PHYSIOLOGICAL RESPONSES TO EXERCISE FOLLOWING DISUSE MUSCULAR ATROPHY IN MAN

by

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"Exercise is not a mere variant of rest ....
.... it is the essence of the machine."

Joseph Barcroft.

ABSTRACT

Measurements were made of the physiological responses to exercise in patients who had had one leg immobilised following bone fracture. As a consequence of immobilisation they had muscular weakness and atrophy of the affected limb. Data were also collected for comparative purposes on normal healthy male subjects. Exercise was performed pedalling a stationary bicycle ergometer with each leg separately and both legs together and a system was developed to enable the pattern of force exerted on the crank by each leg to be measured. Anthropometric data including estimates of total leg and component tissue volumes were also obtained.

Analysis of the pattern of force exerted in cycling established the comparability of 1-leg exercise involving patients' injured or uninjured legs. In 2-leg cycling the patients showed a disproportionate sharing of work between the legs, although the actual 'pattern' of force remained the same in both legs and the same as in 1-leg cycling.

In submaximal exercise with the patients' injured leg the oxygen uptake ($\dot{V}O_2$) for a given work load and cardiac frequency for a given $\dot{V}O_2$ were higher than with the uninjured leg. Rated perceived exertion was also higher for a given $\dot{V}O_2$ during exercise with the patients' injured leg, but this difference was removed when $\dot{V}O_2$ was expressed in relative terms (% $\dot{V}O_{2\ max}$).

Maximum oxygen uptake ($\dot{V}O_{2\ max}$) was reduced by ~ 17% in the injured (cf. uninjured) leg, and was associated with the degree of muscle atrophy estimated anthropometrically. In 2-leg exercise there was a greater reduction of $\dot{V}O_{2\ max}$ for a given leg muscle (plus bone)

volume when comparison was made with normal subjects.

The effect of rehabilitation therapy undertaken by the patients was to restore 1- and 2-leg exercise responses towards normal. The patient data were interpreted in relation to normal data including consideration of the effect of habitual limb preference.

ACKNOWLEDGEMENTS

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CONTENTS

Page

CHAPTER 5

CHAPTER 6

CHAPTER 7

APPENDIX 1

APPENDIX 2

Reprint of: Davies, C.T.M., and Sargeant, A.J., (1975b) Physiological responses to exercise in patients following fracture of the lower limb. Scandinavian Journal of Rehabilitation Medicine 7, 45–50.

APPENDIX 3

Reprint of: Davies, C.T.M., and Sargeant A.J., (1975c) Changes in physiological performance of the lower limb after fracture and subsequent rehabilitation. Clinical Science and Molecular Medicine 48, 107–114.

APPENDIX 4

Reprint of: Davies, C.T.M., and Sargeant, A.J., (1975d) Effects of training on the physiological responses to one- and two-leg work. Journal of Applied Physiology 38, 377–381.

CHAPTER 1

INTRODUCTION

INTRODUCTION

The effect of changing activity patterns on man's capacity for exercise has been observed and exploited since the earliest civilisations. Primarily this exploitation has been aimed at ensuring the survival of society in times of conflict, but at other times it has been channelled into the search for victory in that other war without weapons, sport.

It is, however, only in the last century that scientist have begun to systematically investigate the physiological effects of physical training. The interest of soldiers, politicians and sportsmen as well as the scientific community has prompted studies leading to the creation of an extensive literature on the effects of physical training in man, and to a lesser extent, woman. However, the highly trained individual is only one end of a continuum which ranges down through the "active but untrained" to the sedentary and beyond.

Whilst there have been many studies on the physiological effects of training, the converse, that is the effect of detraining, or immobilisation has received relatively little attention and it is the latter aspect which is the subject of this thesis. Specifically, the thesis sets out to examine the effects of disuse muscular atrophy resulting from prolonged immobilisation on the physiological responses to exercise.

Early investigations into the physiological effects of inactivity in man were primarily concerned with metabolic and regulatory changes occurring at rest (e.g. Cuthbertson 1929, Taylor et al 1945, Deitrick et al 1948). It was not until the arrival of manned space flight in the 1960's that changes in the physiological responses to exercise were systematically studied. The most comprehensive account of the changes occurring was provided by Saltin et al (1968) who immobilised five subjects for three weeks with bed rest and then subjected them to 55 days of physical training. However by the very nature of bed rest studies it is difficult to distinguish between the influence of central and peripheral factors in modifying the exercise response since there is probably a deterioration affecting all levels of the oxygen transporting system (e.g. cardiac function, muscle size, enzyme systems etc.). A different approach was therefore required in order to isolate the effects of disuse of skeletal muscle.

