 1983; DeSmet, 1985b). Angle of kyphosis is measured from a lateral spinal radiograph. The angle of intersection of perpendiculars from lines drawn through the most tilted upper and lower vertebral end plates, yields this value (figure 2.1). Because of difficulty visualizing the upper thoracic vertebrae, the superior end plate of T_3 and the inferior endplate of T_{12} were taken as the reference vertebra for measurement of kyphosis in these studies. This is common practice (Propst-Proctor and Bleck, 1983; DeSmet, 1985b; Shufflebarger and King, 1987). Stagnara et al (1982) reported reciprocal angulations between the upper and lower endplates of various vertebrae in 100 normal adults. From these data, for these vertebrae, the average normal kyphosis would be $\sim 40 \pm 10$ degrees (SD). Angle of kyphosis may be increased (>60°), hyper kyphosis; reduced (0 - 20°), hypokyphosis; or become convex anteriorly (<0°), lordosis. Measurement error for angle of kyphosis is similar to that for angle of scoliosis (Carman et al, 1989).

Dickson and others (Roaf, 1966; Deacon et al, 1984; Deacon and Dickson, 1985; Dickson, 1985; Dickson, 1987) have convincingly argued that idiopathic scoliosis is almost invariably associated with loss of kyphosis or development of

lordosis, when assessed by anatomical measurements rather than by "face value" interpretation of lateral radiographs. Their findings are not disputed, but as the radiographic projections they recommend are not part of our, and most other centres, usual radiographic evaluation, our analysis is of the conventional radiographic views. Furthermore, spinal configuration relative to the body as a whole, as assessed from conventional lateral films, may be physiologically important.

2.2.4 Pulmonary impairment

Pulmonary impairment was assessed with spirometry, maximum inspiratory and expiratory flow volume loops, lung volumes, respiratory muscle strength, carbon monoxide transfer factor (DL_{CO}), arterial O_2 saturation (SaO_2) and mixed venous CO_2 tension ($P\bar{v}CO_2$).

2.2.4.1 Spirometry

FEV_1 and FVC were obtained from the best of three forced expiratory maneuvers, using a dry rolling seal spirometer (S & M, Mijnhardt model VRS2000, Doylestown, PA) according to the standards and recommendations of the American Thoracic Society (Gardner, 1979; Gardner et al, 1987; Nelson et al, 1990). These standards require an accuracy of measurement of $\leq$ 50 mls (SD) or 3% of the measured volume, whichever is greatest.

Reference values for spirometry for subjects ≤15 years were predicted from non-deformed height using logarithmic equations from the Hospital for Sick Children (updated from Weng and Levison (1969)) which have a predictive accuracy (SD) of ~11.7% for FVC and ~13.9% for FEV_1. Reference values for older subjects (≥16 years) were predicted from age, sex and non-deformed height according to the linear equations of Crapo et (1981b). In their study, the SD of the residuals around the predicted values was - males: FVC 644 ml, FEV_1 48 mls; and for females: FVC 393 ml, FEV_1 326 ml.

2.2.4.2 Flow - volume curves

Flows at different lung volumes (between TLC and RV) were examined from three maximal inspiratory and expiratory maneuvers (Bass, 1973; Knudson et al, 1976; Gardner et al, 1987). Maximal inspiratory and expiratory flows were not necessarily recorded from the same loop. If technically satisfactory tracings demonstrating good reproducibility were not obtained on these three attempts, additional maneuvers were performed. Flow - volume relationships were determined with the same equipment which was used to record spirometry, flow being derived from differentiation of volume. Calibration was performed by delivering known syringe volumes, against which integrated flow rates were compared. Flow recording capabilities complied with ATS accuracy requirements of ± 0.200 l/sec or 5% of the true value (Gardner et al, 1987).

Standards for normal expiratory flow rates for all age groups were predicted from age, sex and non-deformed height using Knudson et al's linear equations (Knudson et al, 1976). The SD around the predicted flow is ~25% of the predicted value at 75% of VC, and ~35% at 25% VC (Leech et al, 1983). Reference standards for maximal inspiratory flows for different sex and age groups were obtained from Bass (Bass, 1973). Variability around predicted peak inspiratory flow rate is ~22% (SD).

2.2.4.3 Lung volumes.

Absolute lung volumes were measured using a steady state Helium dilution technique (Morgan Systems) (McMichael, 1939; Ferris, 1978). At the end of a quiet expiration (FRC), subjects were switched into a spirometer containing a gas of known volume and He concentration. After equilibrium of He between the spirometer and the subjects lungs has occurred, the initial volume of the lungs at the point of being switched in to the circuit can be calculated.

$VOL_{SPIROM} \times [He]_{SPIROM} = VOL_{(SPIROM + FRC)} \times [He]_{EQUILIBRIUM}$

During the procedure, CO_2 is "scrubbed" from exhaled volumes and O_2 added to maintain a constant volume within the system. After additional measures of expiratory reserve volume, tidal volume and inspiratory reserve volume are made, TLC and RV are calculated from FRC.

The SD of FRC measured with this technique is ~90 - 160 mls (Holmgren, 1954; Schaanning and Gulsvik, 1978; Ferris, 1978). Reference lung volumes for subjects ≤ 15 yrs were predicted from non-deformed height using logarithmic equations from the Hospital for Sick Children, Toronto (updated from Weng and Levison (1969)). The SD around these predicted values (coefficient of variation) corresponds to ~16% of the volume for FRC; ~12% for TLC; and ~25% for RV. Reference lung volumes for subjects ≥ 16 years were predicted from age, sex and height using the linear equations of Crapo et al (1982) (single breath He dilution technique) which have a SD for the residuals of - females: 540 ml for TLC; 520 ml for FRC; 380 ml for RV; and for males: 790 ml for TLC; 720 ml for FRC; 370 ml for RV.

2.2.4.4 Diffusing capacity

Lung diffusing capacity was assessed by quantifying the amount of CO which was taken up from alveolar gas each minute per unit driving pressure ($D_{L_{CO}}$)(mls/min/mmHg) (Krogh, 1915; Ogilvie et al, 1957; Crapo and Morris, 1981a; Van Kessel, 1982; Crapo, 1988; Crapo and Forster, 1989). A single breath technique was used which involves inhaling a gas mixture with a known concentration of CO and He from residual volume, breath holding for approximately 10 sec., and collection of an alveolar sample on exhalation. From the change in concentration of the inert gas, He, from inspired to alveolar air samples, the initial CO concentration at the start of breath holding can be

determined, and the rate of fall in CO concentration calculated per mmHg driving pressure. As lung volume during the breath hold has a major influence on the alveolar-capillary area available for diffusion, diffusion capacity was also expressed per litre of lung volume, termed the KCO. Using these techniques, the coefficient of variation for duplicate measures has been reported as 4.6% (Crapo and Morris, 1981a).

Reference standards for children (≤15 yrs) were calculated from age and predicted TLC (from non-deformed height) according to equations from the Hospital for Sick Children (updated from Weng and Levison, 1969) which have a SD of 4.3 mls/min/mmHg. Diffusing capacity was measured by a steady state method for the calculation of these standards, whereas a single breath method was used by our subjects. Although in adults, diffusing capacity may be ~33% lower by the steady state method than by single breath (Van Kessel, 1982), this is not known for children. Predicted D_LCO for an 11 year old child of 160 cms is 22.8 mls/min/mmHg according to Bucci et al (1961) (single breath method) and 23.6 mls/min/mmHg according to the Hospital for Sick Children equations, suggesting that the comparison is appropriate.

2.2.4.5 Respiratory muscle strength

Respiratory muscle strength was measured by recording maximal inspiratory and expiratory pressures at the mouth, in a manner similar to that

reported by Black and Hyatt (1969). Inspiratory pressures were generated at FRC, and expiratory pressures at TLC. Subjects used a flanged rubber mouthpiece which had a small air leak designed to prevent force generation by the buccal musculature which may exceed respiratory pressures. Pressures were measured by an aneroid manometer which was calibrated from -160 to +160 cms H_2O by water manometry. The maximum pressure sustained for 2-3 seconds was recorded. Measurement error (c.v.) for these measurements is ~9% (Bass, 1973; Gaultier and Zinman, 1983; Wagener et al, 1984).

Well established reference standards for respiratory muscle strength measured at these lung volumes (MIP from FRC) are not available. Respiratory muscle strength is greater in post pubertal males than in females and, after increasing to maximum values in adolescents and young adults, thereafter decreases with advancing age (Bass, 1973; Leech et al, 1983; Smyth et al, 1984a; Gaultier and Zinman, 1983; Wagener et al, 1984; Inman et al, 1987). To account for major differences in respiratory muscle strength due to sex, and to allow for comparison of strengths with normal subjects, the following sex specific standards were selected on the basis of similarity of method and population age group in the reference studies. Reference maximal inspiratory pressure from FRC for males - 126 cm H_2O; for females 76 cm H_2O (Inman et al, 1987). Reference maximal expiratory pressures for males, 133 cm H_2O; for females, 95 cm H_2O (Leech et al, 1983).

2.2.4.6 Mixed venous CO_2

Adequacy of alveolar ventilation at rest was assessed from oxygenated mixed venous carbon dioxide tension ($P\bar{v}CO_2$) as originally described by Collier (Collier, 1956; Hackney et al, 1958) and subsequently adapted by Campbell (Campbell and Howell, 1960; Campbell and Howell, 1962; McEvoy et al, 1974; Powles and Campbell, 1978). This involves patients rebreathing from a bag with a PCO_2 marginally higher than the expected $P\bar{v}CO_2$ and a high O_2 concentration. During rebreathing, fluctuations in respired CO_2 concentration are recorded from a rapidly responding infrared analyzer (Godard capnograph, Bilthoven, Holland) which has an accuracy of 0.02 - 0.05% (Collier, 1956). Equilibration between bag and lungs is indicated by loss of CO_2 fluctuations with respirations. This occurs after 4-5 breaths, ~10-20 seconds after the start of the maneuver. Accuracy of the estimate is better than ±2 mmHg (SD) (McEvoy et al, 1973). In the absence of impaired cardiac output, marked arterial desaturation and anaemia, there is a predictable relationship between P_aCO_2 and P_vCO_2 ($P_aCO_2 = 0.8\ P\bar{v}CO_2$) (McEvoy et al, 1974; Powles and Campbell, 1978). When SaO_2 and Hb are markedly abnormal, their effect on the relationship between pressure and content of CO_2 can be adjusted for (McHardy, 1967; Powles and Campbell, 1979), but this was not necessary in any of these subjects.

2.2.5 Incremental exercise testing

Cardiac, pulmonary, metabolic and symptomatic responses to work performance were evaluated during an incremental exercise test which, in addition to being central to these studies, was part of each subject's clinical assessment. Exercise was performed on an electrically braked cycle ergometer (Siemens Elema) as described by Jones (Jones, 1988).

The procedure and possible risks were explained to subjects and/or their guardians, and written informed consent obtained. Subjects first performed loadless pedaling at 60 rpm for one min, after which they were required to increase power output by 100 kpm/min each min until they were no longer able to sustain pedalling. The test could be stopped by the supervising physician before exhaustion if indicated (Jones, 1988), but this was not necessary for any of the subjects.

2.2.5.1 Measurements made at rest and during exercise

Subjects breathed through a unidirectional, low dead space valve (Hans Rudolph) with expired air going to a microprocessor-controlled exercise testing system (SensorMedics Horizon System) which performed the following measurements:

1. **Ventilation:** Expired ventilation ($\dot{V}E$), tidal volume (VT), frequency of breathing (f) and peak expiratory flow rates were measured as expired gas moved through a jewel mounted turbine incorporating electrooptical detectors which were volume and flow calibrated before each period of testing. These measurements correlate closely with reference standards using syringe volumes and Tissot spirometry recordings (r^2=99.2%) and have a coefficient of variation of ~1.4% (Jones, 1984a).

2. **Gas exchange:** Expired gases were sampled from the mixing chamber within the exercise testing system. O_2 concentration was measured by a polarographic sensor and CO_2 concentration by an infrared optical system. Gas temperature and pressure were monitored at the level of the sensors and their influence on concentration continuously adjusted for. A two point gas calibration was performed prior to testing with reference gases composed of N_2=100% (O_2=0%, CO_2=0%) and N_2=80%, O_2=16%, CO_2=4%. O_2 and CO_2 concentrations measured by this system correlate closely (CO_2, r^2=98.8%) with mass spectrometer values. The SD for the relationship was 0.059% for O_2 and 0.085% for CO_2 corresponding to a coefficient of variation of 0.52% and 1.94% respectively at physiological expired gas concentrations (Jones, 1984a).

Oxygen consumption ($\dot{V}O_2$) and carbon dioxide output ($\dot{V}CO_2$) were derived from the product of mixed expired concentrations and volumes. Similarly strong correlations have been found for $\dot{V}O_2$ and $\dot{V}CO_2$ when compared with values

derived from mass spectrometer concentrations and dry gas volumes (r^2 >98%, SD= ~70 mls/min.) All values were calculated and recorded by the computer each 15 second interval. Reference values for $\dot{V}O_{2\,max}$ were predicted from age, sex and height (power function) as reported by Jones and Killian (1987) (for further discussion see 2.2.5.2).

3. Cardiac response:

In addition to measurements made by the computerized system, continuous electrocardiographic monitoring of heart rate, rhythm and for possible myocardial ischaemia was performed and systemic blood pressure was recorded manually (Bruce, 1984a; Bruce, 1984b; Jones, 1988).

4. Arterial oxygenation:

SaO_2 was monitored noninvasively with an ear pulse oximeter (Ohmeda Biox 3700). Accuracy at rest and during exercise is ~2.5% (SD) (Ries et al, 1985; Warley et al, 1987; Escourrou et al, 1990) when compared with directly measured SaO_2 from arterial blood. Ability of the oximeter to detect within subject changes in SaO_2 (eg. a fall) is probably even better (Ries et al, 1985; Escourrou et al, 1990).

2.2.5.2 Work capacity

Work capacity was measured as the maximal power output (100 kpm/min increments each minute) which was sustained for at least 30 sec during the incremental test. The cycle ergometer was calibrated using a torsion balance dynamometer which has an accuracy of 20 kpm (SD) (Cumming and Alexander, 1968). The reproducibility of work capacity in individual subjects, as measured by this test, has not been precisely defined. Experience with the test is that when the same subjects perform the test twice, there is rarely if ever a difference of greater than 100 kpm between the two occasions (Jones N.L., personal communication). A high level of reproducibility is also supported by the findings of another study of work capacity (Tornvall, 1963) which found that duplicate measurements of estimated maximal work capacity had a SD of 4.1% around the mean value.

Reference values for maximal power output were calculated from age, sex and non-deformed height (power function) as reported by Jones and Killian (1987). The SD of the regression residuals are ~ 10% of the predicted values. Reference values for $\dot{V}O_{2\,max}$ and for maximal power output are not available for adolescents, when performing this protocol. The original reference population of 100 subjects who were studied by Jones et al (1985) were aged between 15 and 71 years. Reanalysis of that data, and a new analysis of a further 480 subjects who were retrospectively judged to be normal (age ≥ 20 years) yielded the reference equations used in this thesis (Jones and Killian, 1987). Independent of height,

Wcap increases as a function of age until maturation occurs (Sprynarova and Reisenauer, 1978) and, after the age of 20, subsequently decreased with advancing years (Jones et al, 1989). Against this physiological background, it was considered justifiable to predict reference values for subjects less than 20 years using the same equations as for the older subjects, using an assigned age of 20 years rather than actual age. As an independent check of the validity of this practice, the relationship of Wcap to age, sex and height was determined for 50 local school children (14-19 years) who had performed a similar (but not identical) incremental exercise test (data provided by Dr O. Bar-Or, personal communication). On average, the maximal power output achieved by these adolescents corresponded to 108 % of that which was predicted by the above approach, suggesting either that this reference population were fitter than usual, or that the adult equations may tend to under estimate disability in the younger subjects.

2.2.5.3 Reproducibility of physiological measurements during exercise.

In addition to defining the limits of precision with which physiological measurements can be made, before attempting to explain between subject differences in these measurements, it is important to have an estimate of physiological variation in the same subjects when exercised on separate occasions. The greater "within subject" variability, the more difficult it is to detect true differences between subjects. Jones and Kane (1979) found the following

within subject variability in physiological measurements when repeat measurements were made days (short term) and years (long term) apart at the same work rate. The average difference of each measurement from each subjects mean value were as follows: **Short term:** HR, 3.0%; $\dot{V}_E$, 8.0%; $\dot{V}O_2$, 3.8%; $\dot{V}CO_2$ 4.2%. **Long term:** HR, 4.7%; $\dot{V}_E$, 5.0%; $\dot{V}O_2$, 5.1%; $\dot{V}CO_2$ 6.2%. Variability was greater when tests were repeated in different laboratories, but this source of error was not operative in the present studies.

2.2.6 Sensory Intensities

The measurement properties of scales used to quantify non-physical continua (eg. sensations or psychological qualities) are more difficult to assess than scales used in physical domains. This is largely because no "gold standard" or reference values are available, against which the proposed scale can be compared (in this case the Borg scale). This leads to problems with validation of the scale (see appendix 2, Borg scale). Reliability, the ability of a scale to make measurements in a reproducible and consistent manner, can still be determined. Accepting that no measurement is made with absolute precision, but can be considered to have a true value and an error term (measured value = true value ± error), reliability can be quantified by expressing the ratio of the true difference between subjects/ total variability between subjects (Streiner and Norman, 1989). The differences of interest may be between subjects under similar conditions of

stimulation (classical reliability), or within subjects with changing conditions of stimulation (classical psychophysics). In either case, assessment of reliability requires that more than one sensory rating is made under identical circumstances (usually twice) and the extent of agreement is then determined (eg. Pearsons r or interclass correlation coefficient).

Reliability of the 10 pt. Borg scale has been addressed in a limited number of studies. In one study (Harms-Ringdahl et al, 1986) eight subjects scaled pain/load following application of different weights at the elbow joint. The sensory range was ~0-5 and the Pearson r for repeated estimates was ~0.85, indicating good reliability. Wilson and Jones assessed reproducibility of Borg scale estimates of breathlessness in two studies. In the first, mean breathlessness scores were the same in ten normal subjects at two points with matched ventilation, during a single exercise session. However, breathlessness ratings were significantly lower on repeat testing within the next 2-6 weeks (Wilson and Jones, 1989). It is worth noting that the same study compared the Borg scale with a visual analogue scale, and judged its reproducibility to be superior under these circumstances. In a follow up study designed to assess long term reproducibility of breathlessness ratings during exercise, significant changes in mean scores at matched ventilations were not observed over a 40 week period (Wilson and Jones, 1991). In agreement with the first of these two studies, Belman et al (1991) reported that in a group of nine patients with severe COPD (FEV_1 1.2 l), breathlessness ratings (Borg $scale_{1-10}$) decreased progressively over a series of

four walk tests. This occurred despite stabilization of physiological measurements. Mahler et al (1991) recently reported good correlations for the slope and intercepts of relationships between $Borg_{1\text{-}10}$ ratings for dyspnea and a number of physiological variables during exercise, when tests were repeated one week apart.

Two further studies evaluated reliability of the 17 pt. Borg scale, a predecessor to the 10 point scale used in these studies, which may have similar psychometric properties. Stamford (1976) found a Pearsons r of 0.76 for rating of exertion during cycling exercise, and an r of 0.9 for ratings at the end of exercise. Arstila et al (1974) found a Pearsons r of 0.9 for perceived exertion at the same heart rate during paired exercise tests. Similarly, Silverman et al (1988) found that sensory ratings of breathing effort during exercise in patients with chronic obstructive pulmonary disease were as reproducible as physical measurements at the same work rates. These studies suggest adequate reliability of the Borg scale ratings for the purpose of these studies.

An index of symptomatic handicap due to breathlessness and leg effort was obtained by determining the intensity of each sensation experienced at 50% of predicted reference exercise capacity, for normal subjects, during the incremental exercise test. When necessary, linear interpolation between 100 kpm increments was performed to obtain this value. Symptom ratings were rounded to the nearest 0.5 Borg units.

2.3 Statistical Analysis

Two computer statistical packages were used to describe and analyze the data (Statpro Version 2.0, Penton Software Inc., 420 Lexington Ave, New york, N.Y. and Minitab Release 7.1, Minitab Inc., 3081 Enterprise Dr., State College, PA 16801). The guidelines for statistical reporting in articles for medical journals, as proposed by Bailar and Mostellar (1988) were followed.

Parametric descriptive analysis has been reported with calculation of the mean, standard deviation (SD) or standard error of the mean (SEM). Non parametric descriptive analysis is reported with calculation of the median, interquartile (Q_1, Q_3), maximum and minimum values.

Comparisons between groups were performed using two tailed unpaired t tests, unless otherwise stated. In addition to hypothesis testing, 95% confidence intervals (both for estimates of the mean and for individual values around the mean) are also reported (Gardner and Altman, 1986), particularly for estimates from single and multiple regression analysis.

Single, multiple and stepwise regression analyses (least squares) were used to assess relationships between variables (Kleinbaum et al, 1988). The regression residuals were examined using the Minitab program to check that the assumptions of randomness, independence, normality, homoscedasticity and linearity, which are a prerequisite of least squares regression analysis, were not unreasonably violated.

Probability of falsely rejecting the null hypothesis, the significance level (p value), are presented in the text, rather than categorizing these values in broad bands. In most cases these probabilities have been presented to one significant figure, unless this value is on the boundary of conventional significance levels, when a second figure is included. p values calculated from partial F values have been termed "partial p values". Recording of a p value as less than X (eg. <0.001 or <0.0001) indicates that the probability was less than the limit of the particular statistical calculator used.

The influence of categorical variables (eg. sex, history of asthma, previous spinal fusion) on continuous outcomes was assessed in multiple regression models using "dummy variables" (Kleinbaum et al, 1988). With this technique categories were coded as 0 or 1, depending on absence or presence of the variable. For example, males have been coded as 0, and females as 1, and in regression equations which include sex (see chapter 5) the coefficient attached to sex applies to females (1) and not to males (0).

Frequencies were analyzed using Chi square, Fishers exact test and binomial distribution probabilities (Woolson, 1987).

As not all measurements were available for every subject, the number (n) of data points used in each calculation is cited with each statistic. To avoid introducing bias due to record selection within the completed data set,

relationships have been analyzed using all subjects in whom measurements were available, unless otherwise stated (eg. for specific comparisons).

Chapter 3

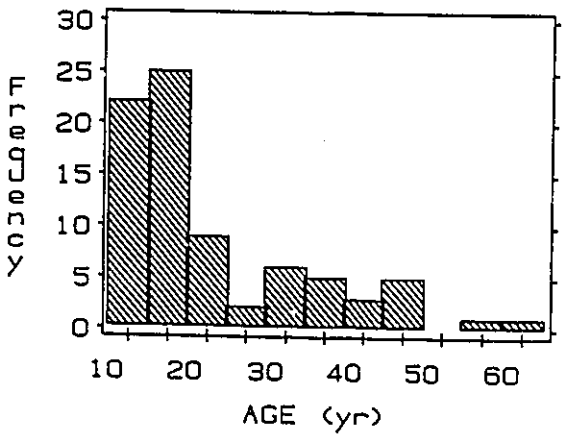
Description of findings

This chapter will first describe the study population, and subsequently the nature and extent of spinal deformity, pulmonary impairment, exercise disability and symptomatic handicap. The relationships between these elements will be analyzed in subsequent chapters.

3.1 Age, sex and anthropometry

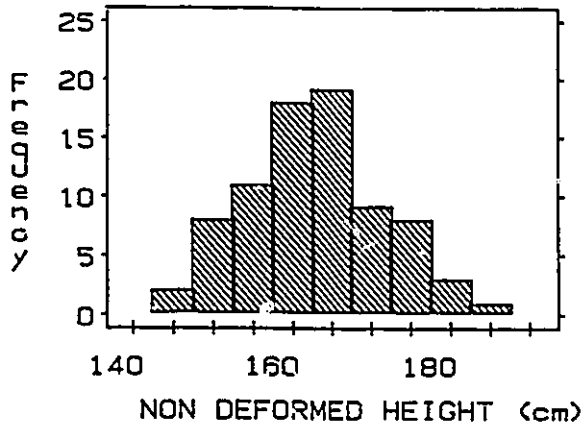
Sex

Male	Female
13	66



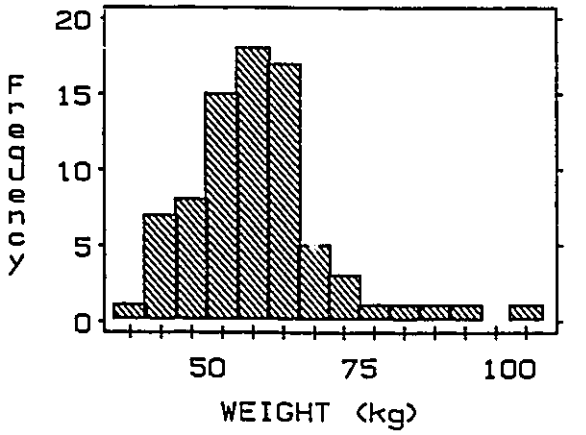
Age (yr)

N	Mean	Median	SD
79	21.4	17.0	10.1
Min	**Max**	**Q1**	**Q3**
11	55	14.0	28.0



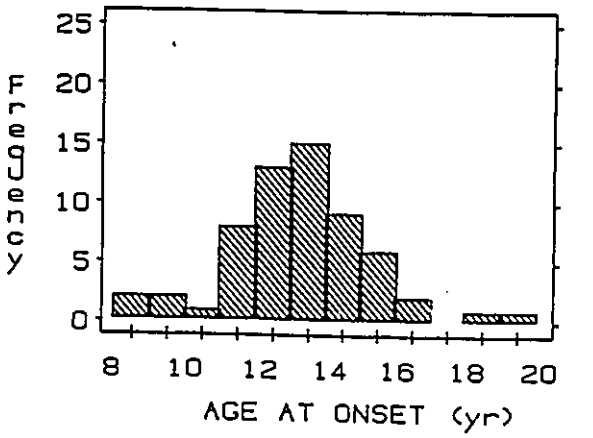
Non-deformed height (cm)

N	Mean	Median	SD
79	165.0	165.0	8.7
Min	**Max**	**Q1**	**Q3**
146.0	186.6	158.2	170.9



Weight (kg)

N	Mean	Median	SD
79	57.7	56.5	11.1
Min	**Max**	**Q1**	**Q3**
38.0	100.0	51.0	62.0



Age first noticed (yr)

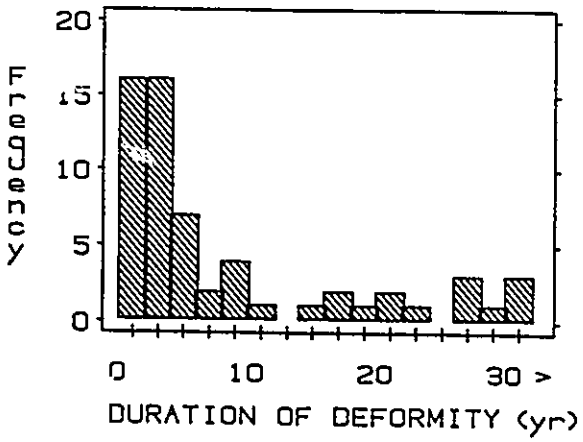
N	Mean	Median	SD
60	12.8	13.0	2.1
Min	**Max**	**Q1**	**Q3**
8	19	12.0	14.0

The 5:1 female to male ratio in these subjects is in keeping with the known predominance of females with idiopathic scoliosis of this severity. Although most subjects were in their teens or twenties (3/4 being 28 yrs or younger), age at the time of being studied was positively skewed with a small number of older cases.

Non-deformed height and weight were compared to normals by plotting these measurements on standard centile charts (Tanner et al, 1966). In the 48 subjects who were 19 years or younger (ages covered by the charts), the median centile for height was 81.5 indicating that, in the absence of deformity, these subjects would have been tall for their age, as has previously been documented (Willner, 1974; Willner, 1975a; Willner, 1975b; Burwell et al, 1977; Buric and Momcilovic, 1982; Archer and Dickson, 1985; Nicolopoulos et al, 1985; Normelli et al, 1985). For a 17 yr old girl, the difference between the 80th and 50th centile corresponds to ~5 cm or 3% of their normal height. The median centile for weight in the same subjects was the 70th, suggesting that although they were heavier than average for their age, subjects were lighter than expected for their non-deformed height (~4 kg or 7%). Using centile charts (≤19 yrs) and Metropolitan Life Tables (≥20 yrs) as reference standards, weight for non-deformed height for the whole group of subjects was 96.5 % of predicted (95% CI, 92.8 - 100.3), not significantly different than normal (p=0.07).

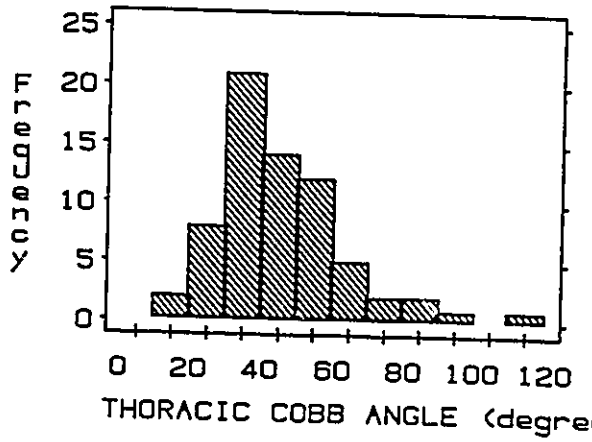
3.2 Spinal deformity

Spinal fusion	Yes	No
	7	72



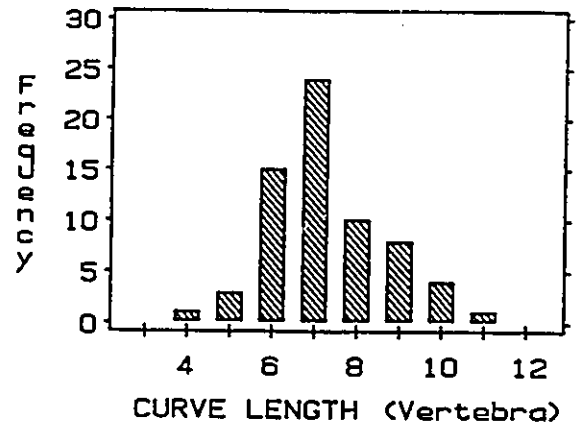
Duration (yr)

N	Mean	Median	SD
60	8.1	3.0	10.6
Min	**Max**	**Q1**	**Q3**
<1	43	1.0	10.0



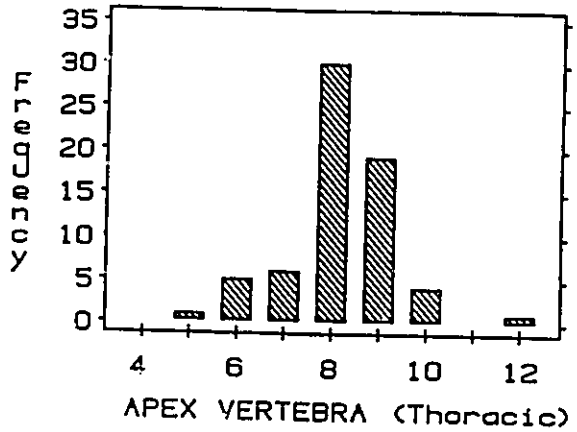
Cobb angle (degree)

N	Mean	Median	SD
68	45.0	41.5	18.4
Min	**Max**	**Q1**	**Q3**
15	118	32.0	55.0



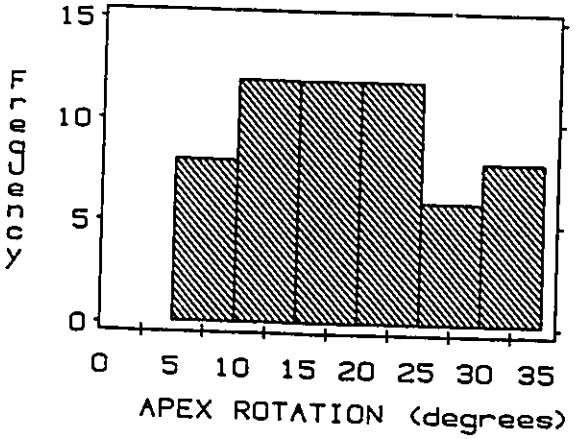
Curve length (number vert.)

N	Mean	Median	SD
66	7.3	7.0	1.4
Min	**Max**	**Q1**	**Q3**
4	11	6	8



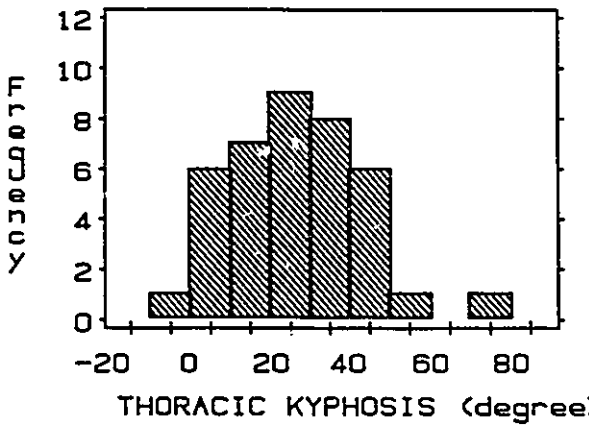
Curve position (Thoracic)

N	Mean	Median	SD
66	8.2	8.0	1.1
Min	**Max**	**Q1**	**Q3**
5	12	8	9



Rotation (degree)

N	Mean	Median	SD
58	16.9	15.0	8.0
Min	**Max**	**Q1**	**Q3**
5.0	30.0	10.0	23.5



Angle of kyphosis (degree)

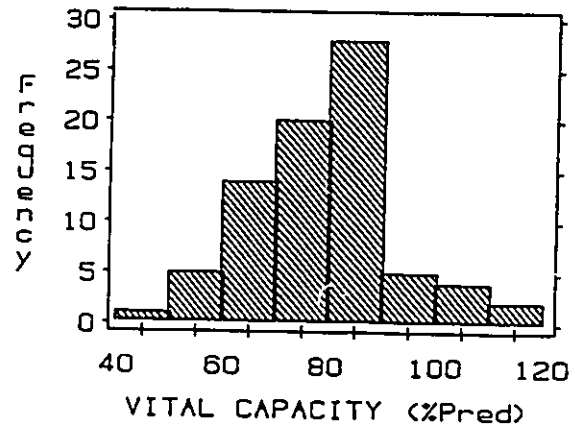
N	Mean	Median	SD
39	25.5	25.0	17.0
Min	Max	Q1	Q3
-5	79	11.0	38.0

The age at which scoliosis was first noticed was normally distributed with a mean of 12.8 yrs. Given the age distribution at the time of being studied, this translated into a short duration of scoliosis for most subjects (median 3 yrs) with a positive skew; 1/4 of subjects had their scoliosis noticed for ≥10 yrs. Seven subjects had spinal fusions, 18 ± 11.9 months prior to being studied.

Cobb angle was < 80 degrees for most curves. All but four curves were convex to the right. More than half of all curves involved 6, 7, or 8 vertebrae. The apex was generally close to or involved the 8th thoracic vertebra; all would have been classified as thoracic except for one, with its apex at T_{12}, which would traditionally have been classified as thoraco-lumbar. Rotation of the apex vertebra was uniformly distributed between 5-30 degrees. On average the angle of kyphosis was normal (Propst-Proctor and Bleck, 1983) but variability was increased with an unusual large number of both hyper and kypokyphotic curves.

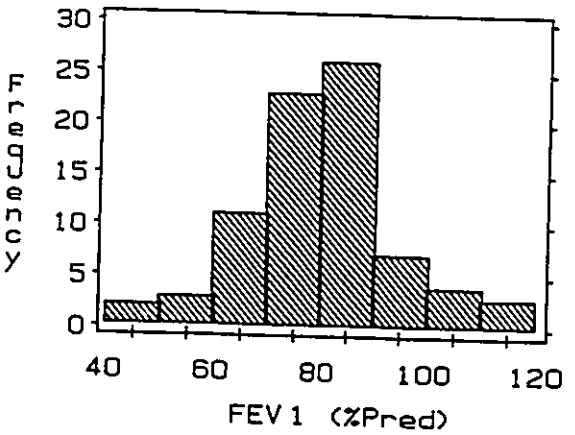
3.3 Pulmonary impairment

3.3.1 Spirometry



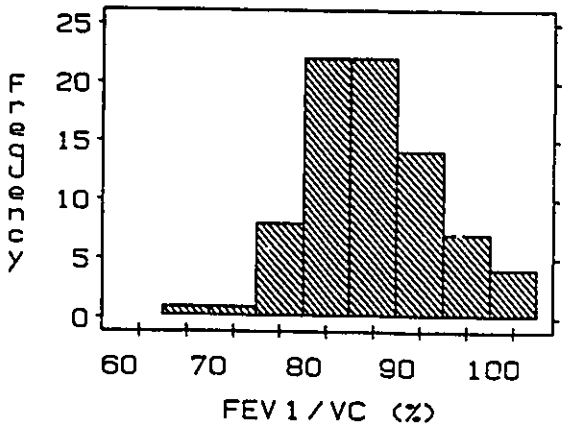
Vital capacity (% predicted)

N	Mean	Median	SD
79	78.8	79.4	13.6
Min	**Max**	**Q1**	**Q3**
46	118	69.5	85.6



FEV_1 (% predicted)

N	Mean	Median	SD
79	79.5	80.4	15.2
Min	**Max**	**Q1**	**Q3**
37	119	71.8	86.8



FEV_1/VC (%)

N	Mean	Median	SD
79	86.9	87.2	6.8
Min	**Max**	**Q1**	**Q3**
67	100	82.4	91.7

	Mean	SD	Min	Q_1	Median	Q_3	Max
VC (l)	3.15	0.74	1.25	2.7	3.10	3.60	5.10
FEV_1 (l)	2.73	0.63	1.09	2.40	2.70	3.10	4.60
TLC (l)	4.20	0.47	2.06	3.56	4.10	4.94	7.37
FRC (l)	2.15	0.66	1.03	1.71	2.14	2.55	4.81
RV (l)	1.04	1.01	0.30	0.74	0.95	1.26	3.14
DLCO (ml/min/mmHg)	24.4	5.4	14.9	21.1	23.5	27.9	37.7
KCO (ml/min/mmHg/l)	5.7	1.1	3.2	5.0	5.6	6.5	9.0
MIP (cm H_2O)	65	24.4	10	50	60	80	140
MEP (cm H_2O)	84	24.6	15	66	80	100	130

Table 3.1 Absolute values for spirometry, lung volumes, diffusing capacity and respiratory muscle strengths in 79 scoliotic subjects.

Spirometry revealed a mild non obstructive ventilatory defect, the FEV_1 and VC being proportionally reduced, with the FEV_1/VC ratio remaining normal. Maximal expiratory flows were reduced at 92% predicted, but this could be fully accounted for by the reduction in the absolute lung volumes at which the recordings were made (table 3.2). Maximal expiratory flows at 50% of vital capacity were 82% predicted $V_{E\,50}$ but were actually 132% of predicted maximal expiratory flow at the same absolute lung volume (figure 3.1). Due to the

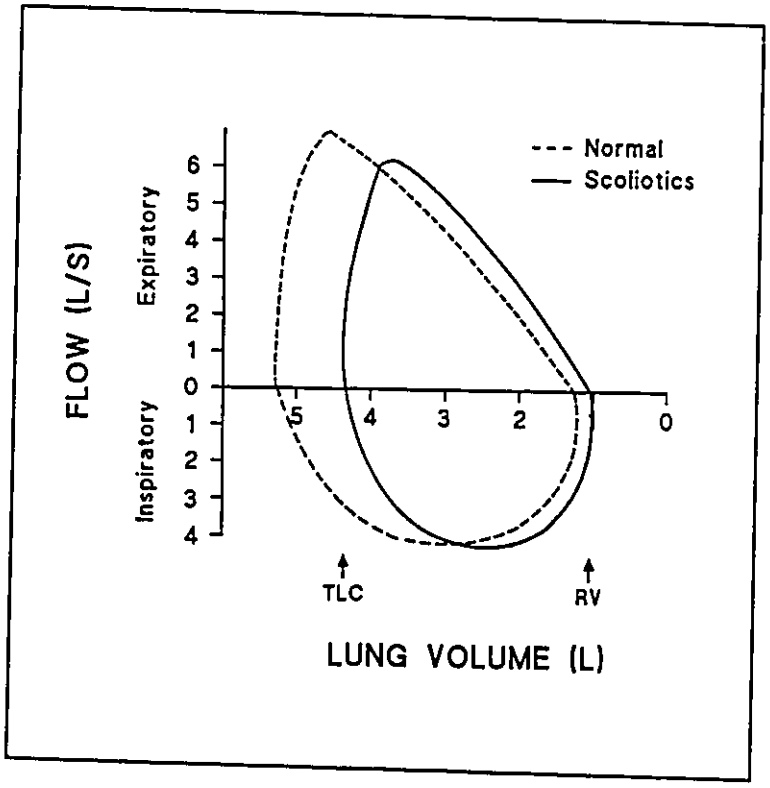


Figure 3.1 **Maximum flow volume loop (averaged) adjusted for absolute lung volume.**

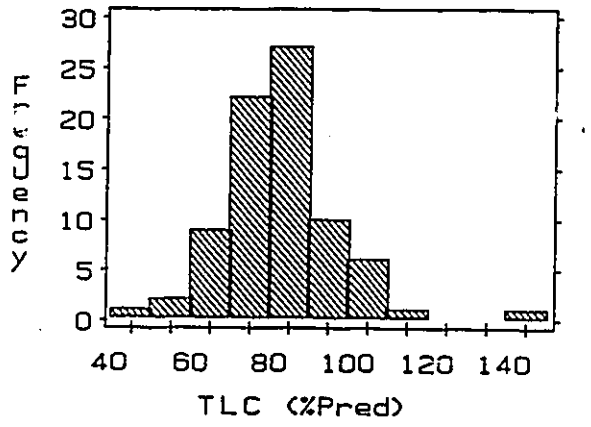
reductions in RV, the volume at which $V_{E\,50}$ was measured corresponded to 76% of normal exhaled VC. Lung volume at mid VC was above predicted TLC in one subject and below predicted RV in another. Maximal inspiratory flows were normal.

	Mean	SD	Min	Q_1	Med	Q_3	Max
$\dot{V}$max (l/sec)	6.2	1.61	3.1	4.9	6.1	7.0	10.8
%$\dot{V}$max	91	17.7	58	80	89	103	135
$\dot{V}max_{50}$ (l/sec)	4.0	1.20	1.2	3.3	3.9	4.8	7.8
%$\dot{V}max_{50}$	82	22.0	28	67	82	98	151
$\dot{V}max_{25}$ (l/sec)	1.9	0.84	0.4	1.3	1.8	2.3	5.3
%$\dot{V}max_{25}$	70	28.3	17	48	67	87	168
$\dot{V}$Imax (l/sec)	4.4	1.41	1.9	3.4	4.3	5.3	8.5
%$\dot{V}$Imax	102	30.5	44	79	98	120	188
$\dot{V}E_{Cap}$ (l/min)	97	22.8	42	82	97	114	145
%$\dot{V}E_{Cap}$	84	15.6	50	73	84	95	119

Table 3.2 Maximum flows and ventilatory capacity.

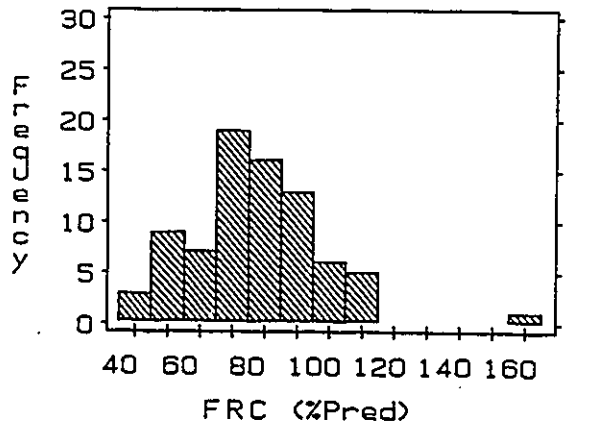
Maximum achievable ventilatory capacity was calculated from each subject's FEV_1 and maximal inspiratory flows (Killian et al, 1992a). Compared to reference values, ventilatory capacity was reduced to 84 ± 15.4% predicted (table 3.2).

3.3.2 Lung volumes



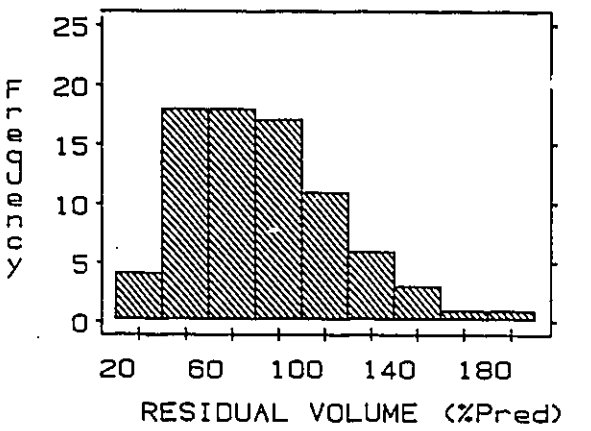
Total lung capacity (% pred.)

N	Mean	Median	SD
79	82.6	81.6	14.0
Min	**Max**	**Q1**	**Q3**
47	143	75.5	89.1



Functional residual capacity (% pred.)

N	Mean	Median	SD
79	81.6	80.5	20.0
Min	**Max**	**Q1**	**Q3**
42	169	70.0	93.8

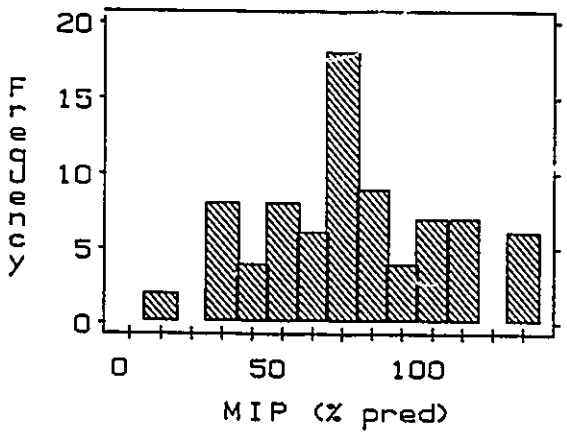


Residual volume (% predicted)

N	Mean	Median	SD
79	83.7	78.9	33.7
Min	**Max**	**Q1**	**Q3**
26	190	58.5	103.0

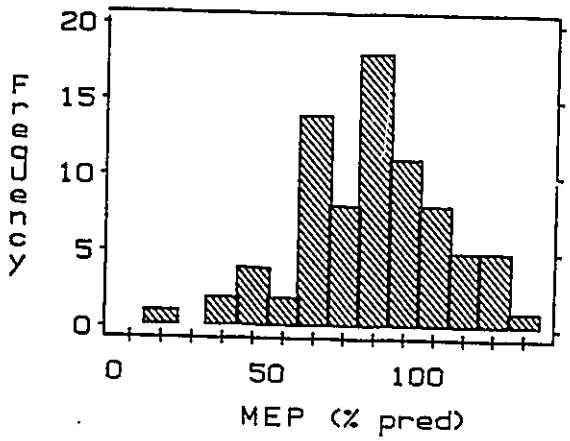
He dilution lung volumes were proportionally reduced to, on average, ~82% predicted. The pattern of lung volume changes was not consistent across subjects, as evidenced by the marked variability in FRC and RV % predicted.

3.3.3 Respiratory muscle strength



Maximum inspiratory pressure (% pred.)

N	Mean	Median	SD
79	78.4	78.9	29.4
Min	**Max**	**Q1**	**Q3**
13	132	56.6	105.3

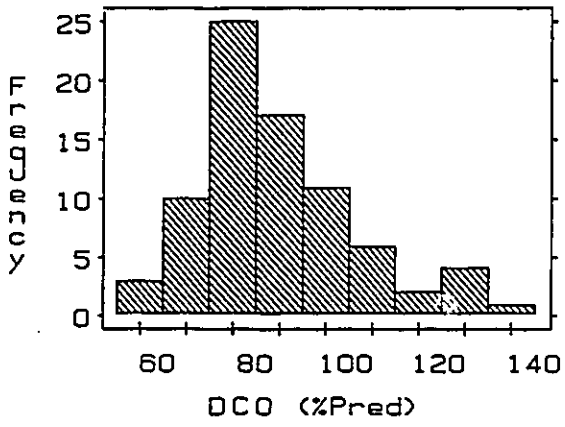


Maximum expiratory pressure (% pred.)

N	Mean	Median	SD
79	83.0	34.2	23.7
Min	**Max**	**Q1**	**Q3**
16	132	68.4	97.7

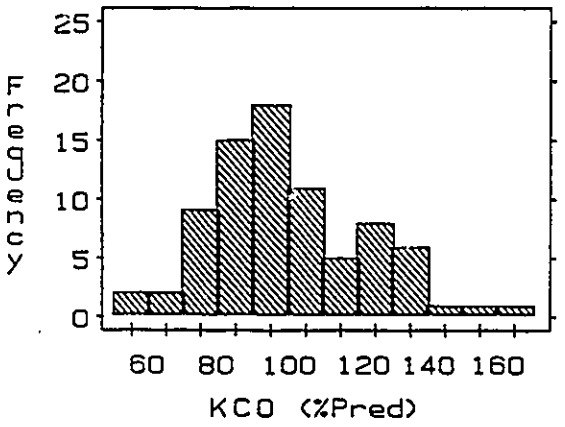
Maximum inspiratory (95% CI, 71.8 - 85.0) and expiratory pressures (95% CI, 77.7 - 88.3) were reduced to a similar extent.

3.3.4 Gas exchange



Diffusing capacity (% pred.)

N	Mean	Median	SD
79	84.4	80.5	17.5
Min	**Max**	**Q1**	**Q3**
50	131	73.0	92.3



KCO (% predicted)

N	Mean	Median	SD
79	100.0	96.4	22.6
Min	**Max**	**Q1**	**Q3**
52	169	84.9	116.0

DL_{CO} was reduced to a similar extent as lung volumes and respiratory muscle strength, but again with wider than expected variability. As the KCO was normal, this reduction could be accounted for on the basis of reduced alveolar volumes during the breath hold manouver. These findings are summarized in figure 3.2.

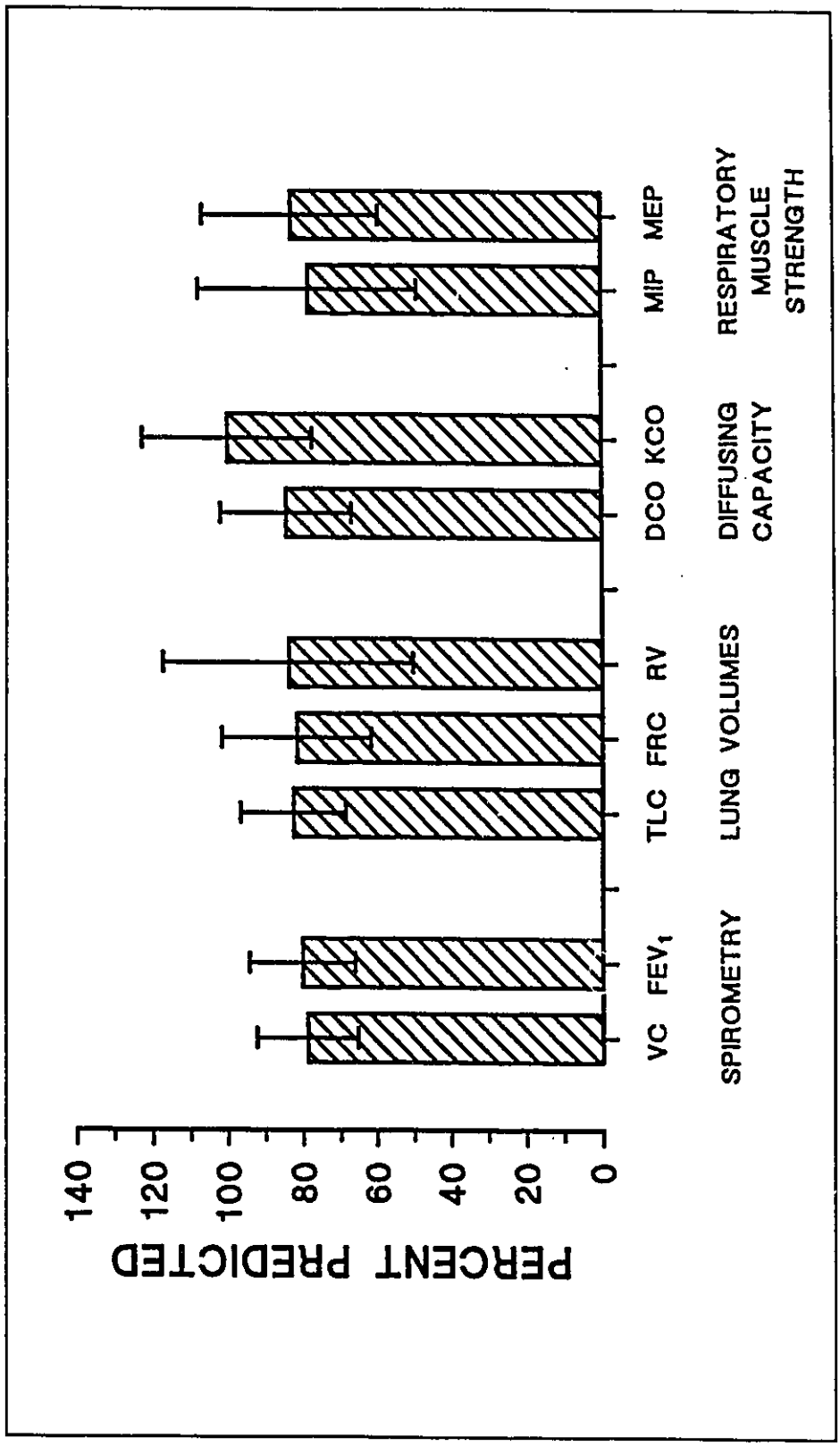
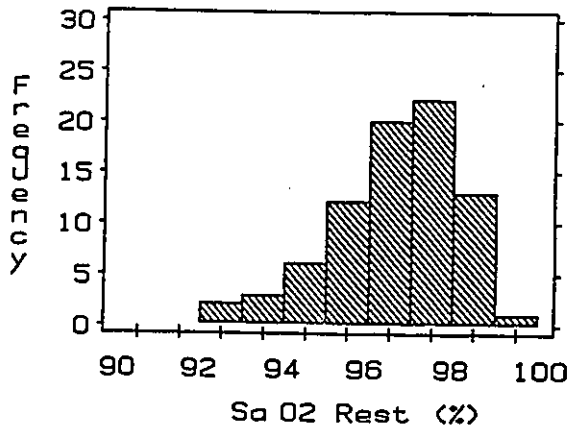
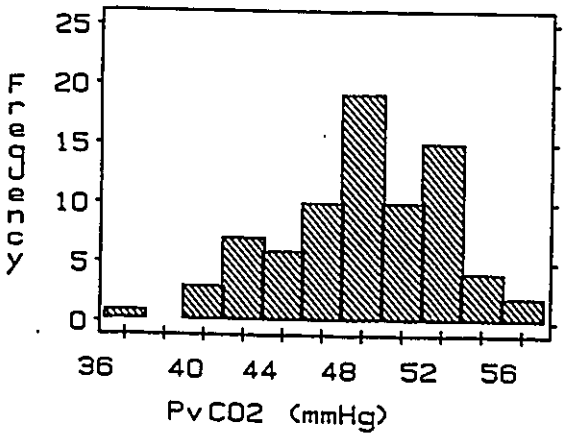


Figure 3.2 Summary of pulmonary function in the 79 subjects. Mean +SD



Arterial O_2 Saturation (%)

N	Mean	Median	SD
79	96.3	96.4	1.4
Min	**Max**	**Q1**	**Q3**
92	99	95.6	97.0

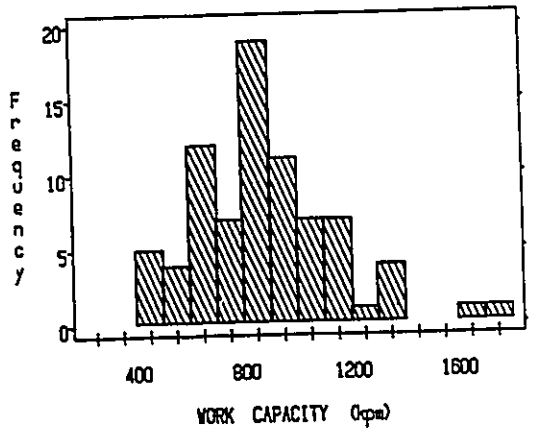


Mixed venous CO_2 (mm Hg)

N	Mean	Median	SD
77	48.4	48	4.0
Min	**Max**	**Q1**	**Q3**
37	57	46	52

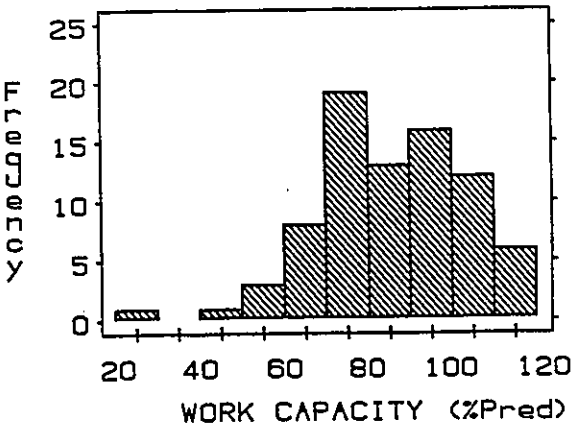
Resting $P\bar{v}CO_2$ and SaO_2 were normal, excluding clinically important abnormalities in gas exchange or alveolar hypoventilation at rest.

3.4 Disability



Work capacity (kpm/min)

N	Mean	Median	SD
79	830	800	260
Min	**Max**	**Q1**	**Q3**
400	1700	600	1000



Work capacity (% predicted)

N	Mean	Median	SD
79	85.8	84.5	17.4
Min	**Max**	**Q1**	**Q3**
26	118	74.7	97.9

Work capacity was significantly reduced (95% CI, 81.9 - 89.7% predicted) with only 18/79 subjects equalling or exceeding their predicted value, calculated from age, sex and non-deformed height.

As previously noted, non-deformed height was above average for age and sex, and this leads to above average predicted work capacities in these subjects.

This in turn inflates the extent of disability. Work capacity as a percent of predicted for subjects of the same sex and age (height being assumed normal) was also reduced ($p = <0.001$) with a mean of 88.4% (95% CI, 87.2 - 91.6%).

3.6 Symptoms during exercise

Symptom intensities were recorded at the end of each minute of exercise, allowing determination of i) an index of handicap for each symptom, and ii) identification of the symptom(s) which limited exercise.

3.6.1 Handicap

Breathlessness and leg effort intensities were determined for each subject at a work rate equal to 50% of their predicted reference work capacity (see figure 3.3).