One interesting approach to the problem of dissociating central and peripheral factors was pursued by Clausen et al (1970), in their case in an investigation into the nature of the training process. In this they studied the effects of training one pair of a subject's limbs, arms or legs, on the response to exercise with the other pair; both the trained and the untrained limbs being connected to the same central cardiorespiratory system. A similar approach applied to studying the effects of muscle disuse seemed a possibility, although there were obviously some difficulties in comparing different pairs of limbs.

A more promising adaptation of this idea seemed to be to study the effects of immobilizing one of a pair of limbs, for example one leg. Thus the response to exercise with that leg alone could be directly compared with the contralateral leg which would act as an intra-subject control; both legs being served by the same cardio-respiratory system and being subject to essentially the same genetic influences.

Fortunately, there was an existing patient group who following leg fracture had had one leg immobilised in a plaster cast for a prolonged period but who were otherwise healthy and ambulatory. After removal of the cast when the fracture had healed the injured leg of these patients showed the typical wasting and muscular weakness associated with prolonged immobilisation whilst the uninjured leg appeared normal in function and size. If satisfactory measurements could be made at this time of the response to exercise using each leg separately, it was clear that these patients would provide a useful experimental model for studying the effects of disuse muscular atrophy on the physiological response to exercise.

Therefore fundamental to the use of this experimental model was the development of techniques for studying the responses to submaximal and maximal dynamic exercise using one leg.

<u>One limb exercise</u>

Whilst exercise performance using both legs or both arms had been studied many times (see Bevegård and Shephard 1967 for a general review) work with a single limb had been largely neglected. Duner (1959) made the first comparative study of one and two leg cycling in normal subjects. In submaximal exercise with one leg he found that oxygen uptake and blood lactic acid level at a given work load, and cardiac frequency at a given oxygen uptake were increased as compared with the responses elicited in two leg cycling. No direct maximal measurements were made in the study. Physical working capacity was taken as the work output occurring at a cardiac frequency of 170 beats/minute; In one leg cycling this was 73-80% of the level achieved in two leg cycling.

Carlson and Pernow in a series of papers presented data on the response to submaximal exercise performed cycling with one leg. However they made no definitive measurements of maximal response or systematic comparison of one and two leg cycling since they were primarily interested only in a form of exercise which would enable them to study patients suffering from circulatory disorders, notably atherosclerosis obliterans (Carlson and Pernow 1959, 1961, 1962, Carlson, Pernow and Zetterquist 1962, Pernow, Wahren and Zetterquist 1965).

Freyschuss and Strandell (1968) were interested in whether the differences in response to exercise with the arms compared with legs were attributable to arm work per se or whether they merely reflected modifications resulting from a smaller muscle mass being utilised. To investigate this question they studied the circulatory adaption to submaximal leg exercise using a reduced muscle mass, that is one compared with two leg cycling. Their findings largely confirm those of Dunér (1959) and led them to the conclusion that the observed differences in circulatory and metabolic adaptation to exercise with the arms and the legs was largely a reflection of the reduction in active muscle mass.

One leg cycling was used by Bergstrom and Hultman (1966) as a simple practical way of depleting the muscle glycogen level in one leg without affecting the other. A similar approach was used in a later study of substrate utilisation in prolonged exercise by Pernow and Saltin (1971). Incidental to their main findings these latter authors report for the first time direct measurements of the response to maximal exercise using one compared with two legs. They found that in one leg cycling their subjects could achieve 75% of the maximum oxygen uptake achieved in cycling with both legs. Coincidentally this agrees with the value found for PWC_{170} by Duner (1959) although this may be somewhat fortuitous since Duner's observations were submaximal and take no account of difference in mechanical efficiency or of the differences noted by Pernow and Saltin in maximal heart rate in the two types of exercise (193 and 183 beats/min respectively in two and one leg cycling).