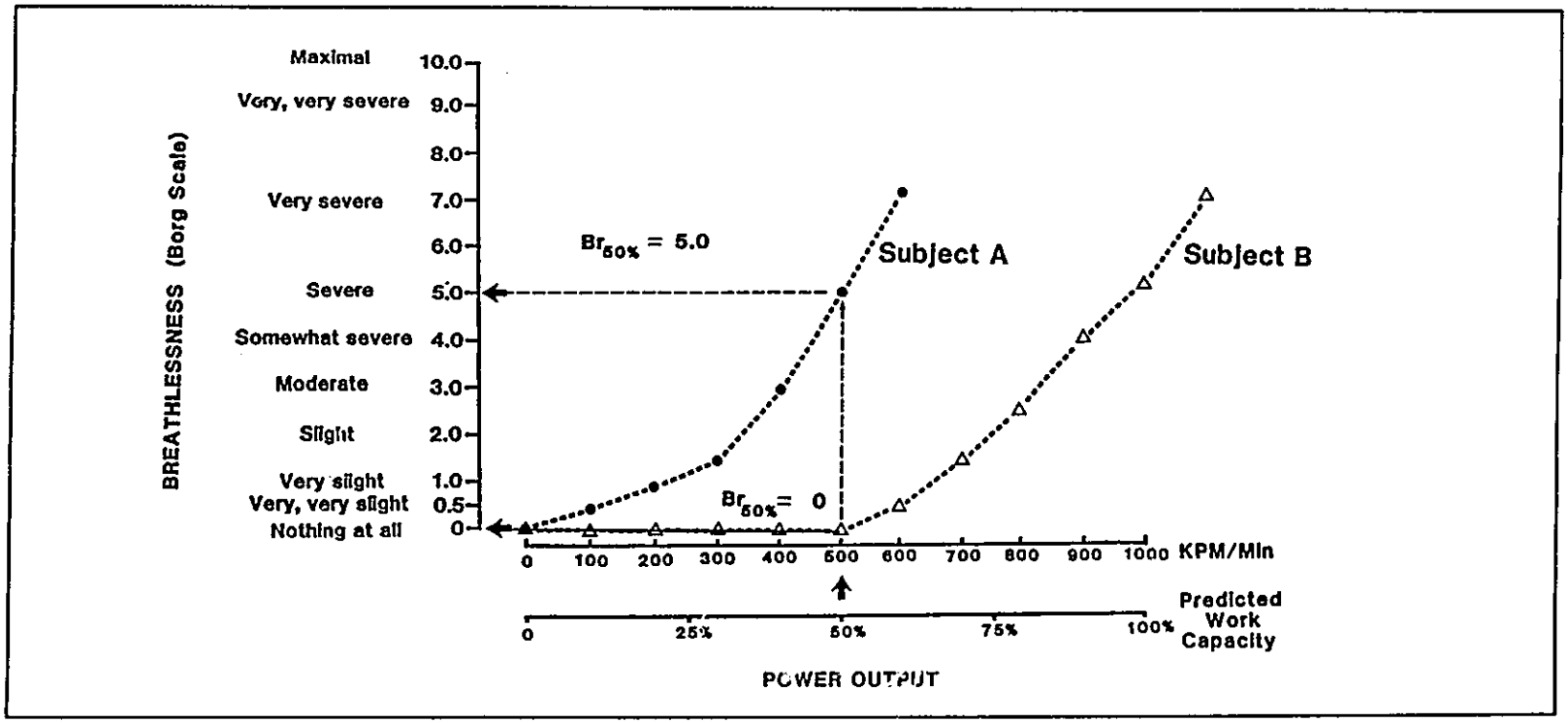
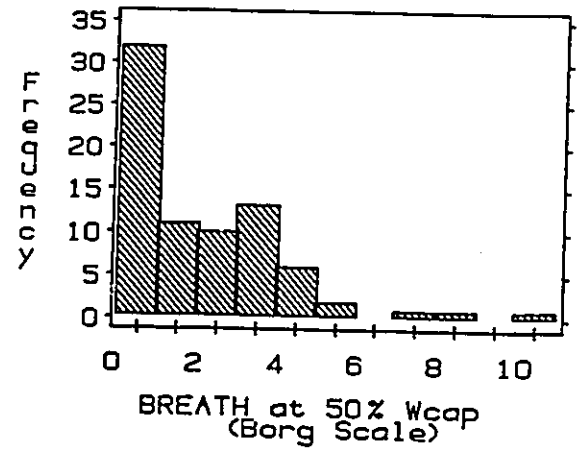


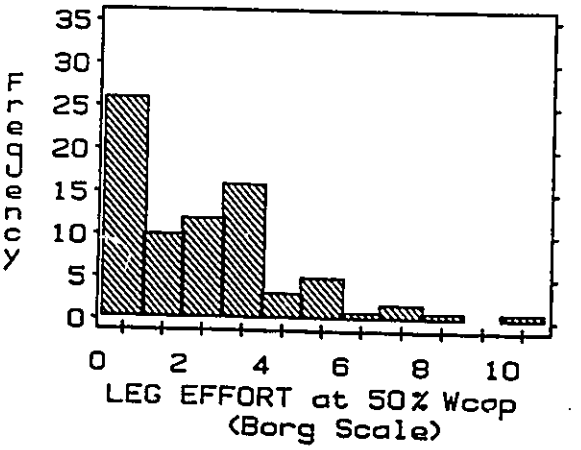
Figure 3.3 Quantification of handicap.

Breathlessness ratings for two hypothetical subjects (same predicted exercise capacity) during incremental exercise. At the index work rate (50 %Wcap) breathlessness ratings for subject A is 5 and for subject B is 0. In this example subject A is disabled with a Wcap of 60 %Wcap and subject B exceeds predicted Wcap (110 %Wcap).



Breathlessness 50 %Wcap

N	Mean	Median	SD
77	1.8	1.5	1.95
Min	Max	Q1	Q3
0.0	10.0	0.5	3.0

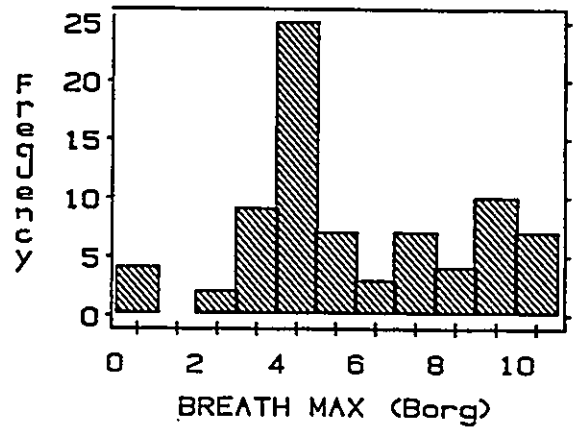


Leg effort 50 %Wcap

N	Mean	Median	SD
77	2.2	2.0	2.06
Min	Max	Q1	Q3
0.0	10.0	0.5	3.0

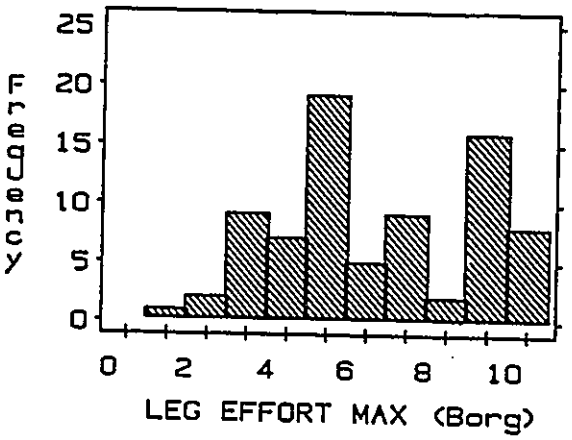
Both symptom intensities were of a similar magnitude, corresponding to "slight" on the Borg scale, although within subject comparisons indicated that leg effort was more severe than breathlessness (paired t, $p=0.0003$). The distribution of these ratings was positively skewed with 13/77 (17%) subjects experiencing discomfort of ≥4 ("somewhat severe") on the Borg scale, for one or both symptoms, even at this relatively low work rate.

3.6.2 Symptom intensities at work capacity



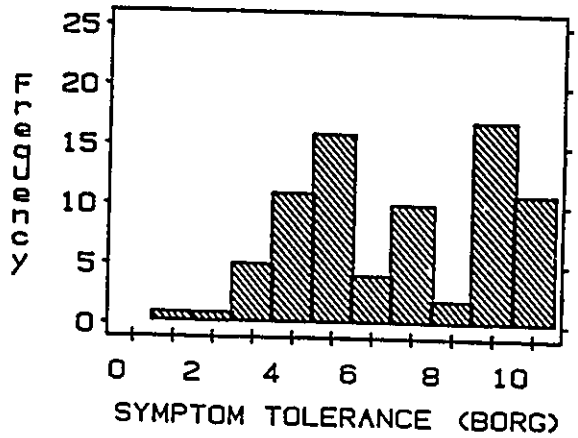
Breathlessness (Borg units)

N	Mean	Median	SD
78	5.5	4.5	2.67
Min	Max	Q1	Q3
0	10	4.0	8.0



Leg effort (Borg units)

N	Mean	Median	SD
78	6.3	6.0	2.43
Min	Max	Q1	Q3
1.0	10.0	4.75	9.0



Symptom tolerance (Borg units)

N	Mean	Median	SD
78	6.6	7.0	2.44
Min	Max	Q1	Q3
1.0	10.0	5.0	9.0

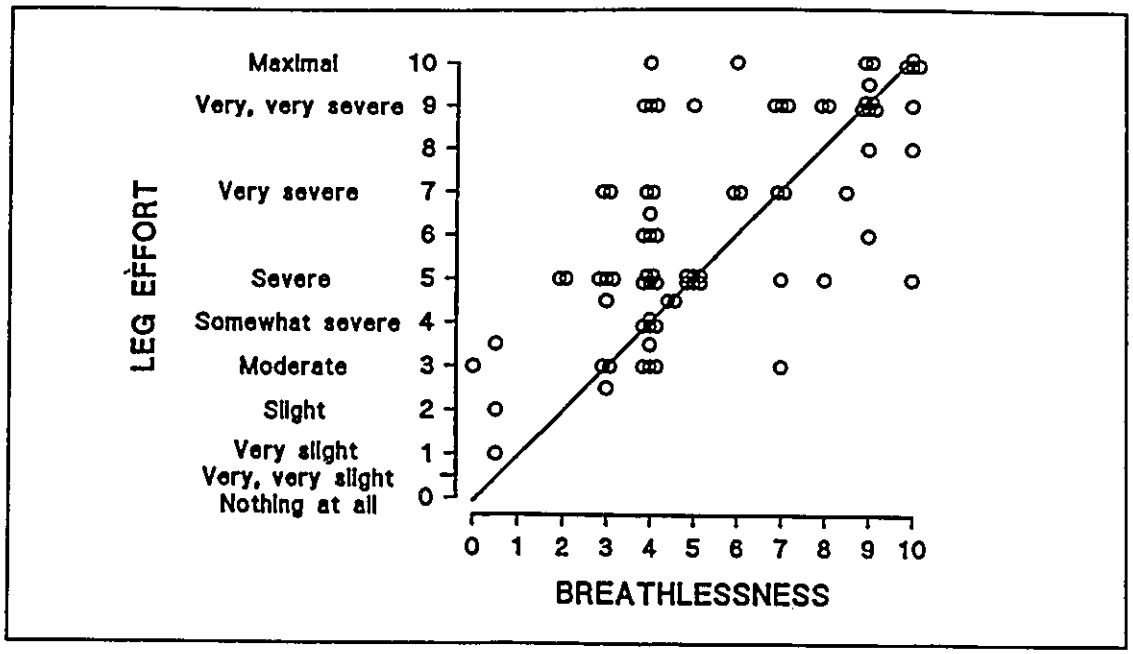


Figure 3.4 Leg effort and breathlessness ratings at Wcap.

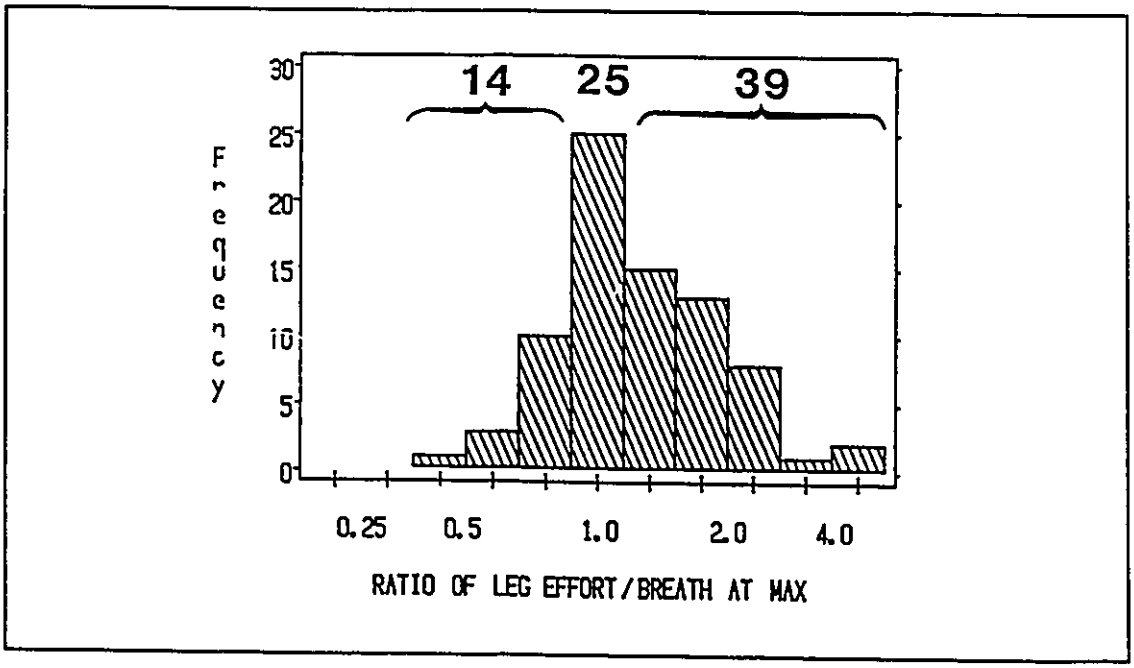


Figure 3.5 Relative magnitude of Leg effort : Breathlessness at Wcap.

At the end of each subject's incremental exercise test, ratings for intensity of breathlessness and leg effort were of a similar magnitude, although higher for leg effort on within subject comparison ($p=0.0005$). The maximum symptom intensity experienced, termed symptom tolerance, corresponded to "very severe". Symptom tolerance was the same as for normal subjects (Killian et al, 1992b).

The relative intensity of breathlessness and leg effort at work capacity is shown below (figures 3.4 and 3.5).

37/78 (50%) of subjects identified leg effort as the limiting symptom. 25/78 (32%) complained of an equal intensity of both sensations, while only 14/78 (18%) were limited predominantly by breathlessness. The proportion of subjects falling into these three symptom categories was no different than for the reference population reported by Killian et al (1992b), who used the same exercise and symptom recording protocol ($Chi^2=4$, $p=0.14$). Using different protocols, earlier studies have also reported that peripheral muscle symptoms usually dominate when normal subjects perform at high power outputs (Strandell, 1964; Slonim et al, 1957; Astrand, 1958; Bruce, 1984b).

In figure 3.6, symptom intensities experienced by these scoliotic subjects at i) 50 %Wcap, and at ii) Wcap, have been compared to normal subjects at the same relative work rates. This figure also shows the proportion of subjects at each of these work rates whose ratings exceeded the 95th centile.

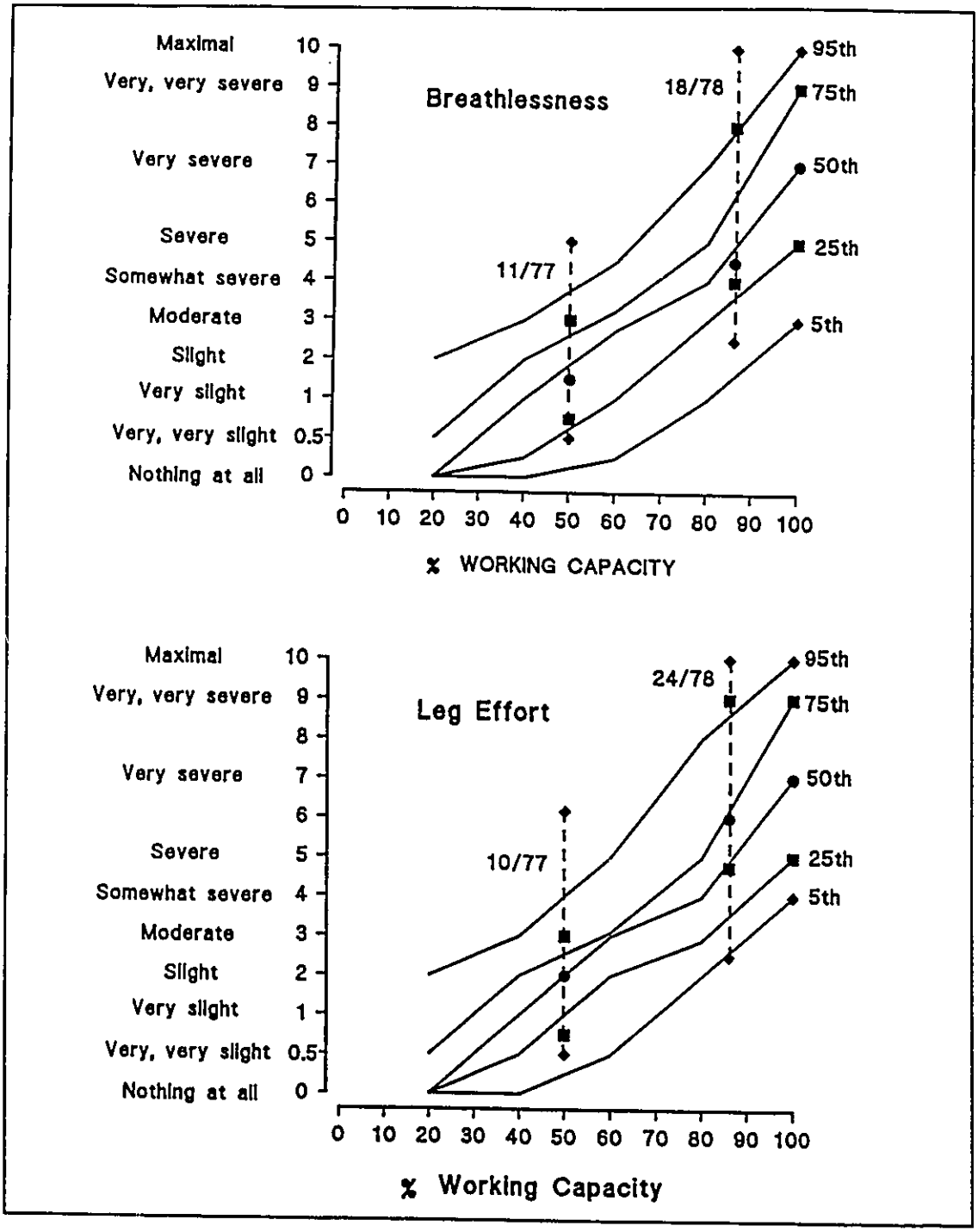


Figure 3.6 Normal ratings for breathlessness and leg effort during incremental exercise, with superimposed ratings for the scoliotic subjects at 50 %Wcap and at Wcap.

Although median ratings for the scoliotic subjects at the two work rates (50% predicted and, on average, 86% predicted) are similar to the normal population, an excessive number experienced discomfort above the upper 95% CI at both work rates (breathlessness, $p = 0.0004$ & <0.0001; leg effort, $p = 0.0015$ & <0.0001 at 50 %Wcap and Wcap respectively) indicating the presence of handicap. For this analysis, two subjects who were unable to achieve a work capacity corresponding to 50 %Wcap were arbitrarily rated as 10 for both symptoms.

Chapter 4

Pulmonary impairment: Analysis of contributors

This portion of the thesis will try to identify factors which contribute to pulmonary impairment in scoliotic subjects. VC, expressed as percent of predicted (%VC) is the primary measure of pulmonary impairment against which the influence of such factors will be analyzed. VC as been chosen because i) it has traditionally been the measure of pulmonary impairment examined in these subjects, facilitating comparison with earlier studies and ii) in the absence of airflow obstruction, as has been shown for these subjects, it is likely to be physiologically as informative as the FEV_1 or any other single measurement of pulmonary function. Directly measured VC (l) and other measures of pulmonary impairment will also be examined to clarify and confirm the findings of this primary analysis.

4.1 Spinal deformity and pulmonary impairment

4.1.1 Single features of spinal deformity and pulmonary impairment

The relationship of %VC to each of the five measured features of spinal deformity is shown in figures 4.1-4.5 with their associated linear regression equations.

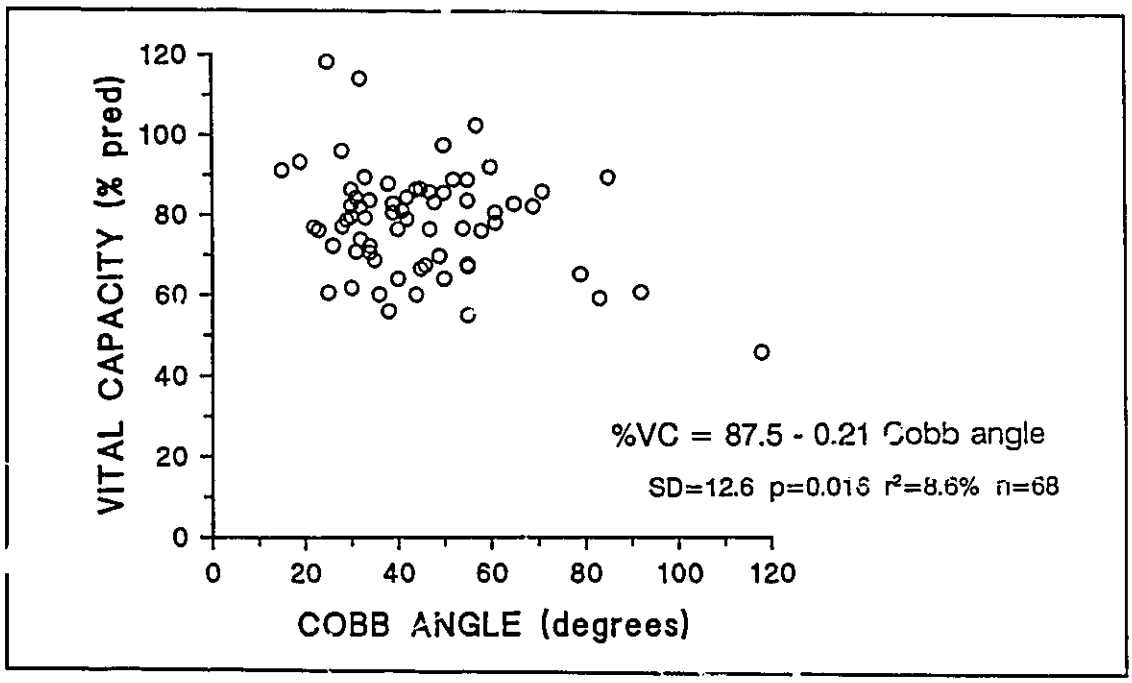


Figure 4.1 %VC as a function of angle of scoliosis.

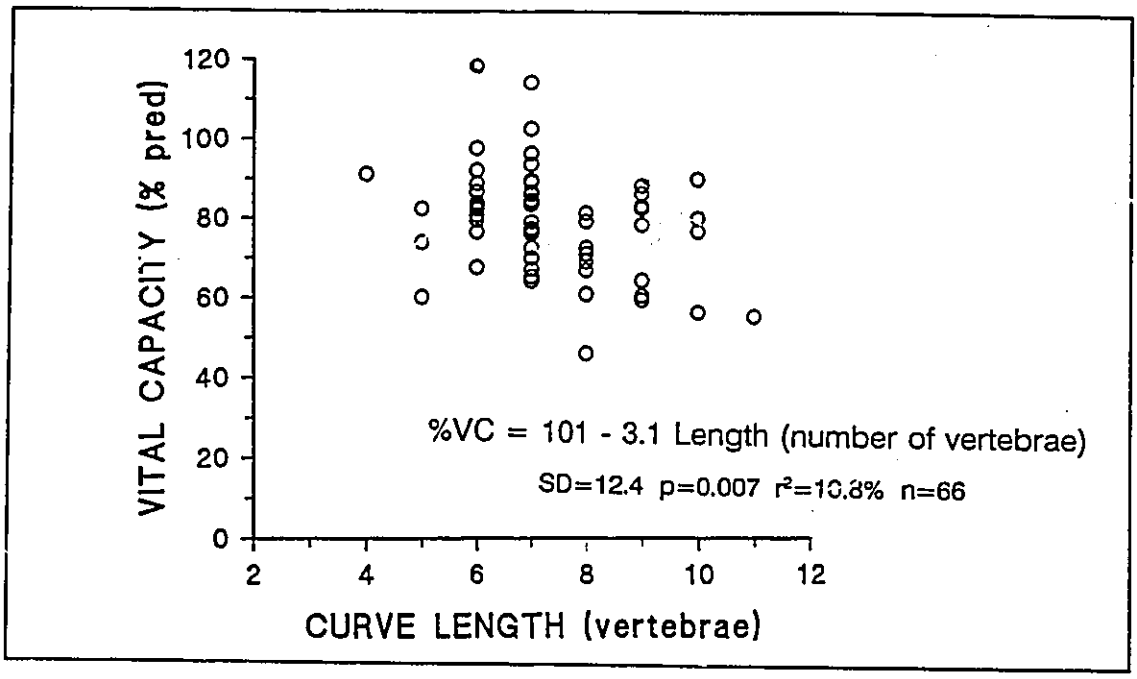


Figure 4.2 %VC as a function of curve length.

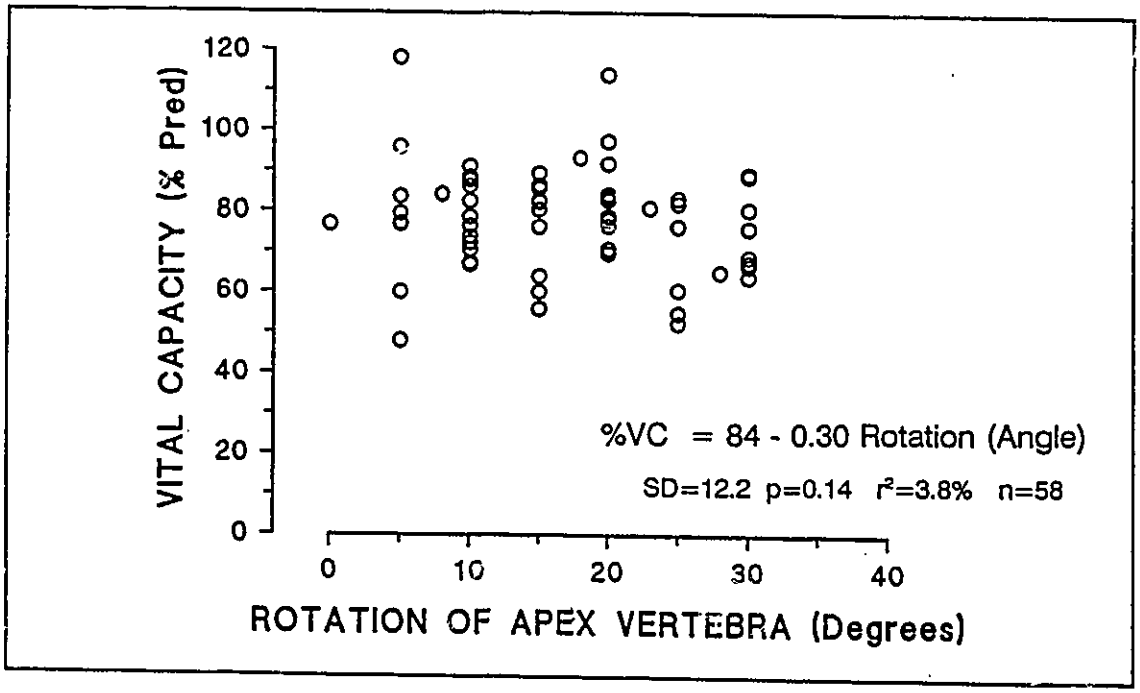


Figure 4.3 %VC as a function of spinal rotation.

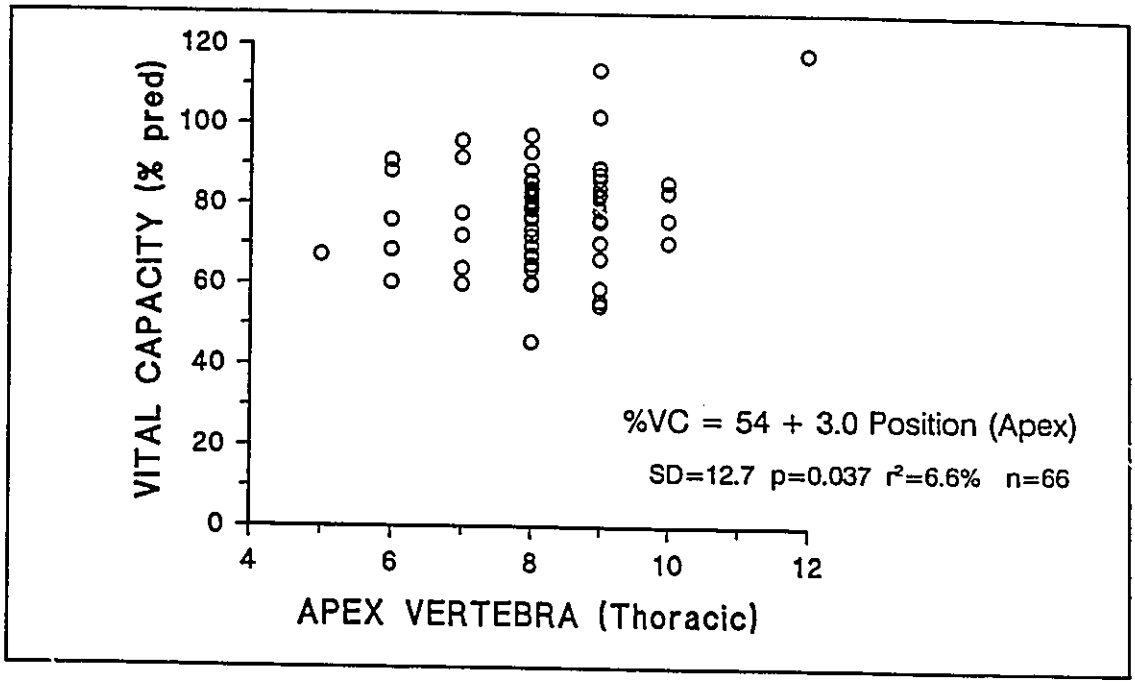


Figure 4.4 %VC as a function of curve position.