It was against this somewhat limited background that I started to investigate the physiological responses to one leg exercise. In particular it should be noted that none of the studies of one leg cycling reviewed attempted to relate the responses to the size of the muscle mass involved although the tacit assumptions have been made since Duner (1959) that the contralateral legs in normal subjects were identical in size and function and that the performance of one-leg cycling employed half the mass of muscle compared with two-leg cycling. The validity of the latter assumption depended upon the pattern of cycling and hence the muscle mass involved being the same, although this had not however been supported by objective measurements.

Effects of Disuse on muscle structure and function

There were no studies of one leg cycling in subjects following periods of muscle disuse. Indeed there was a lack of data generally on the functional and structural effects of disuse of skeletal muscle in man. This was surprising considering that the effect of different activity patterns first found scientific generalization in the "aktivitätshypertrophie" and "inaktivitätrophie" concepts proposed by Roux (1905) at the turn of the century.

There were for example no existing data (with the sole exception of a single case study, Hills and Byrd 1973) on the changes in limb (and component tissues) volume resulting from immobilisation. The only previous data on the effects of immobilisation on limb size were usually based on single circumference measurements of the limb (e.g. [illegible] et al [illegible], [illegible] 1964; [illegible], Friedebold and Strand 1968; Patel, Razzak and Dastur 1969). Fried and She[illegible]d (1970) did attempt to improve on this approach by measuring muscle width from X-rays, hence removing the confounding influence of subcutaneous fat, although again only at one point. All of these measurements fail to take into account any geometric or regional differences in the limb.

Data regarding the effects in man of muscle atrophy on the physiological responses to dynamic exercise and the aerobic function of muscle were lacking. There was only one study (Fried and Shephard 1970) of the response to exercise in patients who were recovering following prolonged immobilisation of one limb in a plaster cast; but unfortunately these authors only measured the responses elicited in two leg cycling. The only other data available was on the effects of whole body immobilisation (see Saltin et al 1968 for general review) but this is difficult to interpret for the reasons indicated at the beginning of this chapter.

Thus the proposed experimental model based on patients recovering from fracture of one leg (illustrated in plate 1) required the development of techniques for assessing the degree of muscle atrophy as well as for measuring the response to one leg exercise.

Plate 1. Patient with disuse muscular atrophy of the left leg. The photograph was taken 7 days after the end of 160 days immobilization of the left leg in a plaster cast, following fracture of the tibia and fibula.

CHAPTER 2

Leg volume and composition following immobilisation.

Introduction

In order to assess the degree of disuse muscular atrophy in a patient's injured leg (see plate 1) a method was sought which would enable an accurate assessment to be made not only of the volume of the whole leg but also of the major component parts; muscle, bone and subcutaneous fat.

Zook (1932) proposed a segmented model for measuring the relative size of various parts of the human body and a number of subsequent investigators have adopted this approach to measure limb volumes using water displacement methods (e.g. Dempster 1955, Carns and Glassow 1957, Drillis and Contini 1964). More recently Jones and Pearson (1969) have developed and validated an anthropometric technique. In this the leg is considered as a series of segments each of which approximate to the form of a truncated cone, the volume of which can be calculated knowing the circumference of the two parallel surfaces and the height (Figure 1). When used in combination with an estimate of subcutaneous fat thickness derived from calliper measurements this technique has the added advantage that it enables the volume of the muscle plus bone tissue to be calculated.

Methodology

I therefore sought to apply and extend this anthropometric technique to the study of the present patient group. 20 patients who had suffered leg fracture were studied initially at the start of exercise therapy following prolonged immobilisation of the injured leg (mean period 117 days). In addition a group of normal healthy males were also studied. Full details of both groups are given in Appendix I. Leg volume was estimated both anthropometrically

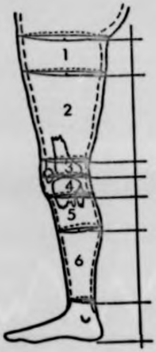


Figure 1. Schematic diagram of the leg illustrating the division into segments and the sites from which anthropometric measurements were taken.

(After Jones and Pearson 1969)

(Jones and Pearson 1969) and independently from leg X-rays (Jones 1970 a).

Estimates of total leg volume based on both anthropometric and X-ray measurements as were calculated in this investigation have previously been shown to be highly correlated with volumes determined by water displacement (Jones and Pearson 1969, Davies, Barnes and Godfrey [illegible], Katch et al 1973, Davies 1974). It was not surprising therefore that in this study independent assessment of leg volumes in patients and normals by X-ray techniques were highly correlated ($P < 0.001$; cv. 4 – 6%) with only a slight and non-significant bias towards underestimation ($\sim 1.5\%$) by anthropometry in the patients (Table 1 of Appendix I).