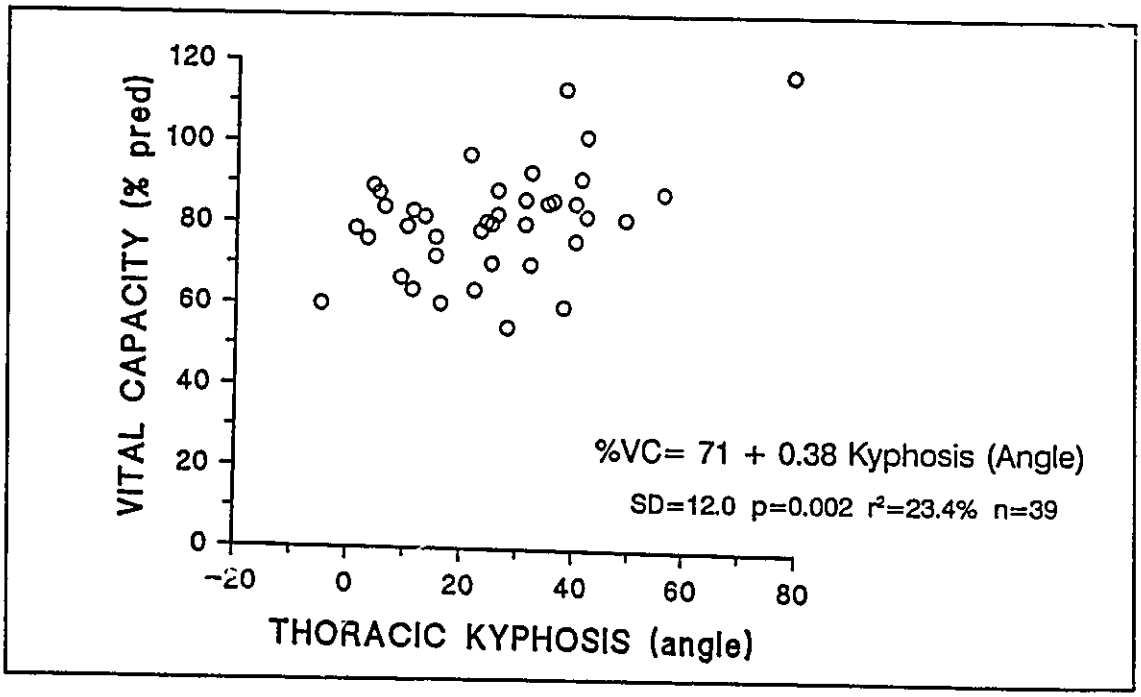


Figure 4.5 %VC as a function of the angle of kyphosis.

Statistically significant reductions in %VC were associated with increasing angle of scoliosis, longer curves, curves positioned higher in the thoracic spine and with reductions in kyphosis. Spinal rotation, as assessed using Bunnell's method, was not associated with pulmonary impairment.

4.1.2 Combined features of spinal deformity and pulmonary impairment

Radiological assessment of spinal deformity is routinely made from a frontal film, with or without a lateral film to assess kyphosis/lordosis. Assessment of the combined influence of features of deformity on pulmonary impairment was first performed using measurements from the frontal film alone, and subsequently the additional influence of kyphosis/lordosis was determined.

4.1.2.1 Frontal film: Combined influence of cobb angle, curve length, position and rotation on pulmonary impairment

Using multiple regression analysis, Cobb angle, curve length and higher curve position were found to independently contribute to pulmonary impairment in the following manner:

%VC = 82 - 0.21 Cobb - 3.2 Length + 3.5 Position			
partial p	0.007	0.003	0.006
SD=11.3	r^2=28.7%	p <0.001	n=66

As with the analysis of individual contributors, rotation of the apex vertebra was unrelated to impairment even in combination with other features of deformity (partial p= 0.4, n=58).

4.1.2.1 Frontal and lateral film: Additional contribution of kyphosis/lordosis to pulmonary impairment

Lateral films suitable for evaluation of sagittal plane deformity were available in 34 subjects. In addition to the features of deformity outlined above, loss of thoracic kyphosis (hypokyphosis) further contributed to pulmonary impairment:

%VC = 64 - 0.17 Cobb - 2.2 Length + 4.0 Position + 0.30 Kyphosis

partial p 0.18 0.17 0.04 **0.02**

SD=11.0 r^2=40.1 p=0.001 n=34

In this subset of 34 subjects, addition of kyphosis/lordosis to the analysis resulted in an increase in the explained variance (r^2) from 29 to 40%. It can be seen from this regression relationship that following the introduction of kyphosis angle, Cobb angle, and length of curve are no longer statistically significantly associated with impairment. This is accounted for by collinearity of these factors with loss of kyphosis; in particular, longer curves were associated with hypokyphosis (p=0.006, n=39).

4.1.3 Lumbar curve and pulmonary impairment

The influence of features of the lumbar deformity on pulmonary function was also examined. There was a significant inverse correlation between the angle of lumbar scoliosis and %VC:

%VC = 88 - 0.32 Lumbar Cobb angle

SD=12.4 p=0.003 r^2=12.4% n=67

No other features of the lumbar curve, either singly or in combination with Cobb angle, were significantly linked to pulmonary impairment.

When the influence of the lumbar curve on %VC was examined after first considering the thoracic curve, lumbar Cobb angle was no longer significantly linked to pulmonary impairment:

%VC = 89 - 0.08 Cobb Tx - 0.26 Cobb Lr

partial p 0.5 **0.08**

SD=12.4 r^2=13% p=0.011 n=67

%VC = 97 - 0.06 Cobb Tx - 3.7 Length + 2.4 Position + 0.29 Cobb Lr

partial p 0.56 0.001 0.073 **0.052**

SD=11.0 r^2=33% p <0.001 n=66

%VC = 80- 0.07Cobb Tx- 2.6Length+ 3.5Posn+ 0.29K/L- 0.23 Cobb Lr

partial p 0.64 0.1 0.23 0.02 **0.21**

SD=11.0 r^2=42.9% p=0.002 n=39

4.1.4 Non-structural variables: The influence of additional factors on pulmonary impairment

It might be expected that spinal deformity would incompletely account for pulmonary impairment due to the presence of additional, non structural, factors which may also compromise pulmonary function. Influence of the following factors was tested for, both singly (probabilities given) and in combination with other factors, all of which were unrelated to pulmonary impairment in these subjects; 1) presence of concomitant disease, particularly asthma (p=0.8, n=79); 2) effects of smoking (p=0.68, n=60); 3) duration of scoliosis (p=0.9, n=60) and the subject's age (p=0.2, n=79); and 4) the influence of inspiratory (p=0.9, n=78) and expiratory (p=0.3, n=78) muscle strength. Younger age at onset (first noticed) was weakly associated with severity of impairment (p=0.03), VC decreasing 1.8

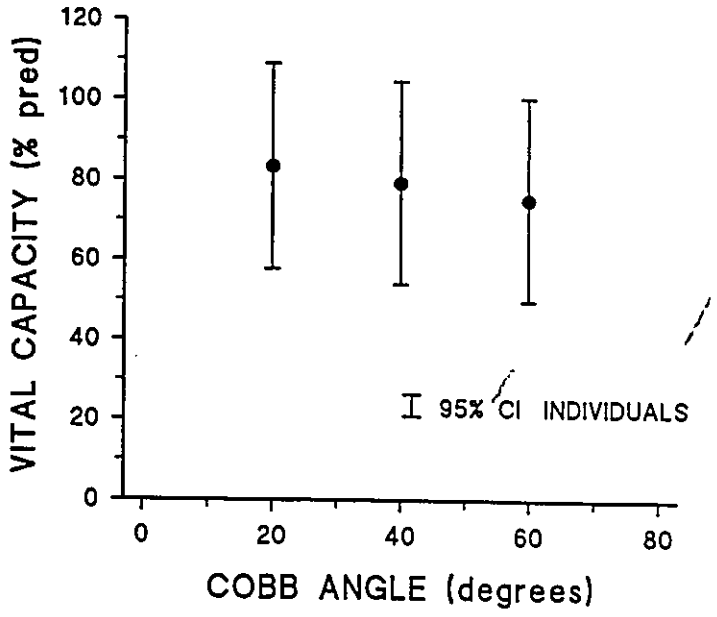
%predicted for each year, but this was no longer significant after features of deformity were controlled for (partial p=1, n=59).

4.2 Discussion

This study found that pulmonary impairment is related to specific features of spinal deformity in idiopathic scoliosis, and that the influence of these factors is additive; no single feature of deformity accounts for impairment to a clinically useful extent. The relationship of Cobb angle to pulmonary impairment was no stronger than that of curve length, position, or angle of kyphosis. In fact, when these features of deformity are considered first, Cobb angle is no longer significantly related to pulmonary impairment. These findings suggest that the relationship between Cobb angle and pulmonary function has been overstated and that assumptions about pulmonary function on the basis of Cobb angle are not justified and may be misleading.

To illustrate the limit of Cobb angle as a predictor for pulmonary impairment, the point estimate and 95% CI for individual predictions are shown for angles of 20, 40, 60 degrees in the following figure (figure 4.6). It is apparent that the 95% CI at any Cobb angle covers a large range of %VC, and that there is near total overlap of the confidence intervals at these angles.

The independent influence of other features of deformity on pulmonary impairment partly explains why Cobb angle is so variably related to pulmonary



Cobb Angle	%VC
20	83.4
40	79.2
60	75.1

Figure 4.6 %VC estimated from Cobb angle alone.

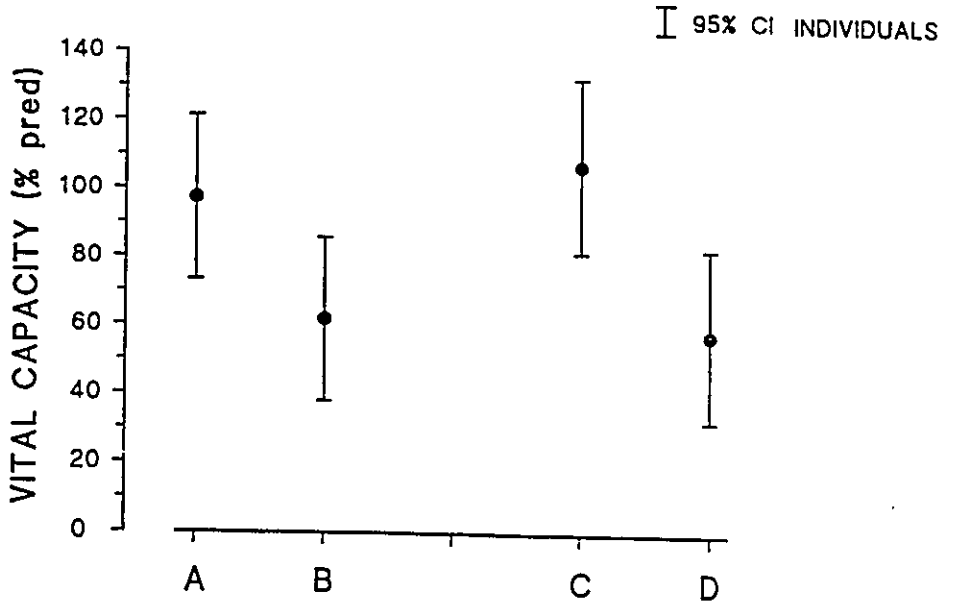
impairment. Curve length and position (evaluated from the same frontal film) yield additional information relating to pulmonary impairment. Position of the curve one vertebra higher in the thoracic spine, involvement of one vertebra more in the curve, or a 15° increase in Cobb angle, each have a roughly equal influence on VC, reducing it approximately 3 %predicted. Their influence on pulmonary

impairment is additive, with close to a 10 %predicted decrease in VC with the combination of these three deformities.

The angle of thoracic kyphosis angle (lateral film) further accounts for observed differences in %VC; an 8° loss of kyphosis is associated with an equivalent reduction in %VC (~3%) as the above increments in deformity. Due to collinearity between kyphosis and other features of deformity, this influence is not fully additive. Figure 4.7 illustrates how combined features of deformity can better account for observed VC.

This figure can be contrasted with figure 4.6. The 95% CI are now narrower and better separated, although they still cover a considerable range. The SD around the estimate is 11 %VC which is now similar to the normal SD around the mean %VC for subjects of the same age, sex, and height (~10%).

The validity of these relationships was further assessed by analyzing the influence of features of deformity on directly measured VC (l) after first introducing age, sex, and non-deformed height into the multiple regression model. Partial p values for the same four features of deformity (but not for rotation) also indicated that these relationships were significant. After the influence of these four features was combined, the SD of the residual was 410 ml, substantially less than the SD around the mean VC alone (742 ml), and similar to the SD around the predicted VC for a given age, sex, and height in normal subjects (males, 644 ml; females,486 ml) (Crapo et al, 1981b).



	Cobb	Length	Position	Kyphosis	VC%
A.	20	5	10	-	97
B.	60	9	6	-	62
C.	20	5	10	60	107
D.	60	9	6	0	57

Figure 4.7 %VC estimated from multiple features of deformity.

Surprisingly, lumbar Cobb angle was associated with pulmonary impairment, in fact it tended to be more closely related to impairment than the thoracic Cobb angle. However, after controlling for differences in features of the thoracic deformity, this relationship was no longer significant, suggesting that it does not contribute directly to impairment but is an epiphenomenon. Lumbar Cobb angle was closely related to the combination of thoracic Cobb angle and

greater curve length ($p < 0.001$, $r^2 = 44\%$). A similar interpretation can be made for the association of younger age at onset with impairment, although in this case age at onset may have influenced the pattern and extent of deformity thereby indirectly contributing to pulmonary impairment.

Assessment of the influence of kyphosis angle on pulmonary impairment needs to be interpreted with some caution. For the reasons previously discussed, this analysis was only performed on a subset of 34 of the 68 subjects who had not previously undergone spinal fusion. All subjects with suitable lateral spinal films were included, but this group may have differed systematically from the rest of the study population eg. assessment re surgery. Cobb angle was the same (45°) for subjects with and without lateral spinal radiographs, suggesting that clinically important differences between these two groups are unlikely.

The best method of radiologically assessing "scoliotic" curves is controversial (previously discussed). The angle of scoliosis and of kyphosis measured from frontal and PA projections is directly influenced by the extent of spinal column rotation (Deacon et al, 1984; Deacon and Dickson, 1985; Dickson, 1987). For example, a lateral view of a spine with a 90° rotation along it's length would yield a kyphosis of 0° regardless of the true kyphosis/lordosis angle. Similarly, a 90° rotation of the scoliotic curve would appear straight on the frontal film. Limitations of the skeletal measurements need to be remembered when

interpreting these results, but as these view are most commonly utilized in clinical practice, they were considered the most appropriate for these analyses.

This study found that non-skeletal factors, other than age at onset, failed to account for between subject differences of pulmonary impairment. This is at variance with the findings of previous authors who have suggested that respiratory muscle strength (Smyth et al, 1984b), age, and duration of deformity (Bergofsky et al, 1959; Caro and DuBois, 1961) influence pulmonary impairment in subjects with scoliosis. These discrepancies can probably be explained on the basis of differences in the populations studied. The age at which scoliosis has its onset is particularly likely to influence impairment when it occurs before thoracic cage growth and alveolar development is completed (Reid, 1968; Davies and Reid, 1971; Thurlbeck, 1975; Reid, 1977; Weich, 1979; Boffa et al, 1984); this study was confined to "adolescents" onset scoliosis. Smoking was not common (15/57) and rarely heavy (mean for smokers, 10/day) or protracted (mean for smokers, 9 yrs). The previously reported relationship between respiratory muscle strength and VC in idiopathic scoliosis was weak and was observed in a population of subjects with only mild curves (Smyth et al, 1984b). This association may reflect the normal relationship between VC and respiratory muscle strength which, our study suggests, may be lost as deformity advances. Previous studies suggest that advancing age compounds pulmonary impairment associated with scoliosis, particularly in the 5th and 6th decades (Bergofsky et al, 1959; Branthwaite, 1986). Our findings indicate that up to the age of 30, age or duration of scoliosis is not

an important contributor to impairment, but as there were few older subjects in this study, the influence of longer durations of scoliosis can not be determined.

This study helps to clarify the findings of previous studies and extends these observations by considering the additive influence of various features of deformity on pulmonary impairment. An association between hypokyphosis or lordosis and pulmonary impairment (Nash and Kevins, 1974; Winter et al, 1975; Aaro and Ohlund, 1984; Branthwaite, 1986) has been confirmed but was opposite to that suggested by Bergofsky et al (1959). In agreement with studies which have reported a relationship between curve pattern and pulmonary impairment (Collis and Ponseti, 1969; Weinstein et al, 1981), but in distinction to others which failed to show a relationship of impairment to curve position (Bergofsky et al, 1959; Mankin et al, 1964; Aaro and Ohlund, 1984), this study found that higher thoracic curves were associated with greater pulmonary impairment. This relationship was weak and for this reason differences between studies are not surprising. Furthermore, in the present study, the association between curve position and pulmonary function is partly accounted for by the inclusion of a curve with apex at T_{12} which would traditionally be considered as thoracolumbar rather than thoracic.

Only one previous study commented on the relationship of scoliotic curve length to pulmonary impairment (Bergofsky et al, 1959), suggesting a lack of association. That study was of a group of 29 patients (only 20 had idiopathic

scoliosis) who had much more advanced disease than is commonly seen now. Failure to find an association between the severity of spinal column rotation and pulmonary impairment is perhaps surprising (Mankin et al, 1964; Aaro and Ohlund, 1984). Whereas vertebral column rotation was assessed from radiographs of the apex vertebra in this study, the two studies which previously showed a relationship between rotation and pulmonary impairment did not assess vertebral column rotation directly. Both of these studies used appraisal of thoracic configuration to assessing rotation, either from CT (Aaro and Ohlund, 1984) or from surface measurements (Mankin et al, 1964), probably accounting for this difference.

Previous studies have not attempted to determine the additive influence of different features of spinal deformity on pulmonary impairment. This study does, and these findings are among the most informative aspects of the analysis. Whereas no single feature of deformity has a clinically useful relationship with pulmonary impairment, taken in combination, a clearer picture emerges of the relationship between anatomical changes and subsequent physiology. Failure to consider features of deformity other than Cobb angle probably explains why some studies have failed to find an association between deformity and pulmonary impairment, and may also account for quantitative differences in the relationship between Cobb angle and pulmonary function which have been reported (table 1.1). Given i) the ease and economy of measuring spirometry, ii) the complexity of the relationship between deformity and pulmonary function, and iii) the lack of precision of this relationship, we do not advocate indirect estimation of pulmonary

function from analysis of spinal deformity. Although this multifactorial analysis helps us to understand the basis of pulmonary impairment in this condition, the severity of impairment can only be quantified satisfactorily through direct measurement.

Chapter 5

Disability: Analysis of contributors

This chapter will try to identify factors responsible for disability in these subjects. As previously discussed, disability has been quantified by expressing each subject's work capacity as a percent of predicted normal work capacity (%Wcap). The analysis will be performed in steps similar to those outlined in

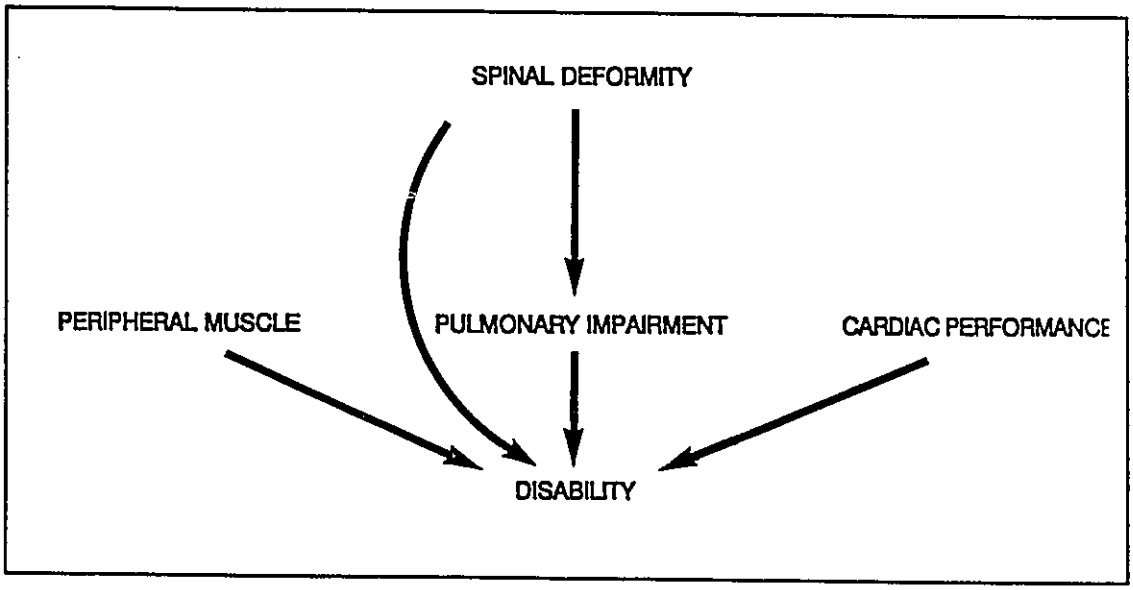


Figure 5.1 Schematic for evaluating disability

figure 5.1. First, the relationship between features of spinal deformity and disability will be determined, and subsequently the relationship of different types of impairment (pulmonary, muscular, cardiac) to work capacity will be explored.

5.1 Deformity and disability

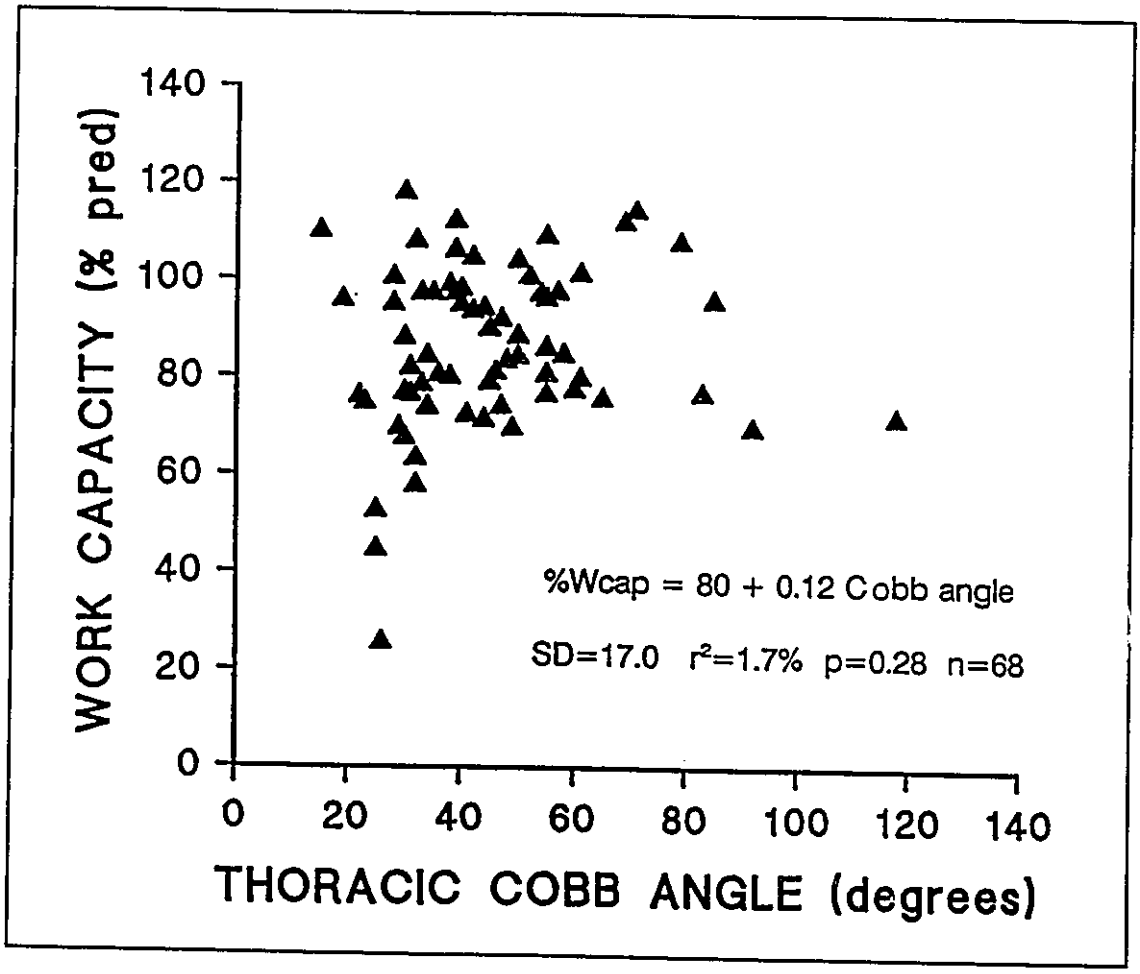


Figure 5.2 Relationship of disability to angle of scoliosis.

Figure 5.2 shows the relationship between angle of scoliosis and %Wcap. Instead of the expected fall of %Wcap with increasing Cobb angle, disability was

unrelated to this feature of deformity. This is emphasized by the wide scatter of work capacities seen in subjects with a Cobb angle of approximately 30°, or alternatively, by considering the marked difference in Cobb angle in subjects with a Wcap of ~75% predicted.

The lack of relationship between thoracic deformity and disability was not confined to Cobb angle; except for curve length, all features of deformity were unrelated to working capacity (**Thoracic curve:** position, p=1.0; rotation, p=0.1; kyphosis, p=0.8; **Lumbar curve**: Cobb angle, p=0.6). The relationship of curve length to %Wcap barely statistically significant (p=0.03), only accounted for 7% of the variability in %Wcap, and in the absence of a consistent relationship with disability in combinations with other features of deformity (see below), was considered clinically unimportant or a chance association.

Given that individual features of deformity were only weakly related to pulmonary impairment, failure to find a convincing relationship between single features of deformity and Wcap may not be that surprising. We might expect that when features of deformity were considered in combination, a relationship between disability and spinal deformity would emerge. This did not occur. Multiple regression analysis failed to identify a significant relationship between combined features of deformity and disability.

To ensure that a true relationship between work capacity and deformity was not missed due to an obscuring effect of expressing work capacity as % predicted,

the analysis was also carried out with directly measured Wcap (kpm/min) as the dependent variable, with age, sex, and non-deformed height being forced into the multiple regression model before features of deformity. Again, no relationship between disability and deformity was evident (**Thoracic curve:** length, partial p=0.07; position, partial p=0.6; rotation, partial p=0.2; kyphosis, partial p=0.8; **Lumbar curve**: Cobb angle, partial p=0.4).

5.2 Disability and pulmonary impairment

5.2.1 Disability and vital capacity

Figure 5.2 shows the relationship between work capacity and pulmonary impairment, when VC is the index of pulmonary impairment and both variables are expressed as % predicted. Despite substantial reductions in both variables, disability was unrelated to pulmonary impairment in this analysis. This finding is contrary to expectation and is at variance with current understanding of the pathophysiology of idiopathic scoliosis. Two possible explanations for this lack of relationship were considered.

Firstly, disability may indeed be due to pulmonary impairment but VC may inadequately characterize pulmonary impairment to reveal this relationship; other assessments of pulmonary impairments such as TLC or DL_{CO} may be more appropriate. Furthermore, whereas single features of pulmonary impairment may

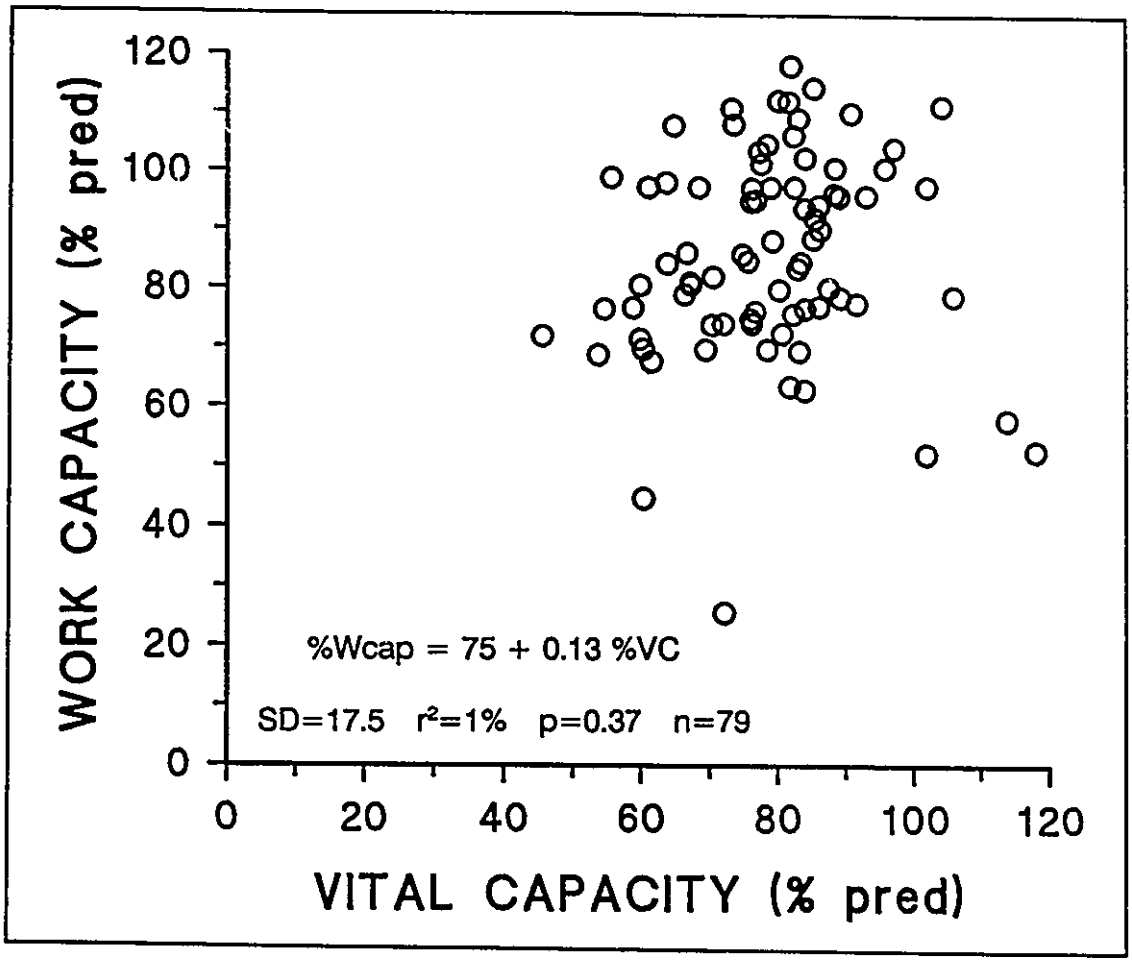


Figure 5.3 Relationship of disability to %VC

not be significantly related to Wcap, perhaps combinations of features, for example reflecting mechanical and gas exchange properties of the respiratory system, would be more closely related to disability.