In order to assess component tissue changes anthropometrically I examined the relationship of skinfold calliper with direct X-ray measurements of subcutaneous fat thickness. This relationship was linear and highly significant (usually at the level of $P < 0.001$) for all four sites measured on the patients' injured and uninjured legs and on the normal subjects' right and left legs (Table 2 of Appendix I). Thus the appropriate regression equation can be used to correct calliper measurements to true thickness. The latter values may then be deducted from the total diameters derived from circumference measurements of the respective limb segments to give a diameter for the calculation of muscle plus bone volume.

In previous studies in normal subjects (see Davies 1974 for general review) 2-leg exercise performance, assessed in terms of maximum oxygen uptake, has usually been related to leg volume corrected for subcutaneous fat, that is, muscle plus bone volume estimated from anthropometric measurements. Since bone constitutes a relatively small proportion of the leg volume it seems reasonable to argue that its inclusion is likely to make only a small systematic difference when estimating the size of the effective muscle mass used in exercise; and that this small systematic error may be preferable to the widespread use of X-ray techniques for non-therapeutic purposes.

The present data confirmed that bone volume as calculated from X-ray measurements by the method suggested by Jones (1970a) was indeed a rather small and remarkably constant proportion (11 ± 1%) of the muscle plus bone volumes of the uninjured legs of patients and normal subjects. This proportion was larger and more variable in the patients injured leg being dependent upon the degree of muscular atrophy. However, the actual volume of bone was the same in the patients injured and uninjured legs.[1] Thus if the bone volume was assumed to be 11% of the uninjured leg muscle plus bone volume, the error involved in using this to derive muscle volume alone of the injured leg, as compared with using an estimate based on direct X-ray measurements was very small indeed (cv. 1%, equivalent to ± 60 ml of muscle volume – Figure 2).

<u>Anthropometric Survey of Patients.</u>

Using the anthropometric techniques described, estimates were made of the total leg and component tissue volumes in 16 young male patients at the beginning and end of a residential course of exercise therapy. This data is given in detail by Table 3 of Appendix 1. At the commencement of therapy the total leg volume of the patients injured leg was

[1] No attempt was made to calculate the volume of callus formed around the fracture site and personal observation indicates that this is in any case very small in the majority of fractures.

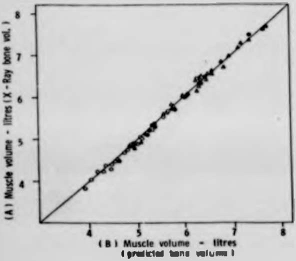


Figure 2. Leg muscle volume derived from anthropometric measurement of muscle plus bone volumes using: (A) the bone volume calculated from X-ray measurements (Jones 1970a).
(B) the predicted bone volume (i.e. 11% of the muscle plus bone volume). In the case of the patient's injured leg the bone volume was calculated as 11% of the uninjured leg muscle plus bone volume.

The line of identity is shown. Data points are for patients injured (o) and uninjured (•) legs, and the right and left legs of normal subjects (▲).

significantly smaller ([illegible] ml; P < 0.001) than the uninjured leg. Considered in terms of the major component tissues it will be seen from Figure 3 that this difference was attributable to a reduction in the muscle volume in the injured leg. In fact the difference in muscle volume was 860 ml (P < [illegible]) but part of this reduction was obscured by a slightly (170 ml) but significantly (P < 0.05) greater volume of subcutaneous fat in the injured as compared with the uninjured leg. Following exercise therapy there was a reduction in the fat volume of the injured leg by 80 ml and in the uninjured leg by 10 ml and as a consequence this significant difference was removed. These observed differences and changes in fat volume are most interesting since they seem to be in opposition to the widely held view (see e.g. Dempsey 1974) that body fat cannot be accumulated or be removed on a local basis as a result of the activity level of underlying muscle. The changes are however admittedly small and until further confirmation is produced the possibility that they are artifacts of the measurement techniques cannot be entirely discounted.

Following exercise therapy (mean length 50 days) the muscle volume of the injured leg had increased by 360 ml (8% - Figure 4). In contrast 7 normal healthy male subjects who took part in an intensive training programme (see Chapter 5) of similar duration showed no significant change in muscle volume. The mean rate of increase in the muscle volume of the injured leg was 1.2% per 10 days and this rate seemed relatively constant in a given individual over the period studied (Table 3 and Figure 1 of Appendix 1). It should be borne in mind however that the data presented is based on patients

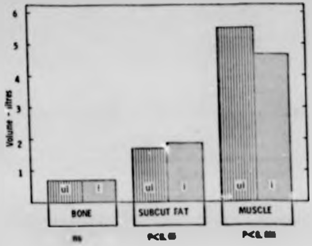
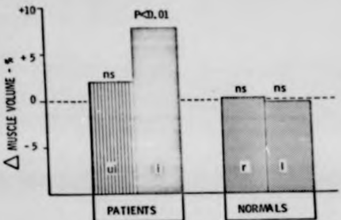


Figure 3. The volume of bone, subcutaneous fat, and muscle, in the injured (i) and uninjured (ui) legs of the patients at the start of rehabilitation therapy. The statistical significance (paired 't') between the legs is given below each column (ns = not significant).



+10
+5
0
-5
Δ MUSCLE VOLUME - %
ns
P<0.01
ns
ns
ui
i
r
l
PATIENTS
NORMALS

Figure 4. The change (expressed as a percentage increase over the initial value) in the muscle volume of the patients uninjured (ui) and injured (i) legs after a mean period of 50 days exercise therapy.

Data are also shown for the right (r) and left (l) legs of 7 normal subjects who underwent endurance training for a similar period.

Statistical significance (paired 't') of the changes is indicated above each column (ns = not significant).

undergoing "active" rehabilitation therapy: clearly this constancy of rate will not be seen if following removal of the immobilising cast patients are unable to effectively exercise the injured leg due for example to reduced joint movement or unsatisfactory union of the fracture. An example is shown in Figure 5 of data collected on such a patient who following removal of the plaster cast had $< 45^{\circ}$ degrees of movement at the knee joint until manipulation under anaesthetic was performed.

Some of the increase during rehabilitation in the muscle volume of the injured leg was offset by a simultaneous, though non-significant, increase (2%) in the uninjured leg, (Figure 4). This finding would seem to indicate that as a result of the consequent restriction of activity imposed by having one leg immobilised in a plaster cast there is some slight muscular atrophy, even in the uninjured and otherwise 'normal' leg.

The exact nature of the loss occurring from the muscle mass is not yet clear, although it is interesting to note that Helander (1958) studying the effects of immobilisation in rabbits observed in the muscle of the immobilised limb a 21% loss of weight which was almost entirely due to a decrease of myofibrillar protein. In an attempt to provide more conclusive evidence in man I have recently embarked on a collaborative study with Drs. R.H.T. Edwards and A. Young of the Royal Postgraduate Medical School, Hammersmith Hospital. In this study muscle specimens are being obtained by percutaneous needle biopsy (Edwards 1971) of the quadriceps of both the injured and uninjured legs. Preliminary findings indicate that

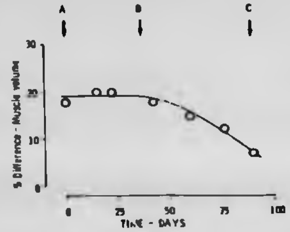


Figure 5. The time course in one subject (AS) of the percentage difference between the muscle volume of the injured (i) and uninjured (ui) legs; i.e. (ui - i / ui x 100)

A - Date of admission to Rehabilitation Centre (plaster removed four days previously).

B - Manipulation under anaesthetic to increase knee joint mobility (prior to manipulation $< 45^{\circ}$).

C - Final measurement at discharge.

in the injured leg there is a marked reduction in the cross sectional area of both type I (slow twitch) and type II (fast twitch) muscle fibres, with some indication of a relatively greater atrophy of the type I fibres (Figure 6).

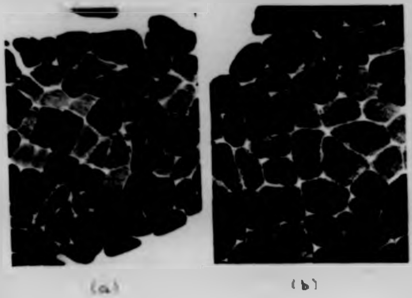


Figure 6. Example of biopsy specimens obtained from the lateral part of the quadriceps muscle of the (a) injured and (b) uninjured legs. Biopsy was performed in both legs immediately following 12 weeks immobilization of the injured leg in a plaster cast.
Transverse 10 μm sections are shown stained for myosin ATPase activity to identify type I (light staining) and type II (dark staining) fibres.