Secondly, work capacity in persons with idiopathic scoliosis may in fact be unrelated to the extent of pulmonary impairment. This explanation is supported by the finding that most subjects identified muscle discomfort (leg effort) as the

symptom which curtailed their work capacity, rather than breathlessness. Each of these options will be considered in turn.

5.2.2 Disability and features of pulmonary impairment other than VC.

There were no statistically significant relationships between %Wcap and $\%FEV_1$ ($p=0.4$), %TLC ($p=0.9$), %FRC ($p=0.3$), %RV ($p=0.3$), or $\%DL_{CO}$ ($p=0.3$). %MIP was weakly related ($p=0.047$). This indicates that failure to find a relationship between pulmonary impairment and disability is not merely a reflection of the inability of VC to adequately reflect pulmonary function. Work capacity was also regressed against each of these variables directly, after first controlling for differences in age, sex and non-deformed height. Again, no significant relationships were found with single variables (VC, partial $p=0.4$; FEV_1, partial $p=0.07$; TLC, partial $p=0.2$; FRC, partial $p=0.7$; RV, partial $p=0.3$; DLCO, partial $p=0.3$; MIP, partial $p=0.06$).

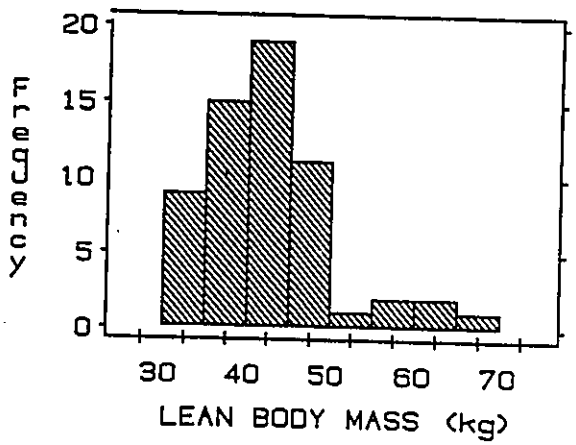
5.2.3 Disability and combined features of pulmonary impairment

Even when features of pulmonary impairment were considered in combination, no convincing relationship to Wcap could be identified. This was also true when the relationship was analyzed using directly measured Wcap (kpm/min), after first controlling for differences in age, sex and height.

5.3 Disability and peripheral muscle impairment

Prominence of leg muscle symptoms during incremental exercise (figures 3.4 & 3.5) focused attention on the role of the peripheral muscles as contributors to disability. In an attempt to quantify this contribution, the relationship of Wcap to lean body mass, leg muscle volume, quadriceps and handgrip strength was evaluated. Unlike pulmonary function, there are no widely accepted reference values for these muscular measurements. This precluded expressing values in the standardized form of % predicted for age, sex, and height. For this reason, inter-relationships have been analyzed using the directly measured units, with or without first controlling for differences of age, sex, and height, in the regression model. Before examining these relationships, the values obtained will be described.

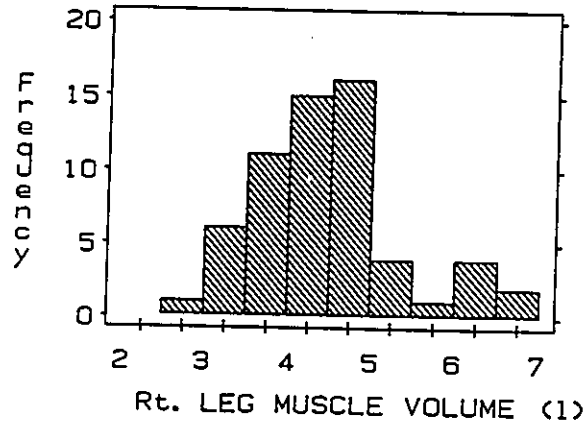
5.3.1 Muscle structure and function: Description of values



Lean body mass (kg)

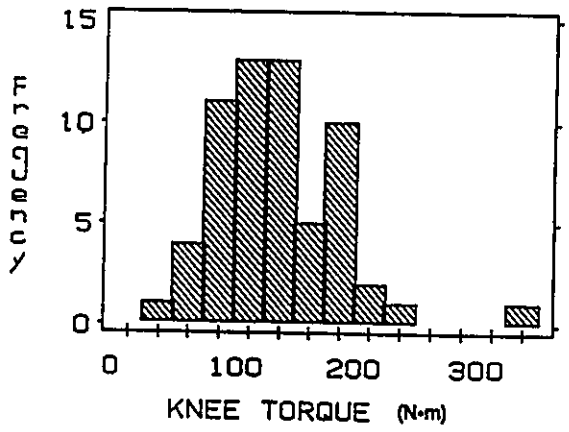
N	Mean	Median	SD
60	42.5	41.7	7.91

Min	Max	Q1	Q3
31.7	69.6	37.0	45.7



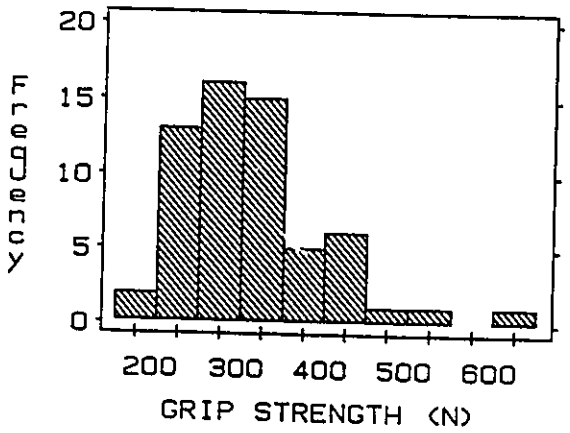
Leg muscle volume (l)

N	Mean	Median	SD
60	4.46	4.30	0.85
Min	**Max**	**Q1**	**Q3**
2.96	6.78	3.90	4.82



Knee extensor torque (N•m)

N	Mean	Median	SD
61	132.0	125.1	49.81
Min	**Max**	**Q1**	**Q3**
41	327	99.2	161.0



Grip strength (N)

N	Mean	Median	SD
61	315	298	93.3
Min	**Max**	**Q1**	**Q3**
165	654	251	346

5.3.2 Disability and the peripheral muscles: Analysis

The relationship of Wcap (kpm) to each of these muscular variables is shown in figures 5.4 - 5.7. The direct relationship of VC (l) to Wcap is also shown for comparative purposes (figure 5.8). As standardization for age, sex, and non-deformed height has not yet been performed, it is not surprising that each variable, including VC, is significantly related to work capacity. The relative strengths of these relationships can be assessed by comparing the r^2 value (proportion of the variance in work capacity accounted for) and the narrowness of the SD of the regression residuals associated with each equation.

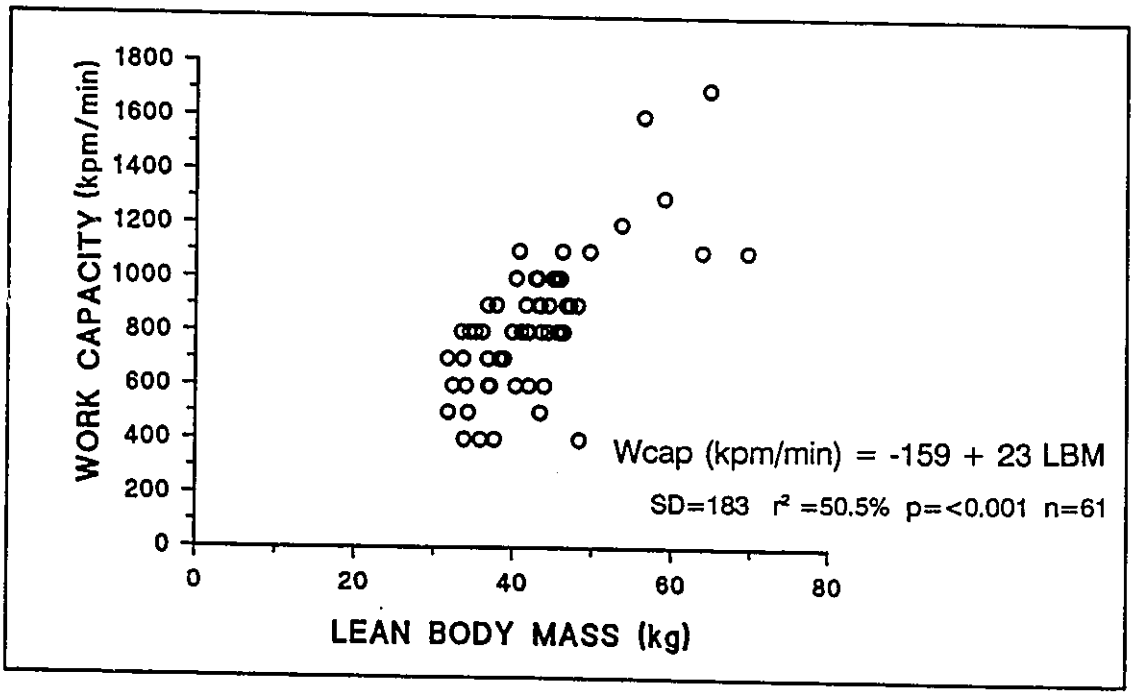


Figure 5.4 Relationship of work capacity to lean body mass

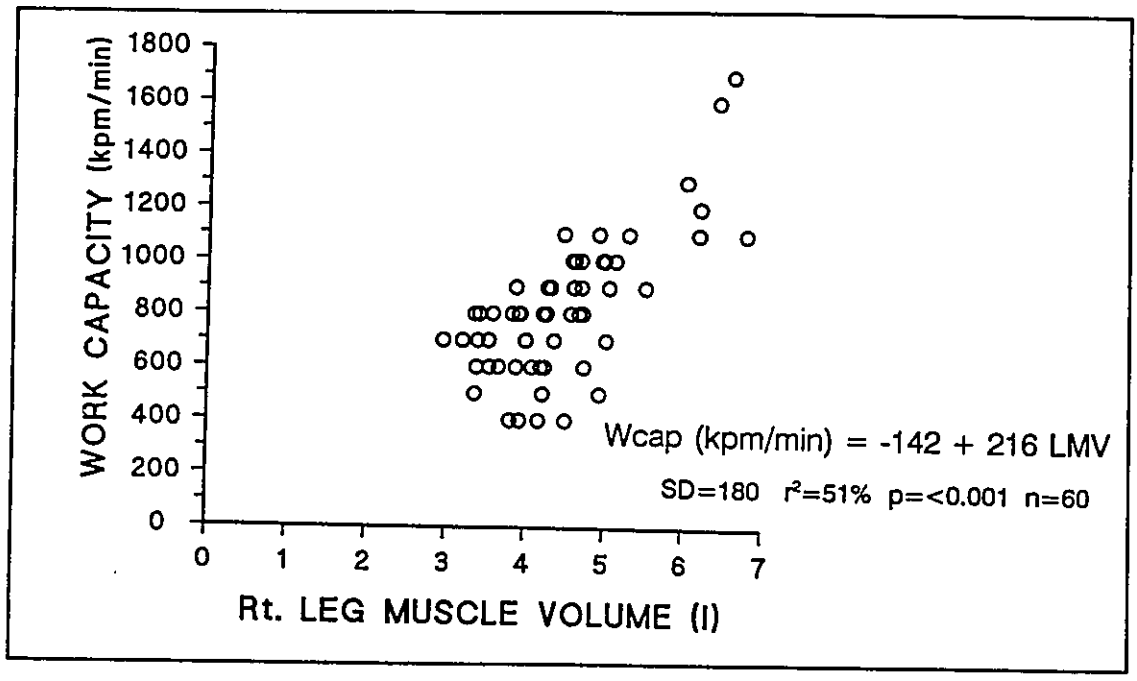


Figure 5.5 Relationship of work capacity to leg muscle volume

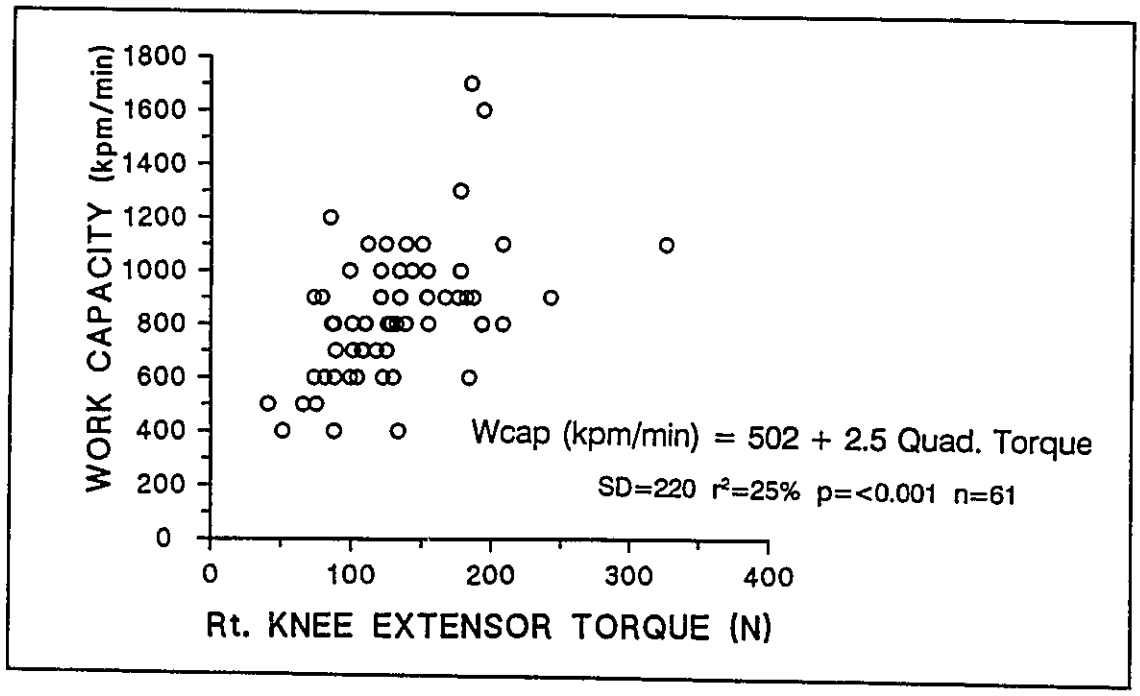


Figure 5.6 Relationship of work capacity to knee extensor torque

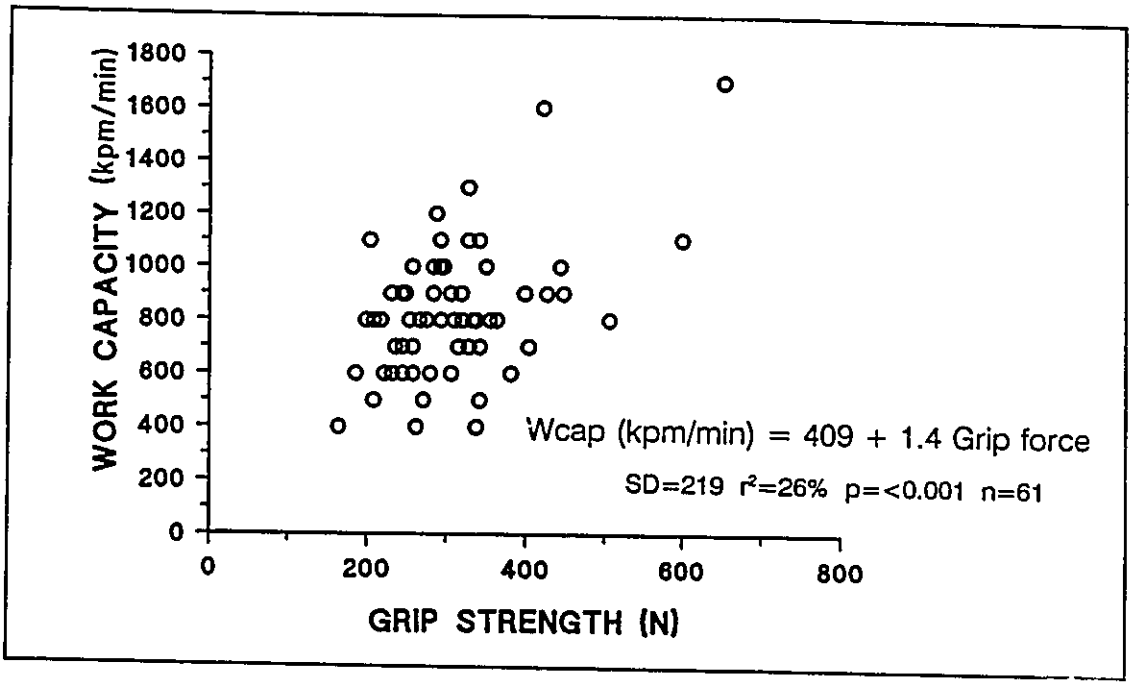


Figure 5.7 Relationship of work capacity to hand grip strength

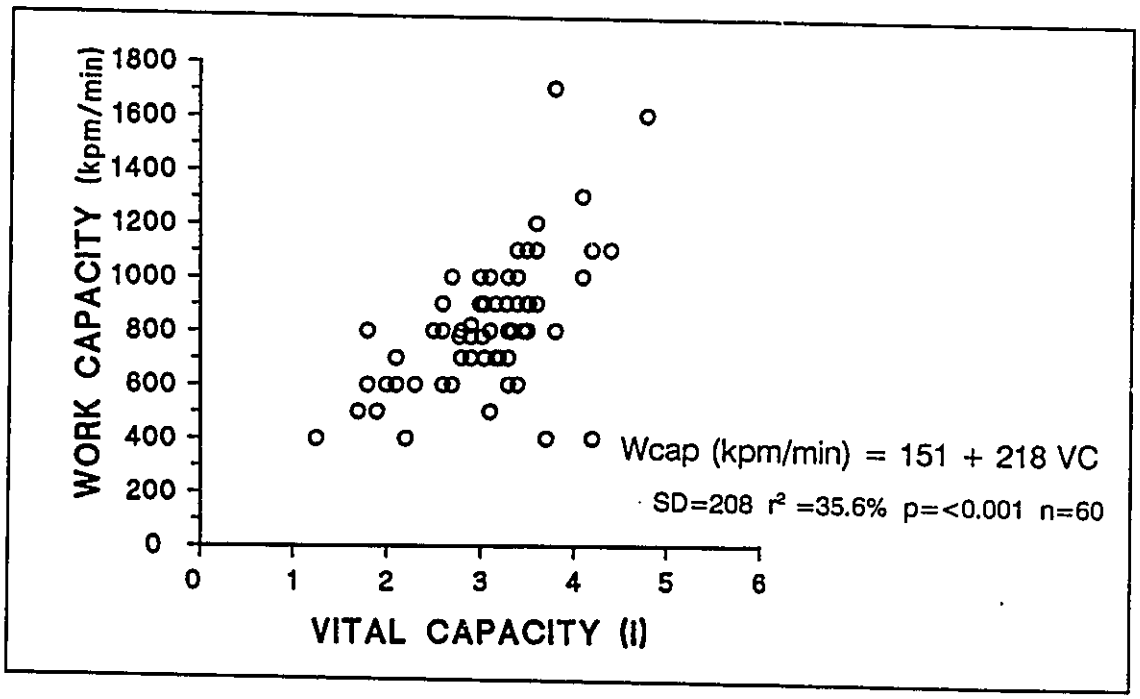


Figure 5.8 Relationship of work capacity to VC

Leg muscle volume and lean body mass are both closely related to work capacity, each accounting just over 50% of the variance in Wcap. The relationship of knee extensor torque and handgrip strength to Wcap is much less impressive, each accounting for only ~25% of the variance. For the same 60 subjects in whom peripheral muscle assessments was performed, differences in age, sex (male=0, female=1), and height account for 46% of the variance, with a residual standard deviation of 195 kpm/min:

Wcap (kpm/min) = -1050 + 5.2 Age -186 Sex + 13.0 Height

partial p 0.04 0.04 <0.001

SD=195 r^2 =46% p <0.001 n=60

This differed somewhat from the same relationship for the whole group:

Wcap (kpm/min) = -627 + 5.4 Age - 256 Sex + 10.8 Height

partial p 0.011 <0.001 <0.001

SD=183 r^2 =52% p <0.001 n=79

After age, sex and height have been considered, leg muscle volume further increases the r^2 to 61% with a fall of the standard deviation to 167 kpm/min:

Wcap (kpm) = -779 - 5.7 Age - 33 Sex + 6.2 Height + 163 LMV

partial p 0.008 0.7 0.08 **<0.001**

SD=169 r^2 =61% p <0.001 n=60

Similar increases occur with consideration of lean body mass:

Wcap (kpm/min) = -390 - 7.3 Age - 43 Sex + 1.7 Height + 22.5 LBM

partial p 0.001 0.6 0.7 **<0.001**

SD=169 r^2 =60% p <0.001 n=60

This analysis also shows that once leg muscle volume (l) or lean body mass (kg) have been considered, height and sex are no longer predictive of work capacity. This indicates that the influence of height and sex on Wcap is expressed through differences in muscularity. This is not the case for age, it continues to be a significant predictor of work capacity:

Wcap (kpm/min) = 15 + 23 LBM - 7.2 Age (yr)

partial p <0.001 **0.001**

SD=167 r^2 =60% p <0.001 n=60

Wcap (kpm/min) = 30 + 208 LMV - 6.4 Age (yr)

partial p <0.001 **0.003**

SD=170 r^2=58% p <0.001 n=60

After consideration of age, sex, and height, knee torque (partial p=0.054) and handgrip strength (partial p=0.04) were minimally predictive of work capacity. The combination of leg muscle volume and lean body mass was more predictive of work capacity than either alone:

Wcap (kpm) = -225 + 12.2 LBM + 119 LMV

partial p 0.04 0.03

SD=117 r^2=54.5% p <0.001 n=60

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but this effect was small, the r^2 only increasing ~4%, due to marked co-correlation of these two muscle measurements:

LMV (l) = 0.56 + 0.092 LBM (kg)

SD=0.44 r^2=73% p <0.001 n=60

As before, age still significantly influenced work capacity:

Wcap (kpm/min) = -53 + 13.4 LBM + 100 LMV - 6.7 Age

partial p 0.01 0.04 0.001

SD=162 r^2=62% p <0.001 n=60

5.3.3 Disability and combined respiratory and muscle impairments

The preceding analysis of the factors which contribute to disability identified a much closer relationship of Wcap to muscle mass than to pulmonary impairment. This section will explore how combinations of both respiratory and peripheral muscle impairment influenced work capacity.

When considered in addition to leg muscle volume and age, VC had a further small but significant influence on Wcap (figure 5.9):

Wcap (kpm/min) = -70 + 164 LMV - 6.0 Age + 92 VC

partial p <0.001 0.004 **0.02**

SD=163 r^2=62% p <0.001 n=60

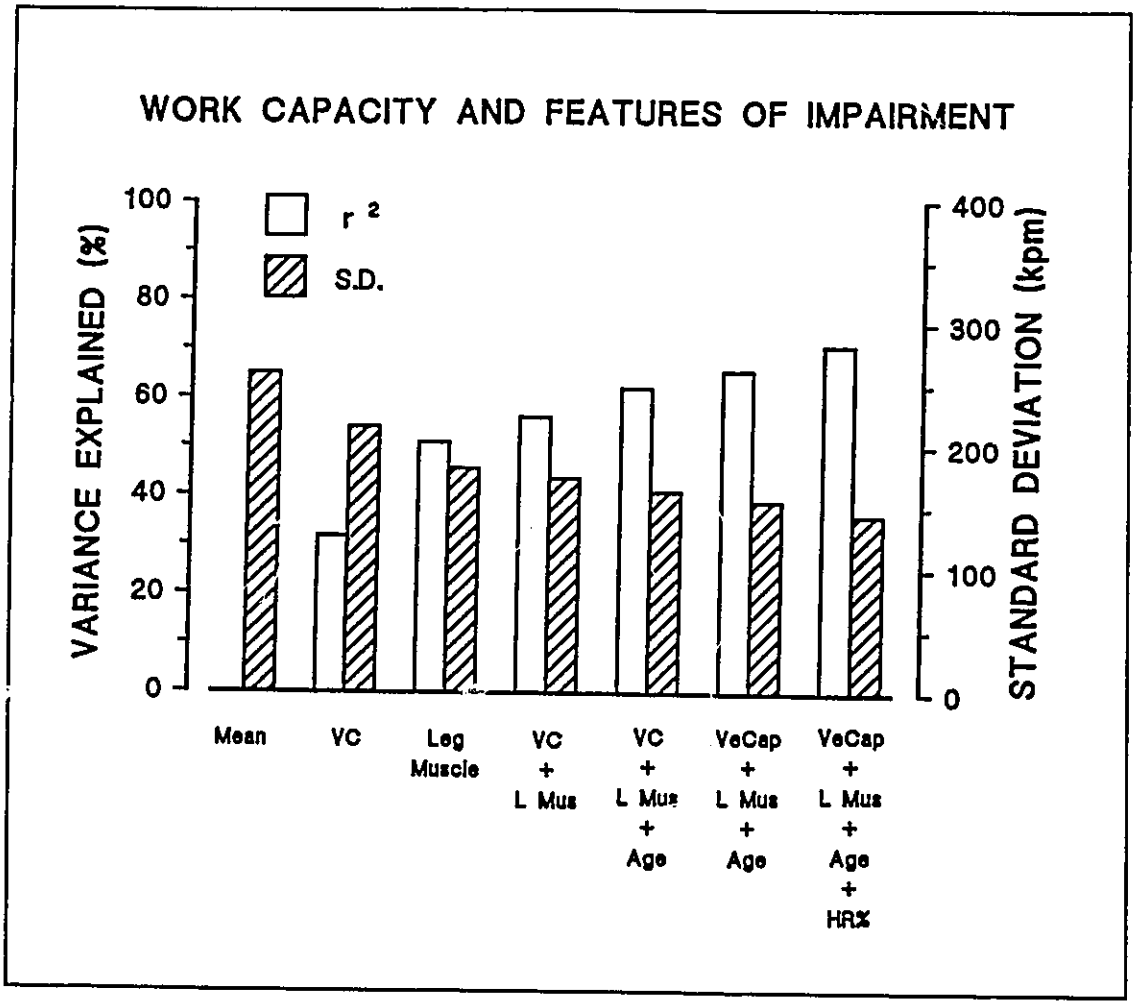

Figure 5.9 **Proportion of variance accounted for, and SD of the regression residuals, when Wcap was related to multiple factors.**

When ventilatory capacity ($V_{E\ CAP}$) was considered instead of VC (physiologically more relevant), the influence of pulmonary function on work capacity was more pronounced (figure 5.9):

Wcap (kpm/min) = -68 + 136 LMV - 6.1 Age + 4.4 $\dot{V}E_{Cap}$			
partial p	<0.001	0.002	**0.001**
SD=155 r^2=66% p <0.001 n=60			

Indices of gas exchange at rest (SaO_2, $P\bar{v}CO_2$, DL_{CO}, KCO) or the inclusion of lung volumes (TLC, FRC, RV) did not further improve prediction of work capacity beyond these three factors.

5.4 Discussion

This study found that disability was unrelated to the extent and nature of spinal deformity in this group of mostly mild to moderate idiopathic scoliotic subjects. Although specific features of deformity were associated with pulmonary impairment, the relationship between pulmonary impairment and disability was so variable that deformity was not related to work capacity. Deformity could have been related to work capacity independent of pulmonary function, but this was not found. Peripheral muscle factors, particularly leg muscularity, had a dominant relationship with work capacity; in fact, until this effect was controlled for, the influence of pulmonary function on Wcap went undetected. Ventilatory impairment was the aspect of pulmonary function associated with disability. Gas exchange at

rest ($Sa\bar{O}_2$, $P\bar{v}CO_2$) was generally normal and did not account for differences in work capacity. The influence of gas exchange efficiency during exercise and cardiac performance has not been assessed in this analysis but will be returned to when the physiological response to exercise in these subjects is considered.

Standardized reference values for peripheral muscle indices in subjects of different age, sex, and height are not available, making it impossible to express these measurements as % predicted. For this reason, the influence of muscular factors on disability could not be assessed in the same manner as the impact of the pulmonary impairment on disability (both expressed as % predicted). To circumvent this problem, the relationship of muscular indices to work capacity was assessed directly, a similar analysis also being performed for work capacity and pulmonary impairment to facilitate comparisons and assessment of their interactions. Independent of age, sex and height, the influence of these variables (pulmonary and muscular) on work capacity was also assessed using multiple regression analysis. After first considering differences in work capacity due to age, sex and height, a significant relationship of muscular or pulmonary variables to work capacity suggests that these factors contribute to disability.