Chapter 3

The pattern of force applied
in one and two-leg cycling.

INTRODUCTION

In previous studies (Dunér 1959, Freyschuss and Strandell 1968, Pernow and Saltin 1971) it has been tacitly assumed that one-leg cycling was comparable to 2-leg cycling in so far as it involved the same movements using the same muscle groups in the same pattern. There was however no objective data to support this assumption. Furthermore it has been known since the work of Dunér (1959) that there is a significant difference between the mechanical efficiency of one and two-leg cycling; on the basis of this evidence it could be suggested that there is a prima facie case for the existence of real differences in the pattern of one and two-leg cycling. Clearly such differences could invalidate direct comparison of the two types of exercise.

Similarly it was not known whether one-leg cycling performed by the patients with their injured and uninjured legs would be comparable. Neither was it clear what the implications of a functional and structural asymmetry as seen in the patients would be for the performance of cycling exercise involving both legs.

Therefore the aim of the investigation reported in this chapter was to examine both in normal subjects and patients the pattern of force applied to the cranks of a bicycle ergometer during one and two leg cycling.

SUBJECTS

Data was collected on four normal subjects and six patients. Although they could all cycle none of them had taken part in competitive cycling and none had cycled on a regular basis for a number of years. However in order to overcome any initial habituation effect (Davies, Tuxworth and Young 1970) all of the subjects were allowed uninstructed practice of one and two leg cycling on the ergometer before the collection of definitive data.

The patients were six young servicemen who had suffered tibia and fibula fracture of one leg which had consequently been immobilised in a plaster cast for an average of 145 days (range [illegible]). They were seen 62 days (range 49–110) post-mobilisation at which time they were fully weight bearing on the injured leg and had good union at the fracture site, although they were still suffering from muscle weakness due to atrophy.

The normal subjects were four healthy young males who were employed at the rehabilitation unit attended by the patients.

The physical characteristics and maximal oxygen uptakes of the normal subjects and patients are given in tables 1a and 1b respectively.

Table 1a Age, weight, height, leg (muscle plus bone) volume (LV), and the maximum oxygen uptake ($\dot{V}O_{2\ max}$) achieved in exercise with the right (r) and left (l) and both legs together by the four normal subjects studied.

SUBJECT	Age Yr	Weight kg	Height cm	LV (m + b) l		$\dot{V}O_{2\ max}$ (Absolute) l/min		
				r	l	r	l	2-legs
A	20	60.0	167.8	6.15	6.25	1.94	1.94	2.54
B	20	90.7	181.4	7.75	7.42	2.59	2.44	3.33
C	31	73.3	179.3	7.22	7.41	2.05	2.27	3.20
D	34	69.0	177.0	7.01	6.96	3.34	3.30	4.47
Mean	26	73.2	176.4	7.03	7.01	2.48	2.49	3.39
± SD	±7	[illegible]	±6.0	±0.67	±0.55	[illegible]	[illegible]	[illegible]

Table 1b Age, weight, height, leg (muscle plus bone) volume (LV), and the maximum oxygen uptake ($\dot{V}O_{2\,max}$) achieved in exercise with the injured (i), uninjured (ui) and both legs together (2-legs), of the six patients studied.

PATIENT	Age yr	Weight kg	Height cm	LV (m + b) l		$\dot{V}O_{2\,max}$ (Absolute) l/min		
				i	ui	i	ui	2-legs
N	19	84.7	170.9	6.74	6.92	2.19	2.35	2.89
O	21	63.4	176.8	5.12	6.27	2.22	2.68	2.93
P	20	57.2	172.8	4.87	5.92	1.96	2.33	2.63
Q	17	62.6	166.3	5.58	5.91	1.99	2.09	2.43
R	25	69.7	178.0	5.19	6.20	1.97	2.20	2.70
S	29	81.0	181.6	6.88	7.31	2.44	2.87	3.04
Mean	21.8	73.1	174.4	5.73	6.42	2.13	2.42	2.77
± SD	±4.4	±13.6	±5.5	±0.87	±0.57	±0.19	±0.30	±0.22

[redacted]

The subjects were required to pedal at fifty revolutions per minute a van Dobeln type friction braked bicycle ergometer (Signwall Limited). Starting at zero load each subject performed a continuous progressive exercise test with each leg separately and both legs together. The test was aimed to span the range of the subjects work capacity in 4 or 5 work loads lasting five minutes each. The subjects were fitted with specially adapted plimsolls which were attached to the pedals by means of two metal plates and bolts situated under the ball of the foot. Since the bicycle had a fixed wheel this arrangement enabled a smooth natural action in one leg cycling when the momentum of the heavy flywheel carried the exercising leg through the inactive phase of the cycle. Care was taken that the saddle height was correctly adjusted for each subject ensuring that the leg was properly extended during the cycling movements. Once selected the saddle height was recorded and used for all subsequent tests. In one-leg exercise the inactive leg was rested on a low stool by the side of the ergometer.

Cardiorespiratory and force measurements were made over the final two minutes of each work load. Where appropriate net values of oxygen uptake and work were calculated by subtracting the value obtained when the subject was pedalling against zero load (Hill 1965, Whipp and Wasserman 1968).

<u>Force Measurement</u>

The force exerted on the right and left cranks of the bicycle were measured simultaneously and separately by a system based on one described by Hoes et al (1968).

The basis of the system (illustrated in Figure 7) is a standard friction braked ergometer. Silicone strain gauges (Pye Dynamics Ltd.) were bonded to flat ground surfaces approximately halfway along the trailing and leading edges of both cranks. The input and output to these was effected by mounting discs containing three concentric brass slip rings on the inside and fixed to each crank so that the disc and crank rotated together. Connection was made with the strain gauge by tapping into the brass rings from the outer face of the disc. The pick-ups from the brass slip rings were mounted on either side of the bicycle frame just behind the bottom bracket. These pick-ups consisted of sets of four phosphor-bronze metal strips 5 x 50 x 0.3 mm sandwiched together and clamped at one end to an insulated base plate. The strips were bent to an angle and the unit mounted on the bicycle frame so that each set of strips was in contact with one of the brass slip rings under a slight spring pressure. The output from each crank was fed to separate Wheatstone bridge circuits and balanced at zero load before recording began. The output was displayed on an ultra violet oscillograph (S.E. Laboratories Ltd. - Type 3006) on which records were made at [illegible] mm/sec and [illegible] mm/sec paper speed (See Figure 8). Indication of the relative position of the cranks was obtained on the same recording by mounting a small photoelectric transistor on the outside of the rim of the left slip ring disc in which a series of holes had

Figure 7. The force measuring equipment mounted on the bottom bracket of the bicycle ergometer.

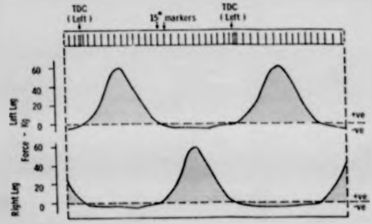


Figure 8. Force recording at fast paper speed to permit calculation of work performed. Timer marks have been omitted and the areas measured to give the work performed (positive and negative) have been shaded. The 15° interval markers appear along the top of the record. Left hand crank top dead centre (TDC) is given by a triple marker. Subject E performing 2-leg pedalling at 1500 kpm/min.

been drilled at 15° intervals to coincide with the position of a small light source mounted inside the disc on the bicycle frame. The impulses generated by the cell appear along the top edge of the force record. As a reference point top dead centre (TDC) of the left hand crank was indicated by a triple marker (Figure 8).

The system was calibrated statically by hanging weights from the pedals with the cranks fixed in the horizontal position. Over a period of six weeks' use there was no significant or systematic change in the response characteristics of the system and the co-efficient of variation of 20 calibrations made during that period was < 2%.