Few studies have evaluated work capacity and its relationship to either deformity or physiological impairment in idiopathic scoliosis. Bjure et al (1969) did not comment on the relationship between Cobb angle (mean,87°) and maximal oxygen consumption, but noted that there was no correlation between $\dot{V}O_{2\,max}$ and

VC in their study of 9 subjects. Chong et al (1981) reported a significant negative correlation between percentile performance on a Bruce protocol exercise test and Cobb angle (mean 33°), and "a definite trend" between $\dot{V}O_{2\,max}$ and the angle of scoliosis, in 38 subjects. Relationship of work capacity to pulmonary function was not assessed. Although $\dot{V}O_{2\,max}$ was reduced in DiRocco et al's (1983) study of 14 subjects with a mean Cobb angle of 28°, the extent of this reduction was not related to severity of deformity. Again, relationship to pulmonary function was not assessed. In a subsequent study using a more intense exercise testing protocol, DiRocco and Vaccaro (1988) found a reduction in $\dot{V}O_{2\,max}$/kg/min in 19 adolescent subjects, and suggested that this was more marked in the eight curves greater than 25°. From the data presented in DiRocco and Vaccaro's paper, it can be calculated that there was a weak relationship between $\dot{V}O_{2\,max}$/kg/min and Cobb angle ($p=0.014$), but the relationship between $\dot{V}O_{2\,max}$ and Cobb angle was not significant ($p=0.2$) after standardizing for differences in age, sex and height. Similarly, after standardizing for age, sex and height, VC and $\dot{V}O_{2\,max}$ were not related in that study. No relationship between $\dot{V}O_{2\,max}$ and angle of scoliosis was found in Leech's study either, but exercise capacity was judged to be normal in this group of very mild scoliotics (Cobb angle ~10°). Stoboy (1978) implied that there was no relationship between Cobb angle and $\dot{V}O_{2\,max}$ in 11 subjects who were exercised before and after surgery. Smyth et al (1986) reported that mean $\dot{V}O_{2\,max}$ was within normal limits in adolescents with mild idiopathic scoliosis (Cobb angle <35°) but, due to the exclusion of 8/44 study subjects who were judged to

have exercised submaximally (RER_{max} <1.1), the validity of this assessment is uncertain.

Although various aspects of the cardiorespiratory response to exercise have been reported in a number of additional studies, data relating exercise capacity to extent of deformity or pulmonary impairment was not included (Mankin et al, 1964; Shneerson and Madgwick, 1979; Shneerson, 1980; Kumano and Miyashita, 1986; Kesten et al, 1991).

It has previously been established that there is a close relationship between work capacity or $\dot{V}O_{2\,max}$ and leg muscle volume in healthy children and young adults (Buskirk and Taylor, 1957; Cotes et al, 1969; Davies, 1971; Davies, 1972a; Davies, 1972b; Sargeant and Davies, 1977). This relationship becomes less tight with advancing age and was not significant in older adults (Davies, 1972a). Part of the reason for a weaker relationship between work capacity and leg muscle volume in adults probably relates to a reduction of work capacity per unit muscle volume with advancing age (Davies, 1972a). The decrease in work capacity of ~7 kpm/yr in this study is similar to the normal reduction with age reported by Jones et al (~8.7 kpm per year or 0.7% per year, (Jones et al, 1985; Jones and Killian, 1987)).

Although the relationship between work capacity (expressed as either $\dot{V}O_{2\,max}$ or as maximal power output) and muscular factors has not previously been addressed in idiopathic scoliosis, from the data presented by DiRocco and

Vaccaro (1988), it is possible to determine the relationship of $\dot{V}O_{2max}$ to lean body mass in their 19 subjects. As in the present study, there was a close relationship between $\dot{V}O_{2max}$ and LBM:

$$\dot{V}O_{2\,max}\ (l/min) = -672 + 62\ LBM\ (kg)$$

$$SD=340 \quad r^2=63\% \quad p<0.001 \quad n=19$$

The relationship of $\dot{V}O_{2\,max}$ to LBM was still significant after adjusting for differences in age, sex and height (partial p=0.003), whereas VC was not significantly related to $\dot{V}O_{2\,max}$ after adjusting for these factors (partial p=0.14). Therefore, in agreement with the findings of the present study, DiRocco and Vaccaro's data support that muscular factors are more predictive of work capacity than is pulmonary impairment. Unlike the present study, VC did not have a significant predictive relationship with $\dot{V}O_{2\,max}$ (p=0.15) when combined with LBM and age. Failure to demonstrate an additive influence of VC and muscular factors on $\dot{V}O_{2max}$ with DiRocco and Vaccaro's data probably reflects the small number of subjects in their analysis.

In children with chronic airflow limitation due to cystic fibrosis, in addition to the severity of airflow obstruction, differences in nutritional status or muscularity were found to contribute to disability (Coates et al, 1980; Marcotte et al, 1986). It is not surprising therefore that muscle volume is closely related to work capacity

in the present study. It was unexpected that the relationship of work capacity to pulmonary impairment would be so weak and variable in subjects of a given age, sex, and height; knowledge of pulmonary function alone gives little indication of the likelihood or severity of disability. From the findings of this study, the relative impact of different combinations of respiratory and peripheral muscle impairment

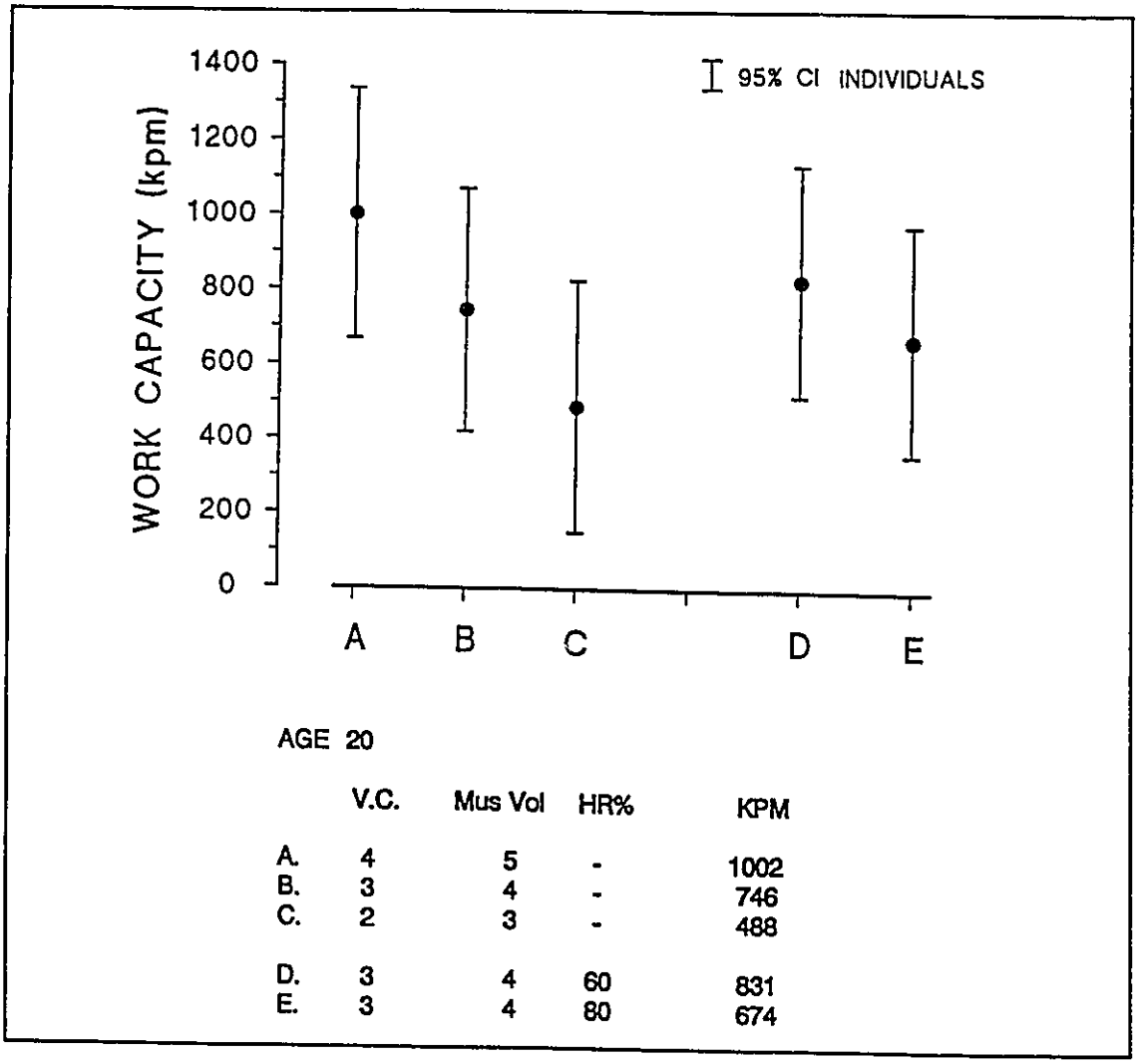

Figure 5.10 %Wcap estimated from different severities of impairment

on work capacity can be estimated, as shown for subjects A, B, and C in figure 5.10. Subjects D and E illustrate the added influence of submaximal heart rate response to %Wcap, which will be addressed in the next chapter.

Given that values for leg muscle volumes were obtained from one leg only in this study, and that differences in muscle volumes between legs is small in the absence of focal disease (~2% (Sargeant and Davies, 1977)) , the true coefficient describing the relationship of total leg muscle volume to work should be approximately half of this value presented above. It is evident therefore that a one litre reduction in VC has a roughly equivalent impact on work capacity as a 1.12 litre reduction in total leg muscle volume. It should be noted that although lung and leg volumes were correlated across the population as a whole:

$$VC\ (l) = 0.95 + 0.48\ LMV\ (l)$$

$$SD=0.58 \quad r^2 = 33\% \quad p < 0.001 \quad n=60$$

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this relationship is accounted for almost entirely by differences of age, sex, and height between these subjects. After controlling for these three factors, there is no longer is a significant relationship between VC and LMV ($p=0.08$), indicating that for subjects of the same age, sex, and non-deformed height, pulmonary and muscle impairments are independent. Interestingly, Marcotte et al also found that

lung function and nutritional status were independent in advanced cystic fibrosis (Marcotte et al, 1986).

Weakness of association between static quadriceps strength and work capacity, and the lack of association between the two after controlling for differences of age, sex, and height, was unexpected. This is probably due to a limited relationship between static strength and work capacity in individual muscles (Tornvall, 1963), and may also reflect muscle specificity with the two maneuvers. Whereas extensor knee strength specifically tests the quadriceps, cycling involves different thigh and calf muscles. The finding that handgrip and quadriceps strengths were not closely correlated in these scoliotic subjects (r^2=30%), indicates that the distribution of individual muscle strengths differs widely between subjects. In keeping with this observation, Tornvall also found highly variable relationships between the static strengths of different muscle groups in military recruits (Tanner et al, 1966). The r^2 value for the relationship between finger flexion (hand grip) and leg extension strength in Tornvall's study was also 30%.

Cardiovascular support of the active muscle and adequacy of arterial oxygenation during exercise has not been addressed by the above analysis. These variables are difficult to assess from measurements made at rest but can be measured either directly (SaO_2) or indirectly (heart rate response, oxygen pulse) during exercise. Physiological response to exercise will be considered in the next chapter.

Cycle ergometry was used to measure work capacity in this study, and it is possible that the type of exercise performed may influence the quantification of disability and its relationship to the variables which have been considered (eg. pulmonary function, leg muscle volume). Treadmill exercise, which may use a larger muscle mass, is associated with a higher $\dot{V}O_{2\ max}$ at Wcap than cycle ergometry (~ 7% (Shephard 1971)) but ventilation tends to be slightly higher with cycling (Shephard 1966). Therefore, it appears that specific mode of exercise involving large muscle groups is unlikely to have much influence on the findings of these studies.

A further component which may influence support of the active muscle and exercise capacity is the hemoglobin level (Davies, 1973). Although this was not measured in all patients, values were evaluated in 25 females (mean, 13.2) and 6 males (mean, 14.8). In this subgroup, hemoglobin level was unrelated to work capacity, either directly or in combination with other factors.

Reductions in $\dot{V}E_{Cap}$ appear to be partly responsible for the observed reduction in Wcap in these patients. Mean $\dot{V}E_{Cap}$ was 97 l/min (table 3.2), corresponding to 84% of the predicted $\dot{V}E_{Cap}$ (calculated from the reference FEV_1 and inspiratory flows). On the basis of the observed relationship between $\dot{V}E_{Cap}$ and Wcap (age and leg muscle volume considered), this reduction in $\dot{V}E_{Cap}$ of ~18 l/min would be expected to reduce Wcap by ~80 kpm/min and would therefore incompletely account for the extent of disability in these subjects (predicted Wcap

(977 kpm/min) - Wcap (830/min) = 147 kpm/min). The remaining reduction in Wcap may be due to i) an absolute reduction of muscle bulk relative to age and height in these subjects ("small muscles"), or ii) a normal muscle bulk but reduced work capacity per unit muscle volume ("unfit muscles"). The first of these options appears to be more important. Davies reported the following relationship between maximum oxygen consumption and leg muscle volume in children and young adults of both European and African origin combined (Davies, 1972a; Davies, 1972b; Davies et al, 1973):

$$\dot{V}O_{2\,max}\ (l/min) = 0.36 + 0.22\ LV\ (l)$$

This is very similar to the equivalent relationship for these scoliotic subjects (coefficient for LV halved to adjust for bilateral leg volume):

$$\dot{V}O_{2\,max}\ (l/min) = -0.423 + 0.24\ LV\ (l)$$

$$SD=0.375\quad r^2=54\%\quad p<0.001\quad n=55$$

Jones et al (1985) reported the following relationship between bilateral thigh muscle volume and $\dot{V}O_{2\,max}$:

$$\dot{V}O_{2\,max}\ (l/min) = 0.082 + 0.306\ \text{Thigh Mus Vol}\ (l)$$

in a group of 100 normal adults. The same relationship for these scoliotic subjects is

$$\dot{V}O_{2\,max}\ (l/min) = 0.039 + 0.279\ \text{Thigh Mus Vol (l)}$$

The coefficient of $\dot{V}O_{2\,max}$ against thigh volume in these scoliotic subjects is 91% of that reported by Jones. The 95% CI for this coefficient in the scoliotics is 0.19 - 0.37 O_2 (l)/ thigh muscle volume (l), suggesting a normal or only mildly reduced $\dot{V}O_2$/LV relationship in these subjects. Shephard et al (1988) found the following relationship between $\dot{V}O_{2\,max}$ and muscle volume (MV) when exercise is performed by different combinations of arm and leg muscles:

$$\dot{V}O_{2\,max}\ (l) = 0.8 + 0.158\ MV\ (l)$$

The findings of a close relationship between muscularity and Wcap in idiopathic scoliosis is clinically important. Symptom intensities reported at Wmax indicate that excessive leg effort commonly limits activity in these subjects. In most of these patients, interventions directed at improving pulmonary function without also attempting to improve peripheral muscle bulk and conditioning, are unlikely to improve functional capacity.

Chapter 6

Cardiorespiratory response during exercise

This chapter describes the cardiac, respiratory and metabolic response to incremental exercise in subjects with idiopathic scoliosis. Initially, average cardiorespiratory responses at Wcap will be described and compared with reference values obtained from a control group who completed the same incremental exercise test in this laboratory. Variability in cardiorespiratory response at Wcap will then be analyzed to determine if differences are systematically related to deformity, pulmonary impairment and severity of disability.

In a subsequent analysis, cardiorespiratory variables recorded at 50% of each subject's predicted work capacity (50 %Wcap) will be examined. This work rate was chosen to avoid difficulties of interpretation which may be associated with comparisons of values recorded at each subjects Wcap, or at a specified absolute work load. Work capacity exceeded predicted values in some scoliotic subjects, while for others, the power output achieved fell far short of normal; therefore, differences in cardiorespiratory variables at Wcap are likely to be dominated by relative work rate (% predicted), which may obscure more subtle influences of

deformity or pulmonary impairment on cardiorespiratory response. Similarly, the same absolute work rate represents different relative stresses for subjects, depending on their age, sex and size.

The cardiorespiratory response at a power output equal to 50% of each individuals predicted maximal power output (50 %Wmax) was selected for the following reasons. Firstly, it corresponds to power outputs which subjects achieve when performing the more strenuous tasks of daily living. Examples might include walking while carrying objects such as children or groceries, or walking up slopes. (Power output during these activities is determined by the rate of movement, in addition to the weight of the subject and their loads.) Secondly, most subjects achieved this work rate, so that comparisons across nearly the whole study population (n=77) were possible. A wide scatter of symptom intensities was also anticipated at this work rate, facilitating comparison of physiologic and sensory responses.

6.1 Measurements at work capacity

Wcap was 830 kpm/min which was 86% of predicted Wcap (chapter 3.4). Base line data and cardiorespiratory variables recorded at Wcap, with accompanying comparisons, are shown in table 6.1 for subjects with scoliosis and for controls. Controls were obtained by selecting exercise tests of normal subjects, between the ages of 11 and 30 years, who were studied in this

	Scoliotics			Normals			
	Mean	SD	n	Mean	SD	n	p
Age (yr)	21	10.1	79	26	4.7	82	.0011
Sex (M:F)	13:66			11:71			0.6
Height (cm)	165	8.7	79	167	7.3	82	0.11
Weight (kg)	58	11.1	79	66	15.7	82	0.0002
FEV_1 (l)	2.7	0.63	79	3.6	0.60	82	<0.0001
VC (l)	3.2	0.74	79	4.2	0.67	82	<0.0001
MIP (cm H_2O)	65	24.4	79	84	26.3	82	<0.0001
MEP (cm H_2O)	84	24.5	79	97	21.6	82	<0.0003
Hand Grip (N)	320	93	61	360	92	47	0.027
Knee Ext. (N)	380	128	61	490	177	47	0.0002
At Wcap							
f	38	8.6	79	35	8.5	77	0.051
V_T (l)	1.5	0.39	79	2.0	0.50	77	<0.0001
$\dot{V}_E$ (l/min)	55	17.8	79	70	25.3	79	<0.0001
V_T/VC_N (%)	36	6.8	79	47	7.6	77	<0.0001
V_T/VC (%)	47	7.9	79	47	7.6	77	0.7
$\dot{V}_E/\dot{V}_{E_{cap}}$	58	16.1	79	56	16.5	77	0.4
HR	173	17.3	79	175	12.9	82	0.5
%HR	88	7.7	79	91	6.4	82	0.051
BP_{sys} (mmHg)	163	20.7	79	169	24.5	79	0.09
BP_{dia} (mmHg)	79	9.7	79	83	16.0	79	0.09
$\dot{V}O_2$ (l/min)	1.72	0.569	71	1.99	0.474	43	<0.0001
RER	1.01	0.103	71	1.13	0.097	43	<0.0001
$\dot{V}_E/\dot{V}CO_2$ (l/l)	31.5	3.82	71	30.5	3.58	43	0.17
Br (Borg)	5.5	2.67	78	6.3	2.32	82	0.04
LE (Borg)	6.3	2.43	78	7.0	2.27	82	0.054
Wcap (kpm/min)	830	260	79	1100	308	82	<0.0001

Table 6.1 Baseline data and cardiorespiratory variables at Wcap, for the scoliotic subjects and controls.

laboratory during the course of this study. Criteria for selection of this reference group were as follows: i) normal pulmonary function (VC and FEV_1 ≥ 80 %predicted, FEV_1/VC ≥ 75%); ii) normal exercise capacity (≥ 80 %predicted); iii) absence of conditions which might be expected to modify Wcap or exercise response (eg. arthritis or exertional chest pain). Although controls were well matched with the study population for sex and height, they were significantly older (table 6.1). This age discrepancy means that comparison of variables known to be influenced by age, for example Wcap, should be performed with caution. Expressing findings for the control and study group as their age adjusted value helps to minimize this problem.

At Wcap, oxygen consumption was related to work performance (across the population) as follows:

$$\dot{V}O_{2\,max}\ (ml/min) = 0.010 + 2.1\ Wcap\ (kpm/min)$$

$$SD = 0.196 \quad r^2 = 88\% \quad p<0.001 \quad n=71$$

The intercept of this relationship was not significantly different than in controls (1.8 ml, p=0.25), but the slope of this relationship in the controls was less (1.7 ml/kpm/min, p=0.009).

$\dot{V}E$ max was 55 l/min, with a mean VT_{max} of 1.46 l and f of 38 breath/min. Given that relative to normal subjects, maximal power output of the scoliotic subjects was reduced, the higher f at Wcap in the scoliotic subjects probably represents a true though small difference. The 25% reduction in VT may in part be due to the lower work rates achieved, but more likely primarily reflects an altered pattern of breathing in these subjects (Jones, 1984b; Jones et al, 1985). Although VT at Wcap, when expressed as a proportion of predicted reference VC (Vt/VC_N), was low at 36% ($p < 0.001$), it accounted for the same proportion of actual VC (47%) as in the controls ($p=0.7$).

HR reached 173 beats/min which was 88% HR_{max} (predicted by: 210 - 0.67 age). HR at Wcap was the same as for the control group (175 beats/min), but tended to be marginally lower than controls after age adjustment (table 6.1), however this difference still was not statistically significant ($p=0.051$). Blood pressure at Wcap was normal, with a mean value of 163/79.

A small but statistically significant reduction in SaO_2 occurred between rest (96.2% SD 1.35) and Wmax (95.8% SD 1.79) (paired t, $p = 0.007$). SaO_2 at rest and at Wcap was not available for the control group for comparison with the study population, but a similar marginal fall in SaO2 has previously been noted in normal subjects in this laboratory (Killian, personal communication) .

$\dot{V}E_{max}$ was 57% (SD 14.6) of ventilatory capacity as calculated from a maximum inspiratory and expiratory flow volume loop, or 58% (SD 16.1) of

ventilatory capacity calculated from FEV_1 x 35. This proportion was the same as for the controls (table 6.1).

Efficiency of gas exchange at Wcap was assessed by i) calculating the ventilation required per litre of CO_2 output (ventilatory equivalent for CO_2, $\dot{V}E/\dot{V}CO_2$) and ii) monitoring SaO_2 during exercise. $\dot{V}E/\dot{V}CO_2$ at Wcap was 31.5 l/l which was not significantly different than the controls (table 6.1). The ventilatory equivalent for O_2, $\dot{V}E/\dot{V}O_2$, was 31.8 l/l (SD 3.75). RER at Wcap was 1.01 which was substantially less than the value of 1.09 for the controls ($p<0.001$, table 6.1).

6.1.1. Deformity and cardiorespiratory response at Wcap.

Frequency of breathing ($p=0.5$) and VT at Wcap (both absolute volumes ($p=0.9$) and as a proportion of reference VC (VC_N) ($p=0.9$)) did not vary systematically with Cobb angle. However, VT as a proportion of VC (VT/VC) did increase marginally as Cobb angle increased:

$$VT/VC\ (\%) = 40 + 0.15\ \text{Cobb angle}$$

$$SD=7.8\ \ r^2=11\%\ \ p=0.006\ \ n=68$$

When multiple regression was performed to determine if other features of deformity influenced breathing pattern at Wcap, the only statistically significant

relationship found was the association of longer and higher curves with a reduced V_T/VC_N (curve **position** coded according to the vertebra at the **apex** eg. 6th thoracic vertebra = 6):

$$V_T/VC_N\ (\%) = 34 + 1.7\ \text{Apex} - 1.6\ \text{Length}$$

$$SD=6.0\ \ r^2=18\%\ \ p=0.001\ \ n=73$$

Efficiency of gas exchange at Wcap did not vary with severity of the scoliosis ($\dot{V}E/\dot{V}CO_2$, p=0.2; SaO_2, p=0.2) or with other single or combined features of deformity.

Neither systolic (p=0.2) or diastolic (p=0.2) blood pressure at Wcap varied systematically with Cobb angle, or with other single or combined features of deformity.

Similarly, $\%HR_{max}$ (p=0.5) and $\%O_2\ pulse_{max}$ (predicted $O_2\ pulse_{max}$ calculated from $\dot{V}O_{2max}$ predicted / HR_{max} predicted) at Wcap were not related to Cobb angle (p=0.07, positive slope) or to other single or combined features of deformity.

6.1.2 Pulmonary impairment and cardiorespiratory response at Wcap

For clarity, %VC is the sole measure of pulmonary impairment against which differences in cardiorespiratory response will be evaluated. $\dot{V}E_{max}$ was related to VC as expressed by the following equation:

$$\dot{V}E_{max}\ (l/min) = 11.3 + 13.8\ VC\ (l)$$

$$SD=13.8\ \ r^2=33\%\ \ p<0.001\ \ n=79$$

The proportion of an individual's ventilatory capacity utilized at Wcap increased as pulmonary function deteriorated, although the relationship was not strong:

$$\dot{V}E_{max}/\dot{V}E_{cap}\ (\%) = 88 - 0.39\ \%VC$$

$$SD=13.6\ \ r^2=13\%\ \ p=0.001\ \ n=79$$

Alternatively stated, the proportion of $\dot{V}E_{cap}$ utilized at Wcap was inversely related to $\dot{V}E_{cap}$. Small but statistically significant differences in breathing pattern at Wcap also occurred with more severe pulmonary impairment; VT_{max}/VC_N decreased and f increased, but VT as a proportion of VC increased.

V_T/VC_N (%) = 14 + 0.28 %VC

SD=5.7 r^2=31% p <0.001 n=79

f_{MAX} (breaths/min) = 56 - 0.22 %VC

SD=8.1 r^2=12% p=0.001 n=79

V_T/VC (%) = 65 - 0.23 %VC

SD=7.3 r^2=16% p <0.001 n=79

Surprisingly, efficiency of gas exchange at Wcap did not vary with %VC ($\dot{V}_E/\dot{V}CO_2$, p=0.4; SaO_2, p=0.5).

No relationship was found between cardiac measures at Wcap and severity of pulmonary impairment ($\%HR_{max}$, p=0.7; $\%O2pulse_{max}$, p=0.3; BP_{sys} p=0.9; BP_{dia} p=0.07)

6.1.3 Disability and cardiorespiratory response at Wcap

$\dot{V}E_{max}$ was related to Wcap as expressed as follows:

$$\dot{V}E_{max} \text{ (l/min)} = 4 + 0.061 \text{ Wcap (kpm/min)}$$

$$SD=7.9 \quad r^2=80\% \quad p= <0.001 \quad n=79$$

This was not significantly different from the control group (intercept: - 5 l p=0.2; slope: 0.068 l/kpm p=0.2)

Despite the association of pulmonary impairment with disability, the proportion of an individual's ventilatory capacity which was utilized at Wmax fell with greater disability:

$$\dot{V}E_{max}/\dot{V}E_{cap} = 30 + 0.31 \text{ \%Wcap}$$

$$SD=13.6 \quad r^2=14\% \quad p= 0.001 \quad n=79$$

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further emphasizing how poorly disability was linked to ventilatory limitation. As would normally be expected, V_T/VC_N at Wcap was greater in the less disabled, at least partly accounted for by the greater relative work loads and ventilatory demands in these subjects at Wcap:

$$V_T/VC_N = 30 + 0.19\ \%Wcap$$

$$SD=6.0 \quad r^2=14\% \quad p<0.001 \quad n=79$$

In contrast, f at Wcap was not linked with disability ($p=0.09$).

Gas exchange, as assessed by ventilatory equivalent for CO_2, was less efficient in more disabled subjects:

$$\dot{V}_E/\dot{V}CO_2\ (l/l) = 30 - 0.08\ \%Wcap$$

$$SD=3.6 \quad r^2=12.4 \quad p=0.003 \quad n=71$$

but SaO_2 was unrelated to %Wcap ($p=0.09$).

At Wcap, $\%HR_{max}$ and $\%O_2\ pulse_{max}$ were higher in less disabled subjects, again at least partly accounted for by the normal increase in these variables with higher relative work loads:

$$\%HR_{max} = 74 + 0.17\ \%Wcap$$

$$SD=7.2 \quad r^2=14 \quad p=0.001 \quad n=79$$

$$\%O_2\ pulse_{max} = 28 + 0.69\ \%Wcap$$

$$SD=12.2 \quad r^2=49 \quad p<0.001 \quad n=71$$

Systolic (p=0.1) and diastolic (p=0.4) blood pressure at Wcap did not vary systematically with extent of disability.

6.2 Cardiorespiratory response at a standardized submaximal work rate (50 %Wcap)

Cardiorespiratory variables measured at 50 %Wcap are shown in table 6.2. In addition to showing the absolute values, a number of standardization, which adjust for expected differences on the basis of age, sex and non-deformed height, are also presented. Values at exhaustion have been included for the two subjects who did not achieve 50 %Wcap.

	Mean	SD	n
f (breath/min)	28.1	6.92	79
V_T (l)	1.13	0.373	79
$\dot{V}_E$ (l/min)	30.7	8.94	79
HR (beats/min)	138	17.1	79
HR (% max pred)	71	8.4	79
BP_{sys} (mmHg)	141	19.1	79
$\dot{V}O_2$ (l/min)	1.12	0.318	69
RER	0.89	0.092	69
O_2 pulse (ml)	8.1	2.22	69
O_2 pulse (% max pred)	71	13.0	69
$\dot{V}E/\dot{V}CO_2$ (l/l)	31.5	3.82	71
SaO_2 (%)	96.3	1.89	77
Work rate (kpm/min)	490	135	79

Table 6.2 Cardiorespiratory variables at 50 %Wcap.

6.2.1 Deformity and cardiorespiratory response at 50 %Wcap

No significant relationship was detected between cardiac (BP_{50}, $\%HR_{max\ 50}$) or ventilatory (f_{50}, V_{T50}/V_{TN}) response, or efficiency of gas exchange ($\dot{V}E/\dot{V}CO_{2\ 50}$, $SaO_{2\ 50}$) at 50 %Wcap and features of deformity.

6.2.2 Pulmonary impairment and cardiorespiratory response at 50 %Wcap

HR at 50 %Wcap was unrelated to pulmonary impairment (p=0.4).

There was a weak relationship of systolic, but not diastolic (p=0.4) blood pressure to %VC:

$$BP_{sys\ 50} = 89 - 0.17\ \%VC$$

SD=10.0 r^2=5% p=0.04 n=79

Both a low V_{T50} and a high f_{50} were associated with pulmonary impairment:

$$V_{T50}/VC_N = 14 + 0.18\ \%VC$$

SD=5.9 r^2=15% p <0.001 n=79

$$f_{50} = 43 + 0.19\ \%VC$$

SD=6.5 r^2=14% p <0.001 n=79

Efficiency of gas exchange was not related to %VC ($\dot{V}_E/\dot{V}CO_{2\ 50}$, p=0.9; $Sa\dot{C}_{2\ 50}$, p=0.4).

6.2.3 Disability and cardiorespiratory response at 50 %Wcap

This section of the analysis will try to identify differences in cardiorespiratory response during submaximal exercise which were associated with disability. Whereas the preceding analyses examined the influence of deformity and pulmonary impairment (independent variables) on the cardiorespiratory response (dependent variable), in this section, cardiorespiratory responses at 50 %Wcap are considered the independent variables and their relationship to %Wcap is presented.

Markers of a reduced stroke volume at 50 %Wcap were predictive of disability:

$$\%Wcap = 157 - 1.0\ \%HR_{max\ 50}$$

SD=15 r^2=24% p<0.001 n=79

$$\%Wcap = 48 + 0.52\ \%O2\ pulse_{max\ 50}$$

SD=16 r^2=16% p<0.001 n=69

Disability was not significantly related to the BP response at 50 %Wcap (p=0.06).

Pattern of breathing at 50 %Wcap was largely unrelated to disability: the association of %Wcap with VT_{50}/VC_N was not significant (p=0.27) and with f_{50} was weak:

$$\%Wcap = 105 - 0.79\ f_{50}$$

SD=17 r^2=7% p=0.015 n=79

Reduced efficiency of gas exchange at 50 %Wcap was associated with disability:

$$\%Wcap = 136 - 1.6\ \dot{V}E/\dot{V}CO_{2\ 50}$$

SD=16 r^2=12 p=0.003 n=71

This association can largely be accounted for on the basis of differences in breathing pattern; once f_{50} and VT_{50}/VC_N were accounted for, the relationship of %Wcap to $\dot{V}E/\dot{V}CO_2$ at 50 %Wcap was no longer significant (p=0.1). SaO_2 at 50 %Wcap was unrelated to disability (p=0.5).

A higher RER at 50 %Wmax was predictive of disability:

$$\%Wcap = 136 - 59\ RER_{50}$$

SD=17 r^2=10% p=0.009 n=69

6.3 Discussion

Subjects achieved the same maximal HR as normal subjects, but at a reduced work intensity (86 rather than 100 %Wcap), indicating a higher than normal HR response. This suggests that stroke volume during exercise was reduced in these scoliotic subjects. Similarly, given the reduction in Wcap, systolic BP may have been higher than expected. Ventilatory efficiency was normal at Wmax, as indicated by $\dot{V}E/\dot{V}CO_2$ measurements, and by finding the same relationship between $\dot{V}E_{max}$ and Wcap (kpm/min) in the scoliotic and control subjects. However, there was variability in ventilatory efficiency; subjects with a higher $\dot{V}E/\dot{V}CO_2$ ratio during submaximal exercise were more disabled. This finding could be accounted for by the association between a low VT, high f pattern of breathing and disability. At Wcap, the scoliotic subjects utilized the same proportion of their $\dot{V}E_{cap}$ as normal subjects, but due to the reduction in $\dot{V}E_{cap}$, this was reached at 86 %Wmax. Similarly, although maximum VT was clearly reduced, this could be accounted for by the non obstructive pulmonary impairment; VT as a proportion of baseline VC was the same as in controls.

Given that $\dot{V}E_{max}/\dot{V}E_{cap}$ and %HRmax findings at Wcap were the same as in controls, it is apparent that no clear evidence of having reached predominantly a ventilatory or a cardiac limitation to exercise was observed for the group as a whole. As noted in chapter 3, leg effort was usually more marked than breathlessness, both at submaximal and at maximal power outputs. The analysis

presented in chapter 5 suggests that reduced peripheral muscle bulk is a major contributor to disability, but that pulmonary impairment is also important. As will be addressed later in this chapter, cardiac function may also be implicated in the genesis of disability. Therefore, it seems unwarranted to identify any one factor as "limiting" work capacity in mild to moderate idiopathic scoliosis; the importance of muscular, respiratory and cardiac factors as contributors to disability differs between subjects.

Arterial desaturation did not occur between rest and 50 %Wmax, but there was an approximately half percent reduction at Wmax. Similar reductions have previously been noted in normal subjects in this laboratory which, coupled with the lack of association between Sao_2 at Wmax and any other factor(s), suggests that this marginal desaturation is normal or unimportant.

Analysis of the relationship between features of spinal deformity and cardiorespiratory response to exercise, is notable for the lack of significant associations. It might have been anticipated that nature and extent of deformity would have been closely related to breathing pattern through their influence on rib displacement and operating length of the respiratory muscles. Except for a weak association between reduced Vt and both higher and longer curves, no such relationships were detected. This further emphasises the inappropriateness of using analysis of deformity, particularly Cobb angle, to assess risk of physiological impairment in scoliotic subjects.

As might have been expected, severity of pulmonary impairment, as assessed by %VC, was associated with ventilatory findings during exercise. The more severely impaired had reduced $\dot{V}_{E\ max}$, smaller tidal volumes and higher breathing frequencies. In addition, $\dot{V}_{E_{max}}/\dot{V}_{E_{cap}}$ and $V_{T_{max}}/VC$ were greater in subjects with greater pulmonary impairment. Cardiac response was essentially unrelated to pulmonary impairment.

Reflecting the higher power outputs achieved, $\dot{V}_{E_{max}}/\dot{V}_{E_{cap}}$, V_T/VC_N, $\%HR_{max}$ and $\%O_2\ pulse_{max}$ were higher at Wcap in less disabled subjects. Failure to find the normal gradient of a higher systolic BP in subjects who achieved a higher relative work rate may suggest that increases in systolic BP were excessive in the more disabled subjects.

Cardiorespiratory measurements at a standardized sub maximal work rate of 50 %Wcap differed systematically with extent of disability. Reduced efficiency of gas exchange and a high breathing frequency were linked with reduced work capacity, but the relationship of cardiac and metabolic parameters to disability was more remarkable. An elevated HR was, in the context of the relationships observed, strongly predictive of disability; on average, %Wmax was reduced to the same extent as the HR, expressed as $\%HR_{max}$, was increased at this work rate. The relevance of this observation will be discussed further later in this chapter (see "Cardiac impairment and disability"). A higher RER at 50 %Wcap was also associated with disability, probably reflecting acceleration of anaerobic metabolism

in these subjects at comparatively low power outputs as they approached their work capacity. Maximal power output (%Wcap) was unrelated to RER at Wcap (either directly, or in combination with muscular, ventilatory or cardiac factors), suggesting that the comparitively low RER_{max} for the scoliotic subjects as a whole should not be taken as evidence of sub maximal exercise test.

These findings generally agree with and extend earlier observations made in subjects with idiopathic scoliosis during incremental exercise. Shneerson (1980) reported that $\dot{V}E_{max}$ as a proportion of maximum voluntary ventilation (MVV), was normal at 65% in adolescent idiopathic scoliotic. From Bjure et al's (1969) data (estimated MVV = FEV_1 x 35), this proportion was 68% in eight subjects tested prior to a period of training. Similar calculations on the data provided by DiRocco and Vaccaro (1988), yields a mean value of 105%, which is highly improbable and difficult to account for. Smyth et al (1986) reported a high value of 90%, but for this calculation subjects judged to have made a submaximal effort (8/44) were excluded, probably partly accounting for this high estimate. In a subsequent study from the same institution (Kesten et al, 1991) the $\dot{V}E_{max}/\dot{V}E_{cap}$ ratio was judged to be normal at 70% in adults with moderate scoliosis. Whereas Shneerson's study measured maximum voluntary ventilation directly, $\dot{V}E_{cap}$ was estimated from FEV_1 x 35 in these other studies and by my manipulation of DiRocco and Vaccaro's (1988) and Bjure et al's (1969) data. The present study calculated very similar ventilatory capacities from i) FEV_1 x 35 and from ii) FEV_1 and maximum inspiratory flows. With either methods, $\dot{V}E_{max}/\dot{V}E_{cap}$ was the same as in controls.

The V_T/VC ratio at Wmax was reported as 0.45 by DiRocco et al (1983). In Bjure et al's (1969) study this ratio averaged 0.46 in seven subjects before a period of exercise training. Shneerson (1980) reported a higher value of 0.67, which may have been partly related to more severe pulmonary impairment in his subjects; $V_{T_{max}}/VC$ was inversely related to pulmonary impairment in the present study. Smyth (1986) reported a value of 0.6, but again, nearly 20% of their subjects were excluded from this calculation. This ratio was 0.48 in Kesten's (1991) study. From the present study it is evident that, compared to normals, V_T is reduced at Wcap although the ratio V_T/VC is normal. The reduction in $V_{T_{max}}$ did not quite parallel the reduction in VC; this ratio increased with greater pulmonary impairment. This finding may help to explain inconsistencies in the reported value of $V_{T_{max}}/VC$ in idiopathic scoliosis.

Ramonatxo et al (1988) noted a low V_T, high f pattern of breathing in scoliotic subjects (not exclusively idiopathic) at rest; in addition they reported duty cycle shortening as Cobb angle increased. They argue that these breathing pattern changes would reduce the energy cost of breathing and protect against inspiratory muscle fatigue.

Previous reports have yielded conflicting evidence as to the efficiency of ventilation during exercise in idiopathic scoliosis. Shneerson (1980) reported a slope of 33.6 l/l when $\dot{V}_E$ was regressed on $\dot{V}O_2$ (mean slope for individuals), which was 25% greater than controls. DiRocco et al reported high values of 42.7 and

43.23 l/l (calculated from data presented in the later study) for $\dot{V}E/\dot{V}O_2$ at Wcap in their two studies (DiRocco et al, 1983; DiRocco and Vaccaro, 1988). $\dot{V}E/\dot{V}O_2$ was 35 l/l in Bjure et al's (1969) study and $\dot{V}E/\dot{V}CO_2$ calculates to be ~31 l/l for Kesten et al's study (1991). The present study found that overall ventilatory efficiency was no different than controls. However, within the scoliotic group ventilatory efficiency did vary, with more disabled subjects having a higher $\dot{V}E/VCO_2$. This is in agreement with DiRocco and Vaccaro's (1988) findings.

A high heart response during exercise was found in the present study, and has previously been noted in subjects with idiopathic scoliosis (Bjure et al, 1969; Shneerson, 1980; DiRocco et al, 1983) (see below).

6.3.1 Disability and cardiac performance

In chapter five it was noted that both peripheral muscle and respiratory factors influenced work capacity in idiopathic scoliotic subjects, but the impact of cardiac performance on disability was not assessed. Unlike ventilatory capacity, maximum respiratory or maximum peripheral muscle strengths which can be assessed during a maximum voluntary manouver, as the heart is not under voluntary control, there is no simple assessment of maximal cardiac performance. (Boundaries of cardiac performance which would be equivalent to these respiratory measures, might be maximum voluntary cardiac output or maximum isometric blood pressure!) In the absence of methods which can reliably quantify

cardiac impairment, the cardiovascular response to exercise, particularly the HR response, can suggest differences in stroke volume and overall cardiovascular performance. As previously noted, a high HR response at submaximal work rates was associated with disability. Reduced muscle mass was strongly associated with disability, and is also associated with a high HR response during work performance (Cotes et al, 1973). It is possible therefore that the relationship of high HR response to reduced Wcap is an epiphenomenon, reflecting their common link to reduced muscle mass. To explore this possibility, and to determine if cardiac performance, independent of respiratory and peripheral muscle factors, contributes to disability in idiopathic scoliosis, multiple regression analysis was performed examining for an additional influence of HR response on %Wcap. For this analysis, factors previously shown to influence work capacity (leg muscle volume, $\dot{V}E_{cap}$, age) were forced into the equation before considering the influence of %HR (HR/HR_{max} predicted) or %O_2 pulse (O_2 pulse/O_2 $pulse_{max}$ predicted) at 50 %Wcap on %Wcap. Both factors were still significantly related to work capacity:

Wmax (kpm/min) = 456 - 6.6 Age + 130 Mus Vol + 4.5 V_{ECAP} - 7.1 $\%HR_{MAX\ 50}$

<0.001 <0.001 <0.001 **0.003**

n=60 SD=144 r^2=71 p<0.0001

$$\text{Wmax (kpm/min)} = -96 - 7.7\ \text{Age} + 79\ \text{Mus Vol} + 3.1\ V_{ECAP} + 49\ \%O_2\ \text{Pulse}_{max\ 50}$$

$$0.006 \qquad 0.04 \qquad 0.03 \qquad \mathbf{0.002}$$

$$n=53 \quad SD=148 \quad r^2=70 \quad p<0.0001$$

---

implicating cardiac performance as a further modifier of performance status (figures 5.9 and 5.10, subjects D & E). Blood pressure (partial p=0.4) and metabolic response (RER, partial p=0.5) at 50 %Wcap were not predictive of %Wcap, independent of age, respiratory and peripheral muscle factors.

Although it is tempting to conclude that a low stroke volume contributes directly to disability in idiopathic scoliosis, attributing causality may not be justified. We have already noted that at Wcap, the more disabled subjects tended to have lower heart rates, which would not support that disability was due to a limit in cardiac output due to a low stroke volume. It is more likely that, due to behavioral changes (less exercise for what ever reason), cardiac conditioning deteriorates in parallel with other determinants of work capacity (eg. qualitative and quantitative skeletal muscle changes). Cardiac deconditioning may exacerbate this process by discouraging subjects from exercising (eg. due to excessive exertional symptoms or palpitations), leading to a vicious cycle of reduced activity and deconditioning.

Alternative explanations for the high HR response during exercise could be the presence of i) structural cardiac abnormalities or ii) complicating pulmonary

hypertension. Although it is recognized that congenital cardiac anomalies may accompany scoliosis, in these cases the scoliosis is rarely idiopathic in nature (Simonds et al, 1989). The present study was confined to cases of idiopathic scoliosis, who had no evidence of cardiac disease on clinical, radiological or electocardiographic evaluation. Therefore, this explanation for the high HR response is extremely unlikely.

Pulmonary hypertension may complicate scoliosis, but only in the presence of marked pulmonary impairment (Bergofsky et al, 1959; Shneerson, 1978). In 23 subjects with thoracic scoliosis of mixed aetiology and severe pulmonary impairment (mean VC ~1.6 l), Shneerson (1978) found that an excessive rise in systolic pulmonary artery pressure during exercise was inversely related to pulmonary function and rarely occurred in subjects with a VC greater than 1.5 l. Only one subject in the present study had a VC less than this value (1.25 l), and furthermore, our analysis found that the relationship of a high HR response to a reduction in Wcap was independent of pulmonary function. This suggests that complicating pulmonary hypertension as a cause for the high HR response and reduced Wcap in these subjects is also extremely unlikely.

Finally, in a training study of 11 girls with severe idiopathic scoliosis (Cobb angle, 91; VC, 2.4; %VC, 60%), Bjure et al (1969) found a high HR response at a submaximal work rate pre training (average: 153 beats/min at 400 kpm/min). Following a three month training period, $\dot{V}O_{2\,max}$ increased by 22% and HR at 400

kpm/min dropped by, on average, 13 beats/min. This improvement in exercise capacity and HR response occurred in the absence of changes in pulmonary function over the same period. It is also interesting to note from this small study, that following training, $\dot{V}E_{max}$ increased in proportion to the improvement in $\dot{V}O_{2\,max}$ ($\dot{V}E/\dot{V}O_2$ remaining constant at 35 l/l) and that VT_{max}/VC increased from 0.46 to 0.54, illustrating how dependent these value are on the maximum power output achieved, and that in general, exercise capacity is not limited by ventilatory factors in this condition.

Chapter 7

Handicap: Analysis of contributors

For the purpose of these studies, handicap has been interpreted in terms of symptom intensities experienced during activity. It has been quantified by measuring the intensity of breathlessness and leg effort at a standardized work rate equal to 50% of each subject's predicted reference work capacity (50 %Wcap). As leg effort and breathlessness are distinct sensations (appendix 3), the two sensations will be evaluated separately, rather than attempting to derive a single quantitative assessment of handicap. In this chapter, we will try to account for the differences in sensory intensities experienced by these scoliotic subjects at 50 %Wcap. It has previously been noted that both breathlessness and leg effort were excessive during exercise in an abnormally large proportion of these subjects.

Section 3.6.1 and figure 3.4 show the severity of breathlessness and leg effort which subjects experienced at 50 %Wcap. Two subjects were unable to exercise to this level, and have been credited with maximal scores of 10 for both

sensations. A value of 10, rather than the actual symptom intensities they experienced at their Wcap (Wcap=47% predicted, Br=4, LE=4; Wcap=26% predicted, Br=5, LE=5), was chosen because, had they been able to achieve the index work rate of 50 %Wcap, their symptom intensities should have increased further. Whereas the assignment of "maximal" symptom intensities seems reasonable for the subject who achieved 26 %Wcap, it may be less suitable for the subject who just fell short of 50% Wcap. With the analysis that has been performed (logarithmic transformation of symptom scores), these assigned values should not bias the findings of the study. It was considered important to include these two cases as otherwise the most disabled subjects would have been systematically excluded, risking i) introduction of bias; ii) loss of some of the most informative data; and iii) reduced generalizability of the findings.

As previously noted, leg effort and breathlessness ratings at 50 %Wcap were not normally distributed; most subjects experienced little or no discomfort at this work rate (41/78 $\leq$ 2 "slight" for both sensations), but there is a positive skew to the right with a considerable number of subjects experiencing marked distress. Rather than use non parametric analyses, symptom ratings were Log (base 10) transformed to normalize their distribution. Although this transformation failed to normalize the raw data completely, it was adequate to normalize the residuals following regression analysis.

7.1 Breathlessness: Analysis of contributors

7.1.1 Deformity

No statistically significantly relationships were found between single or multiple features of deformity and breathlessness. These analyses were performed using single, multiple and stepwise multiple regression analysis; to avoid clutter, they are not presented in the thesis.

7.1.2 Pulmonary impairment

7.1.2.1 Single Features

Breathlessness at 50 %Wcap was not convincingly related to any single feature of pulmonary impairment. %RV ($p=0.03$, $r^2=6\%$) and %FRC ($p=0.03$, $r^2=6\%$) were weakly associated with breathlessness, but perhaps surprisingly, handicap from breathlessness tended to be greater when these volumes were larger ie. less abnormally reduced. In addition, taller subjects were more breathless at 50 %Wcap ($p=0.012$, $r^2=8\%$).

7.1.2.2 Combined features

Multiple regression analysis was used to identify the additive influences of features of pulmonary impairment on breathlessness. Although a great many combinations of factors were statistically significantly related to BR_{50}, the analyses presented here have been confined to the strongest and most physiologically informative of these. The observation that taller subjects tended to be more breathless was consistent and is included with these analyses.

A larger %FRC or %RV and taller stature had an additive influence on breathlessness. As shown in table 7.1, height and FRC together accounted for 13% of the variance in $LgBr_{50}$. Although %VC, when considered alone or in combination with height, was unrelated to breathlessness, it was highly significantly related when considered in combination with %FRC (partial $p=0.001$, $r^2=17\%$). To reduce complexity, this equation is not shown. Similarly, though not as convincingly, %TLC was also inversely correlated with breathlessness after differences in %FRC were accounted for. Although not originally intended to be part of the analysis, it was found that alveolar volume (TLC during a single breath manouver, TLC_{SB}) was not consistently the same as TLC measured using the steady state method, and was more closely related to intensity of breathlessness, particularly in combination with %FRC or %RV (table 7.1). Addition of %DCO or %KCO to this analysis further increased the proportion of variance accounted for, but this effect was small (table 7.1).

c	Ht (cm)	FRC (% pred)	TLC_{ea} (% pred)	TLC_{eb} (% pred)	DCO (% pred)	p	r^2	SD ($Lg_{10}Br$)
-2.9	0.015	0.0055				0.005	13	0.45
part. p	0.014	0.04						
-2.4	0.015	0.013	-0.013			0.002	18	0.44
part. p	0.01	0.005	0.047					
-1.6	0.01	0.014		-0.019		<0.001	33	0.40
part. p	0.02	<0.001		<0.001				
-1.4	0.012	0.019	-0.016		-0.009	<0.001	27	0.42
part. p	0.03	<0.001	0.013		0.004			
-0.9	0.011	0.016		-0.018	-0.007	<0.001	38	0.39
part. p	0.04	<0.001		<0.001	0.014			

Table 7.1 **Relationship of breathlessness to combined measures of pulmonary impairment.**

Equation: Lg_{10} Breathlessness at 50 %Wcap = c + mx, where c is the intercept and m is the slope shown in the table for the variable x.

Example: Lg Br_{50} = -2.9 + 0.015 Ht (cm) + 0.0055 %FRC p=0.005 r^2=13% SD=0.45
partial p values (part. p) are recorded directly under each variable in the table.

No influence of i) age at onset, ii) duration of scoliosis or iii) respiratory muscle strength could be detected on intensity of breathlessness. Nor was there any relationship between Br_{50} and measurements of peripheral muscle strength or mass. These analyses were performed individually, and in combination with the already described significant correlates of handicap due to breathlessness.

7.1.2.3 Cardiorespiratory response

The relationship of respiratory variables at 50 %Wcap to breathlessness ratings at the same work rate was examined. Specifically, analyses were performed to determine if breathing pattern, ventilatory efficiency or SaO_2 at 50 %Wcap were related to intensity of breathlessness.

There was no direct relationship between ventilatory efficiency, as assessed by the ventilatory equivalent for CO_2 ($\dot{V}E/\dot{V}CO_2$), and $LgBr_{50}$ ($p=0.5$). $\dot{V}E/\dot{V}CO_2$was still unrelated to breathlessness (partial $p=0.1$) after controlling for differences in non-deformed height, %VC and %FRC. Similarly, SaO_2 at 50 %Wcap was also unrelated to breathlessness ratings at the same work rate.

Breathing pattern was essentially unrelated to intensity of breathlessness. This was assessed by examining the relationship of i) breathing frequency ($p=0.4$) and ii) VT as a proportion both observed ($p=0.05$) and reference VC ($p=0.4$) for each subject, to $LgBr_{50}$. Given the weakness of the relationship between VT_{50}/VC

and $LgBr_{50}$ and the number of analyses performed, little importance can be attributed to this observation.

7.2 Leg effort: Analysis of contributors

A similar analysis to that outlined above, was performed to identify factors associated with handicap from leg effort.

7.2.1 Deformity

No relationship was detected between features of deformity and leg effort during exercise.

7.2.2 Pulmonary impairment

The features of pulmonary impairment which were associated with breathlessness were also associated with leg effort, as shown in the following equation:

$LgLE_{50}$ = -0.57 + 0.009 Ht + 0.015 %FRC - 0.016 %TLCSB - 0.008 %DCO

partial p 0.06 <0.0001 <0.0001 0.003

SD=0.36 r^2=38% p <0.0001 n=77

There was no relationship between leg effort and SaO_2 at Wcap 50% predicted.

7.2.3 Peripheral muscle factors

The relationship of leg effort at 50 %Wcap to leg muscle volume was determined from multiple regression analysis after first forcing age, sex and height into the equation. This method of analysis was required because leg muscle volume could not be standardized for differences in age, sex and height, whereas the index work rate at which sensory intensities were recorded, was standardized. Surprisingly, no significant relationship was found between LE_{50} and LMV:

$LgLE_{50}$ = - 1.6 + 0.007 Age + 0.013 Ht - 0.14 Sex - 0.04 LMV

partial p 0.3 0.2 0.5 **0.7**

SD=0.47 r^2=7% p= 0.4

In case differences in pulmonary impairment influenced LE_{50} and tended to obscure a relationship between leg effort and LMV, this analysis was also performed after controlling for differences in pulmonary function, but still no relationship was found between LE_{50} and LMV (partial p=0.8). This was also true for the other peripheral muscle assessments: LBM, partial p = 0.6; quadriceps strength, partial p = 0.9; hand grip, partial p = 0.1.

7.2.4 Cardiac response

Handicap from leg effort was weakly associated with a higher systolic BP response during exercise ($p=0.03$) and a tendency to a higher HR response, although the latter was not statistically significant ($p=0.07$).

7.3 Discussion

This study found that features of pulmonary impairment were associated with handicap due to breathlessness and leg effort during exercise. No relationship was found between features of deformity and intensity of either symptom.

7.3.1 Breathlessness

Lack of a direct relationship between %VC or %TLC and breathlessness was unexpected, though consistent with previously noted clinical observations (Mankin et al, 1964; Collis and Ponseti, 1969; Bjure et al, 1970; Weinstein et al, 1981). This lack of association may be partly accounted for by the modifying influence of differences in RV and FRC. Subjects with the same %VC tended to be breathless if RV or FRC were normal or increased. Restated, for subjects with the same %VC, those with a higher TLC tended to be more breathless. The association of a normal or increased FRC or RV with breathlessness may at first seem counterintuitive, but can probably be accounted for by the well recognized

normal relationship between a muscle's length and its force generating capacity (Spiro and Sonnenblink, 1964; Gordon et al, 1966). Shortening of the inspiratory muscles with increases in FRC, or during contraction (V_T generation), may reduce their functional strength (Killian et al, 1984; Leblanc et al, 1986; El-Manshawi et al, 1986). In the presence of scoliotic deformity, the optimal operating length of the inspiratory muscles may be at a lung volume considerably below normal FRC. Lack of association between MIP and breathlessness is also unusual and may suggest that spinal deformity has uncoupled this relationship. This interpretation is supported by lack of the normal association between VC and MIP in these subjects (previously noted in chapter 4).

An alternative explanation for the association between higher FRC and breathlessness could be that compliance of the respiratory system may fall rapidly at volumes considerably below TLC in scoliotics. If this were so, subjects who have failed to reduce FRC and RV may be forced to breathe in this less compliant zone.

In addition to these factors which are primarily mechanical in nature, efficiency of gas exchange would also be expected to correlate with breathlessness. Reduced gas exchanging efficiency should be associated with a relatively high $\dot{V}_E$ during work performance, which in turn would interact with any mechanical abnormalities to aggravate breathlessness. Failure to find a convincing

relationship between breathlessness and $\dot{V}E/\dot{V}CO_2$ suggests that this is not an important contributor to breathlessness in these subjects.

The association between greater non-deformed height and breathlessness may reflect the dominant influence of height in determining the work rate at which sensory ratings were recorded. If the coefficient relating height to predicted Wcap was inappropriately high, or if some subjects were unusually tall, this work rate may be disproportionately high for the tall subjects ie. greater than 50% of the Wcap that they might reasonably be expected to achieve. The finding that subject's armspans corresponded to an above average height, may support the latter of these two options. However, were this the only reason for the association between height and breathlessness, leg effort should also have been greater in the taller subjects, but this was not observed.

7.3.2 Leg effort

Surprisingly, no relationship was found between leg effort at this sub maximal work rate and either leg muscle strength or bulk. Previous studies have established that effort varies proportionally with the magnitude of the task, and inversely with capacity to perform that task (McCloskey et al, 1974; Roland and Ladegaard-Pedersen, 1977; Gandevia and McCloskey, 1977). As cycling work capacity is closely related to leg volume, leg effort was expected to be inversely related to leg volume. Failure to find this relationship is puzzling. It is unlikely to

be due to i) narrow spread of symptom intensities, ii) smaller number of subjects who had leg volume measurements, or iii) low reliability of sensory ratings at this stimulus intensity (50 %Wcap), because leg effort correlated with pulmonary function using the same approach to analysis. It is possible that leg effort may be related to muscle bulk at higher power outputs, accounting for the association between leg volume and disability, but that this does not occur at submaximal power outputs. This explanation is speculative.

Given the lack of association between leg effort and leg volume, the relationship between features of pulmonary impairment and leg effort is surprising. This relationship may be an epiphenomenon. Whereas there was only a limited relationship between intensity of breathlessness and leg effort at Wcap:

$$Br_{max} = 0.67 + 0.76\ LE_{max}$$

SD=1.9 r^2=48% p <0.001 n=78

---

these symptoms were very closely correlated at 50 %Wcap:

$$Br_{50} = - 0.06 + 0.85\ LE_{50}$$

SD=0.86 r^2=81% p <0.0001 n=77

Failure to find i) arterial oxygen desaturation, or ii) a relationship between severity of pulmonary impairment and a high heart rate response (as may accompany right heart dysfunction), suggests that higher ratings for leg effort at 50 %Wcap did not occur secondary to pulmonary impairment.

The role of sensory measurements during exercise in the quantification of handicap due to cardiorespiratory or neuromuscular disease has yet to be defined. If subjects can discriminate and quantify sensations reliably, and if differences in these ratings accurately reflect true differences in the discomfort which they experience, this information would be very valuable in the evaluation and quantification of handicap. As has been reviewed in chapter 2.2.6 and appendices 2 & 3, Borg score ratings are reproducible, and their reliability therefore appears to be satisfactory. The validity of sensory rating during exercise is less satisfactorily defined. If the wide scatter of sensory ratings (both leg effort and breathlessness) reported by normal subjects at the same relative work rates (see fig 3.4) represent true differences in sensory intensities, we would expect that subjects with greater discomfort at sub maximal power outputs would have systematically reduced exercise capacities. This theoretical construct is only partially supported. Killian et al (1992a) reported that in normal subjects, symptom tolerance (highest discomfort rating) at Wcap was only very weakly associated with %Wcap. In the present study, LE_{50} and Br_{50} were quite strongly predictive of %Wcap (LE_{50}: r^2=25%, $p < 0.001$; Br_{50}: r^2=25%, $p < 0.001$).

Finally, the method used to quantify symptomatic handicap in the present study could be criticized for relying on sensory ratings at a single work rate during the exercise test. It might be preferable to develop methods of quantifying handicap which utilize all sensory ratings reported during the exercise test. Such a method could improve the discriminatory function of handicap ratings.

Chapter 8

SUMMARY AND CONCLUSIONS

The series of studies outlined in this thesis help to clarify the relationships between spinal deformity, pulmonary impairment, exercise disability and symptomatic handicap in idiopathic thoracic scoliosis. Traditionally, severity of scoliosis has been assessed solely by the angle of scoliosis (Cobb angle), and it is widely believed that pulmonary impairment and disability are directly related to this assessment of deformity.

In common with earlier studies, we found that pulmonary function deteriorated with increasing Cobb angle, but that this relationship was weak. More importantly, three additional features of spinal deformity were identified (curve position, number of vertebrae involved, angle of kyphosis) which have an equal and additive impact on pulmonary impairment. The finding that pulmonary impairment is associated with multiple features of deformity helps to explain why there is a weak relationship between pulmonary function and Cobb angle alone. Non anatomical factors such as age at which scoliosis develops, duration of the

deformity, and respiratory muscle strength, did not account for differences of pulmonary impairment.

Contrary to expectations, extent and nature of spinal deformity was unrelated to disability or symptomatic handicap. Secondary physiological factors, rather than the primary anatomical disturbance, determined how disabled and handicapped these subjects were. The amount of muscle available to perform work was the single factor most closely related to each individual's work capacity. The relationship of maximum oxygen consumption to leg muscle volume was similar to that previously reported for normal subjects. This suggests that qualitatively, the peripheral muscles of the scoliotic subjects were normal, but that quantitatively, muscle bulk was reduced and contributed to disability.

The relationship of disability to pulmonary impairment was weak. In fact, until differences in muscularity were accounted for, the relationship between pulmonary function and work capacity was not significant for subjects of the same age, sex and height. Multivariate analysis revealed that pulmonary and peripheral muscle factors had a roughly additive influence on disability. Examination of the cardiorespiratory response to exercise found that scoliotics breathed with abnormally low tidal volumes, but that efficiency of gas exchange was essentially normal. Arterial desaturation did not occur, and ventilatory dead space did not appear to be increased. A high heart rate was observed during exercise, and subjects with the highest heart rate response were more disabled. It appears

therefore that disability in idiopathic scoliosis is multifactorial, a combination of peripheral muscle, pulmonary and cardiac factors all contributing to reduced work capacity (figure 8.1).

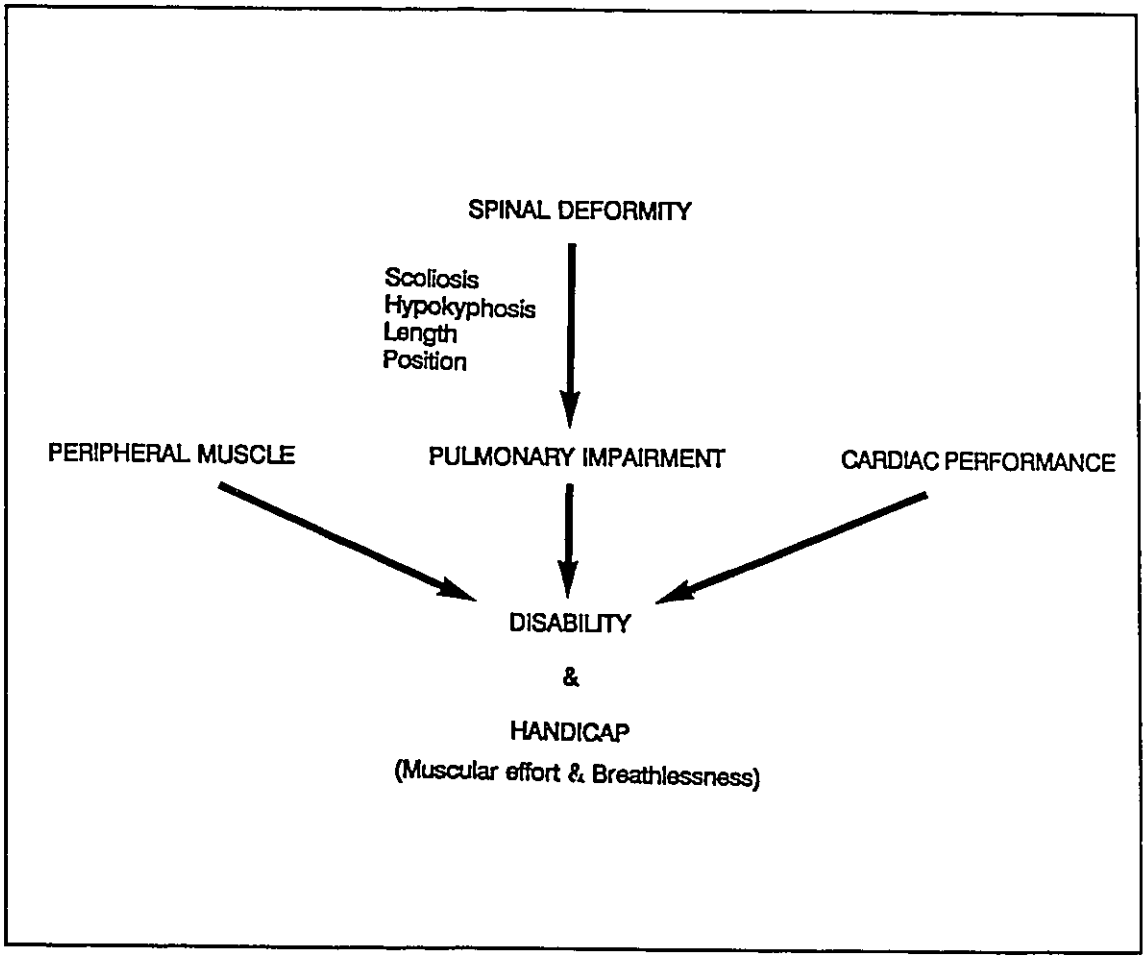

Figure 8.1 Schematic diagram depicting interrelationships of spinal deformity, physiological impairments, disability and handicap in idiopathic scoliosis.

Intensities of breathlessness and leg effort during exercise were abnormally high for many of these subjects. As with a normal population, symptoms relating to the exercising muscle dominated, reaffirming the importance of peripheral muscle factors as contributors to disability and handicap in these subjects. Exertional symptoms during exercise were unrelated to the nature and extent of spinal deformity. Pulmonary impairment was linked to breathlessness and disability primarily through reductions in ventilatory capacity, rather than inefficiency of gas exchange.

This study can not determine the cause of peripheral muscle and cardiac impairment in these subjects, but it seems likely that behavioral adaptations to the cosmetic, physiological or symptomatic consequences of the deformity contribute to deconditioning and a generalized lack of fitness.

There are a number of important clinical implications of these findings. Due to the extreme variability between the angle of scoliosis and pulmonary impairment, predicting pulmonary function from Cobb angle is not justified and will frequently be misleading. When pulmonary impairment is an issue, this should be measured directly. Spirometry is usually adequate for this purpose, although measurement of lung volumes may yield additional valuable information. Presence and severity of disability should not be estimated from either analysis of the spinal deformity or the pulmonary impairment. When severity of disability will influence management, this can be measured directly, simply and safely, using exercise testing. Exercise

testing can also help to identify the symptoms and pathophysiological mechanisms underlying disability and handicap, there by facilitating an individualized approach to their management. These studies also suggest that in addition to preventing progression of spinal deformity and pulmonary impairment, subjects with idiopathic scoliosis should be encouraged to exercise regularly to maintain muscular conditioning. Regular exercise would be expected to increase muscle bulk and fitness, thereby reducing the disability and symptomatic handicap which frequently accompanies idiopathic thoracic scoliosis.

Appendix 1

Calculation of non-deformed height

Height is the anthropomorphic measurement which shows the closest relationship to normal pulmonary function and exercise capacity. For this reason, usually in combination with age and sex, height is used to predict reference physiologic values for individual subjects, against which their own measurements can be compared (chapter 2). Scoliosis is associated with loss of height and if reference physiologic values for subjects with idiopathic scoliosis were to be calculated from deformed height, this would lead to an underestimate of predicted values and an underestimate of impairment or disability. To avoid this bias an alternative method of predicting normal reference values is required for these subjects. A number of options will be considered.

The first is not to use height at all in the in the prediction of reference values; physiological values are predicted from age and sex alone, or from age, sex and some other anthropomorphic measure. The disadvantage of this approach is that reference values obtained from these methods are much less

precise (wide confidence intervals around the estimate) or not available (Zorab and Prime, 1961; Johnson and Westgate, 1970; Helms et al, 1986).

A second, and generally preferred method, is to estimate the height subjects would have been in the absence of spinal deformity, and predict normal physiological function from this value. The best method of predicting non-deformed height appears to be from its relationship to arm span, although there is controversy as to exactly what this relationship is. For the purpose of this thesis, it is important to obtain as precise an estimate of non-deformed height as possible so that accurate assessments of impairment and handicap are obtained. In addition, if arm span to height (AS:Ht) ratio differs systematically with age or sex and this is not taken into account, the validity of the results may weakened.

Hepper et al (1964) studied the relationship of AS:Ht in 288 males and females between the ages of 16-63 years. They found an average AS:Ht ratio of 1.01 for females and 1.03 for males, with a systematic increase in this ratio with advancing age in males but not females. These ratios were in agreement with nine earlier studies which they reviewed. Gazioglu et al (1968) reported values of 1.01 for females and 1.02 for females. Johnson and Westgate (1970) reported a AS:Ht ratio of 1.03 for both males and females, with no age effect between 6-30 years. In an attempt to resolve these uncertainties, Linderholm and Lindgen (1978) studied 209 males and females (5-78 yrs) and found an average AS:Ht ratio of 1.01 for females and 1.03 for males, with a significant increase with aging. They

also described the relationship of Ht to AS and age in separate multiple regression equations for males and females. Kumano and Tsuyama (1982) described the relationship of Ht to AS as sex specific regression equations for children of 6-17 years, without an age adjustment. Hibbert et al (1988) studied 512 children from 8-18 years on repeated occasions and found that although AS:Ht varied statistically with age and sex, but with both variables, deviations from a ratio of 1.00 were trivial over this age range.

A method has also been described for calculating loss of height from radiographically measured angle of scoliosis (Bjure et al, 1968).

On the basis of i) similarity of the age group studied; ii) ability to adjust for differences in AS:Ht ratios with age ,sex and arm span; and iii) consistency of their findings with the literature as a whole; the regression equations of Linderholm and Lindgren were used in these studies to estimate non-deformed height (NDH) from arm span:

Males NDH (cm) = 0.9329 AS (cm) - 0.0732 A (yr) + 8.64 (SD=3.51, r_2=0.96)

Females NDH (cm) = 0.9405 AS (cm) - 0.0848 A (yr) + 9.88 (SD=3.60, r_2=0.94)

In a minority of cases where standing height was greater than estimated non-deformed height, this was used in the calculation of reference values, as abnormalities in arm span have been described in idiopathic scoliosis (Johnson and Westgate, 1970; Burwell et al, 1977; Stirling et al, 1986).

Appendix 2

Psychophysics

" The science dealing with the quantitative relationships between the characteristics or patterns of physical stimuli and the resultant sensations." (Dordand 1981)

Study of the relationship between a physical stimulus and the resultant sensation requires that both elements can be quantified. Whereas the physical stimulus can usually be directly and accurately measured (eg. light intensity, weight), measurement of the resultant sensation (eg. perceived brightness or heaviness) is not as straight forward and is more controversial (Stevens, 1946; Stevens, 1957). As measurement of sensations is fundamental to the assessment of handicap as performed in these studies, the following sections will initially deal with types of measurement scales in general, and subsequently with a description of the Borg scale specifically.

Measurement and Scaling

Measurement may be defined as "the assignment of numbers to objects or events, according to rules, to represent facts and conventions about them" (Stevens, 1946). The array of numbers used, and the rules which are adhered to when assigning these numbers determine the properties of the scale (measurement tool). Stevens (1946; 1951) formalized the classification of measurement scales into four types depending on their quantitative properties, which increase in sophistication in the following sequence: nominal, ordinal, interval and ratio. These four types of scales will be outlined briefly.

Nominal scale: Numbers are assigned according to "sameness", allowing distinctions to be made between subjects or groups, but the numbers do not indicate qualitative or quantitative differences. Eg. registration numbers assigned to participants in a race.

Ordinal scale: Numbers are assigned according to rank or relative position. In addition to distinguishing between subjects or groups, the numbers indicate qualitative differences but do not indicate the magnitude of these differences. Eg. Position (1^{st},2^{nd},3^{rd} ... last.) crossing the finishing line.

Interval scale: The interval between adjacent numbers is constant over the length of the scale, but the origin of the scale is not from an absolute zero. In addition to having the properties of the lower scales, the numbers indicate by how

much two or more measurements differ from each other, but cannot be used to determine their proportionality (see ratio scale). Eg. Time interval between when the winner and subsequent runners cross the finish line.

Ratio scale: In addition to equality of the interval between numbers, a ratio scale has its origin at an absolute zero. The properties of the three lower scales are present but now proportionality or ratio relationships between different measurements can be determined. Eg. Time taken to complete the race. The relative speed of one runner to another can be calculated as all are timed from the same origin, zero time, at the start of the race.

Knowledge of the properties of a scale (ie. type) are important as these properties govern the type of manipulation and analysis which can be performed with the data (Stevens, 1946). Parametric analyses, in addition to assuming a normal distribution of the values for a variable in a population, requires equality of intervals along the scale. It is therefore not meaningful or acceptable to calculate parametric statistics (eg. mean, SD, regression analysis) from data recorded from nominal or ordinal scales. Measurements made on interval scales, although suitable for parametric analysis, should not be manipulated by multiplication or division (ie. determination of ratio relationships) as, in the absence of an absolute zero on such scales, these calculations are not valid.

Historically, different types of scales and mathematical models have been used to describe psychophysical relationships. This introduction will not review the

history of psychophysics in any depth, but instead will describe the evolution, strengths and limitations of the Borg scale which has been used in these studies.

Borg Scale

Whereas there has never been debate that subjects can distinguish sensory intensities (eg. mild as opposed to severe pain), it was generally believed that sensory magnitudes could not be directly measured until this was demonstrated by Stevens. Using open magnitude ratio scaling (eg. matching of freely selected numbers to perceived sensory intensities so that the ratio relationships chosen matched ratio changes of the perceived sensation) Stevens established that valid direct sensory measurements could be made, yielding reproducible psychophysical relationships, both within and between subjects (Stevens, 1957; Stevens and Galanter, 1957; Stevens et al, 1960; Stevens, 1971). Sensory magnitude (Ψ) was shown to increase as a power function (exponent = n) of the physical stimulus (PS) as expressed by the equation:

$$\Psi = k \times PS^n$$

where the exponent (n) is a measure of perceptual sensitivity, indicating proportional changes in sensory magnitude for a given change in stimulus magnitude, and k is a constant. For example, with an exponent of 1.6 (n) relating perceived heaviness (Ψ) to lifted weight (PS), a doubling of weight is associated with a 3 fold increase ($2^{1.6} = 3.0$) in heaviness.

Although reproducible psychophysical relationships are obtained with ratio scaling methods, a serious limitation is the inability of these scales to yield measures of absolute sensory intensities for comparisons between individuals - how did one subject's rating of "10" correspond to another's "500", for example. Stipulating that each subject match the same number (eg. 100) to an initial index physical stimulus (eg. 1 kg. weight) does little to overcome this limitation - there is no reason to believe that the resultant sensory magnitude would be the same in different subjects (eg. perceived heaviness of a 1 kg. weight for a child or an adult).

Borg undertook to develop a new scale which was to have the following desirable properties: i) simplicity of use; ii) ability to measure absolute sensory intensities, thereby permitting valid comparisons between individuals; iii) ratio properties. There were four guiding principles for the development of the new scale: i) acceptance that Stevens' ratio scales were the best scales for deriving psychophysical exponents (description of variations in perceptual sensitivity to different physical stimuli); ii) belief in the "range theory" (see below); iii) knowledge of quantitative semantics (see below); and iv) utilization of known psychophysical relationships (Borg, 1980). According to the "range theory", there is a finite range of perceptual intensities extending from threshold (just noticeable) to maximal, which is common for all subjects, although the corresponding range of physical stimulus magnitudes which results in this sensory range may differ markedly between individuals (Borg, 1961). It follows that a scale ranging from zero to

maximal intensity will cover the perceptual range for all subjects, scaling any sensation. Quantitative semantics required Borg and associates to determine which commonly used descriptors (eg. mild, moderate, severe) were used most precisely in a quantitative manner, and the relative quantitative content of these terms (eg. "somewhat strong" was empirically found to be twice as intense as "weak") (Borg and Hosman, 1970; Borg and Lindblat, 1976).

Against this background, Borg developed a scale from 0 - 10, along which specific descriptor terms were anchored so that use of this category scale would reproduce psychophysical relationships (exponents) previously validated by Stevens' more rigorous scaling methods (Borg, 1980). As such this is a category scale with ratio properties.

The psychometric properties of a scale can be assessed under two headings, the reliability and validity of the measurements obtained (Streiner and Norman, 1989). Reliability reflects the ability of a scale to make reproducible and consistent measurements. Reliability of the Borg scale is reviewed in the methods section when various measurements are discussed. Validity reflects the ability of a scale to measure what we think it is measuring, thereby allowing us to be confident of the conclusions (inferences) we reach from these values.

Validation of the Borg scale is incomplete, it is uncertain whether it does truly have ratio properties and it may exert a ceiling effect - highest sensory values being negatively affected by the upper end of the scale. Extensive experience with

this scale in this laboratory and elsewhere (Borg, 1980; Marks et al, 1983; Killian et al, 1992a; Killian et al, 1992b) has confirmed that it does reproduce valid psycnophysical relationships (though the exponents tend to be marginally smaller than with magnitude estimation (Marks et al, 1983)) suggesting that it has adequate ratio properties. Furthermore, consistency in the relationships between symptom intensities rated on this scale and physiological measurements, also suggest valid measurement of absolute intensities (Marks et al, 1983; El-Manshawi et al, 1986; Leblanc et al, 1986; Killian et al, 1992b; Kearon et al, 1991b; Mahler et al, 1991).

Appendix 3

Muscular sensations

The term "kinesis" denotes movement or motion and "kinaesthesia", the sense by which movement, weight, position etc. are perceived (Dorland, 1981). Although skeletal muscles are the machinery by which movement is performed, their role in kinaethesic sensibility has been controversial. During the early part of this century it was widely believed that muscles had a sensory role, receiving and transmitting sensory information to the cortex and to conscious perception (for review see McCloskey (1978)). This was later rejected when it was demonstrated that "selective" anaesthesia of skin and joint receptors markedly reduce kinaesthetic sensibility. Turning full circle, more recent evidence has challenged these findings and now, not only supports a sensory role for muscles and tendons, but suggests that they are the prime location of receptors for kinesthetic sensations (McCloskey, 1978).

Specifically, these sensations include i) **tension:** perceived force generated either actively or passively within muscle, for which Golgi tendon organs are thought to be the receptor (McCloskey et al, 1974; Roland and

Ladegaard-Pedersen, 1977); ii) **position or displacement:** for which muscle spindles are thought to be the receptors, sensing changes in muscle length (Roland and Ladegaard-Pedersen, 1977); iii) **effort:** the willed motor command to the active muscle, for which interneurons high in the central nervous system are thought to be the receptors, relaying this information to consciousness (McCloskey et al, 1974; Roland and Ladegaard-Pedersen, 1977; Gandevia and McCloskey, 1977). In addition to these specific kinaesthetic sensations, muscles can also sense pain, if pain receptors are stimulated by trauma or over use.

Similarly, the ability to sense changes in i) **intrathoracic pressures** (Bakers and Tenny, 1970) is thought to be due to changes in respiratory muscle tensions, and changes in ii) **pulmonary volumes** (Bakers and Tenny, 1970), due to changes in respiratory muscle length (for review see Killian and Campbell (1985)). As will be elaborated on later, iii) **respiratory muscle effort** appears to be closely related to breathlessness (Killian et al, 1984).

In addition to these primary muscular sensations, deviation from the normal interrelationships of these sensations can also be distinguished, for example, changes in impedance (tension / displacement) (Campbell et al, 1961; Bennett et al, 1962) or muscle strength (tension / effort) (Gandevia and McCloskey, 1977; Campbell et al, 1980).

At rest, the intensity of kinaesthetic sensations is low and usually does not reach consciousness, but during muscular activity these sensory inputs increase

and may lead to a marked feeling of discomfort. As all kinaesthetic sensations increase during activity, the quality of this discomfort depends on the extent and balance of each of these inputs. This varies with the nature of muscular activity. When muscle action is impeded, tension is high and rate of displacement is low; when muscle action is unimpeded, tension is low but rate of displacement is high. Although kinaesthetic sensory quality may differ markedly with circumstances, the intensity of muscular discomfort during activity, both for the respiratory (Killian et al, 1984) and peripheral muscles (Gandevia and McCloskey, 1977), appears to be dominated by the effort component, regardless of the pattern of muscular activity. Therefore, breathlessness and peripheral muscle effort are the dominant symptoms during exercise. During tasks requiring subjects to progressively increase power output, or to maintain a high work rate for a prolonged duration, both symptoms increase progressively and either singly or in combination ultimately limit exercise both in normal subjects (Kearon et al, 1991a; Killian et al, 1992b) and in patients with cardiorespiratory disease (Killian et al, 1992b; Escourrou et al, 1990). The following sections will examine the nature of muscular effort and breathlessness in greater detail.

Muscular Effort

As with kinaesthetic sensations in general, the existence of a sense of effort or "innervation" was for long the subject of debate (for review see McCloskey et al (1974) and McCloskey (1978)), receiving support in the early part of this century,

subsequently losing it, only to regain it following the results of more recent studies (McCloskey et al, 1974; Roland and Ladegaard-Pedersen, 1977; Gandevia and McCloskey, 1977). These studies documented increases in perceived effort when muscles were required to generate the same tension after being weakened by prior activity (fatigue) or partial neuromuscular blockade. Perceived tension and effort were thus established to be distinct sensations. In contrast to the senses of tension and position, effort is enhanced by partial chemical denervation, indicating that the muscle itself does not feed back this sensory information to the cortex. Instead it has been proposed that "efferent copy" from the motor cortex is relayed by interneurons high in the central nervous system, causing the willed command to reach consciousness (McCloskey, 1978).

Muscle contraction results in generation of tension and / or shortening. At one extreme, when muscles contract against an insurmountable impedance, maximal tensions are generated without shortening (isometric contraction). At the other extreme, when muscle contraction is unimpeded, minimal tensions are developed but the rate of shortening is maximal (isotonic contraction). Muscles normally function at neither of these extremes but generate an intermediate tension and extent of shortening, the product of the two being work performance. Similarly, the product of tension and the rate of shortening is muscular power output. The capacity of a muscle to perform work and generate power varies according to the balance of force development (tension) and the velocity of shortening, as was originally described by Hill's force velocity relationships (Hill,

1938). During maximal contractions, velocity of shortening is achieved at the expense of ability to generate tension, and vice versa.

The studies outlined above established the following relationship: effort $\propto$ mechanical task / muscle capacity. From this expression it is evident that perceived effort will increase if either the mechanical task increases, the capacity of the muscle decreases or both occur simultaneously. A muscle's capacity to generate tension and/or rate of shortening, decreases (functional weakness) when muscle length is longer (partially stretched) or shorter (partially contracted) than an optimal value which approximates to resting length (length : tension relationships (Spiro and Sonnenblink, 1964; Gordon et al, 1966)). Therefore, the effort required to achieve a given tension and rate of shortening is also dependent on a muscle's operational length.

In the studies which make up this thesis, subjects cycled on an ergometer at a constant velocity (60 revolutions per min) while the resistance against which they pedalled was incrementally increased each minute, so that the power output of the leg muscles would increase by 100 kpm/min each min. Therefore, a progressive increase of leg effort is to be expected on the basis of increasing mechanical load. In addition, leg muscle capacity to meet these demands may fall due to muscle fatigue during the test. With an incremental exercise test such as the one used in these studies, fatigue is likely to be a minor contributor to leg effort compared to the increases in mechanical demand (Kearon et al, 1991a).

Breathlessness

As previously outlined, respiratory muscles, like skeletal muscle in general, have a kinaesthetic role, sensing volume, rate of change in volume (flow), pressure and ventilatory effort. In addition to muscular sensations, irritation of the airways may invoke the need to cough or, with greater trauma, a poorly localized visceral discomfort. Alhough less well described, subjects may also be aware when breathing is inadequate for gas exchange demands, for example during experimentally induced hypercapnic ventilation, which has been termed the "need to breathe". The overall quality of respiratory sensation depends on the balance of all of these sensory inputs.

During normal breathing at rest, subjects are usually unaware of respiratory sensations. When normal subjects are required to generate large ventilations (eg. exercise) or when, under experimental or pathological conditions, the impedance to breathing increases, respiratory sensations become uncomfortable. Throughout this thesis, the term breathlessness refers to any "discomfort associated with the act of breathing"[1]. Although the quality of breathlessness may vary with the circumstances of its production, the magnitude or intensity of breathlessness has been shown to be closely related to respiratory muscle effort (Killian et al, 1984).

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[1] The term "breathlessness" is sometimes reserved to reflect "the need to breathe" and "dyspnea", to reflect "difficulty in breathing" - this distinction is not implied in the use of this term in this thesis.

The mechanical factors relating the respiratory muscles and their pattern of activity to the intensity of breathlessness have been well described and support this concept (Killian et al, 1984; Killian and Campbell, 1985; Leblanc et al, 1986; El-Manshawi et al, 1986; Mahler et al, 1991; Kearon et al, 1991b). Breathlessness increases when the demand on the respiratory muscles increases, as with large ventilations, resistive or elastic impedances to breathing; or when the ability of the respiratory muscles to meet ventilatory demands is reduced, as with muscle weakness - either absolute, following activity (fatigue), or functional (sub-optimal length:tension, force:velocity relationships). Particularly relevant to scoliotic patients, abnormal coupling of respiratory muscle forces to the chest wall ("mechanical uncoupling"), or chest wall distortion during the act of breathing, would also be expected to increase inspiratory effort and breathlessness. Although there is much support for this mechanical/respiratory muscle approach to understanding the mechanisms which underlie breathlessness, it should be noted that it is not universally accepted (Anonymous, 1986), but further debate of these issues is beyond the scope of this thesis.

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At the end of each subject's incremental exercise test, ratings for intensity of breathlessness and leg effort were of a similar magnitude, although higher for leg effort on within subject comparison ($p=0.0005$). The maximum symptom intensity experienced, termed symptom tolerance, corresponded to "very severe". Symptom tolerance was the same as for normal subjects (Killian et al, 1992b).

The relative intensity of breathlessness and leg effort at work capacity is shown below (figures 3.4 and 3.5).

37/78 (50%) of subjects identified leg effort as the limiting symptom. 25/78 (32%) complained of an equal intensity of both sensations, while only 14/78 (18%) were limited predominantly by breathlessness. The proportion of subjects falling into these three symptom categories was no different than for the reference population reported by Killian et al (1992b), who used the same exercise and symptom recording protocol ($Chi^2=4$, $p=0.14$). Using different protocols, earlier studies have also reported that peripheral muscle symptoms usually dominate when normal subjects perform at high power outputs (Strandell, 1964; Slonim et al, 1957; Astrand, 1958; Bruce, 1984b).

In figure 3.6, symptom intensities experienced by these scoliotic subjects at i) 50 %Wcap, and at ii) Wcap, have been compared to normal subjects at the same relative work rates. This figure also shows the proportion of subjects at each of these work rates whose ratings exceeded the 95^{th} centile.

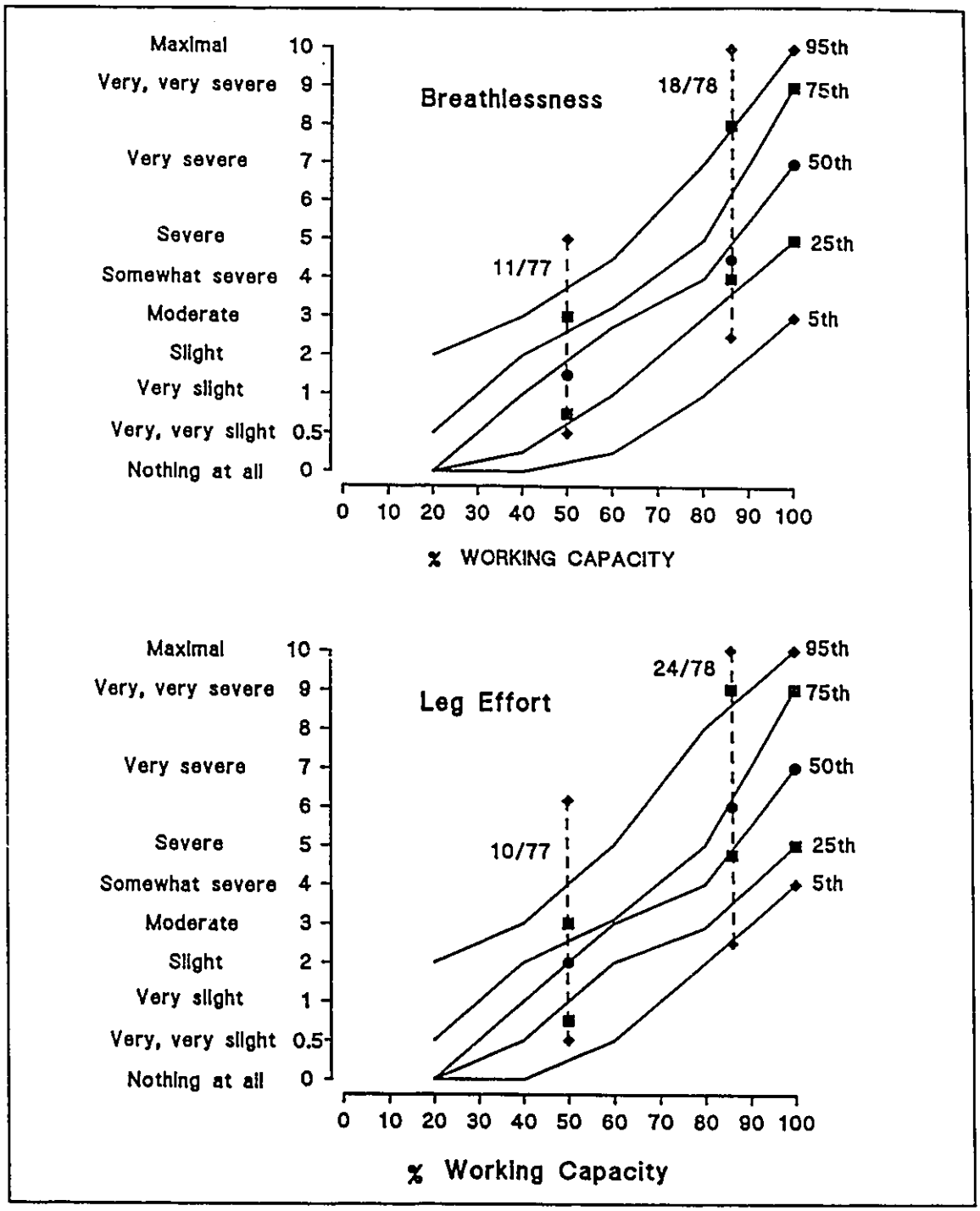

Figure 3.6 Normal ratings for breathlessness and leg effort during incremental exercise, with superimposed ratings for the scoliotic subjects at 50 %Wcap and at Wcap.