The force measurements were analysed in two ways: In the first (based on the slow paper speed recording) the peak force generated on a crank during each cycle was measured over the last two minutes of each work load and a mean value taken, this is referred to as the mean peak force (MPF); in the second analysis, the work[1] performed on the crank ($\dot{W}_{CR}$) was calculated in a typical cycle by integration of the area between the force record and the zero baseline (Figure 8). The force was measured at each 15° marker position (which are not equidistant due to changes in speed through the normal cycle) and the area between them calculated assuming a mean force and a constant speed. The work performed in each 15° segment (positive or negative) was added together to give the total work performed on the crank ($\dot{W}_{CR}$) over 360°. In addition, $\dot{W}_{CR}$ was calculated separately for the first 180° of each cycle (starting at top dead centre) and the second 180°, these sections

[1] N.B. Throughout the text 'work' is standardised per unit time (i.e. expressed as a rate, kpm/min).

corresponding to the leg extension and flexion phases respectively of the cycling movements. The cycle measured was selected from a fast paper speed recording of 10 complete cycles taken at the end of each work load. The cycle closest in peak force to the mean measured over the previous two minutes of recording was used.

Cardiorespiratory Measurements

At submaximal work loads oxygen uptake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$) and pulmonary ventilation ($\dot{V}_E$) were measured using a continuous sampling open circuit technique.

Subjects breathed through an Otis-McKerrow low resistance mouthpiece which was connected on the inspired side by wide bore tubing (35 mm I.D.) to a dry gas meter (Parkinson Cowan CD4). The gas meter dial was fitted with a photoelectric relay which enabled volumes to be read on a digital counter. Expired air passed via wide bore tubing from the mouthpiece to a 5-litre polyethylene bottle designed to produce mixing of the tidal air. Near the outlet of this container a sample line was inserted and air was sucked at 500 ml/min over a drying agent (magnesium perchlorate) and through an infra red CO_2 analyser (Beckman LBI) and flow meter by an electric pump. Finally the sample gas was pumped through a paramagnetic oxygen analyser (Servomex OA 150) before exhausting to atmosphere.

The dry gas meter was calibrated against a standard wet gas meter. The CO_2 analyser which was fitted with a linearizer was calibrated at the beginning of each test using outside air and a cylinder gas with a nominal gas mixture of 4% CO_2, 17% O_2 and 79% N_2:

the exact concentrations were determined by Haldane analysis. The linearity was checked periodically with gas mixtures containing different CO_2 concentrations but this did not change during the course of the investigations. The oxygen analyser was calibrated at the beginning of each test using O_2 free nitrogen and outside air: in addition the cylinder gas was used to check meter function in the respiratory gas range.

Lightweight adhesive electrodes (Devices Sales Ltd.) were used to pick up an ECG signal which after suitable amplification was fed to a counter triggerred by the 'R' wave; in addition a continuous write out of the signal was obtained on an ultra violet oscillograph recorder (S.E. Laboratories Limited).

During submaximal exercise cardiorespiratory measurements were made over the last two minutes of each five minute work load. Inspired gas volume, cardiac frequency and CO_2 and O_2 concentrations were recorded every fifteen seconds and mean values calculated. Breathing and pedalling frequency were counted during the same period by an observer with a stop watch.

Maximal measurements were made using a standard Douglas bag technique. ECG was recorded and cardiac frequency counted from the oscillograph record. In two leg exercise performed by the normal subjects the "VO_2 plateau with increasing work load" criterion was used to confirm maximum. However, in two leg work with the patients and in one leg work by both patients and controls this was not always easy to apply. The patients in particular although they were encouraged to keep going for as long as possible could often only sustain maximal levels for a relatively short period. In order to overcome this difficulty when it arose duplicate measurements were made on subsequent days at different final supramaximal loads.

Anthropometry

Height was measured with a portable stadiometer (Holtain Limited) and weight with a beam balance (Herbert and Sons Ltd.).

Leg muscle (plus bone) volume was assessed by the anthropometric technique described in detail in Chapter 2. Briefly this involves measuring the leg as a series of segments which are considered for the calculation of volumes to approximate to truncated cones (Jones and Pearson 1969); correction is made for the thickness of subcutaneous fat.

RESULTS – NORMAL SUBJECTS

The principal indices of the response to progressive one and two leg exercise tests are summarised in Tables 2 and 3.

Cardiac frequency was consistently higher for a given $\dot{V}O_2$ in one compared with two leg exercise, as was $\dot{V}O_2$ for a given $\dot{W}$: the latter phenomenon indicating a reduction in apparent mechanical efficiency in one compared with two leg exercise (Figure 9).

Peak Force

The peak force of each cycle was measured over the last two minutes of each work load: The coefficient of variation (cv) of these measurements for a given subject, leg and work load was ~ 7%. The coefficient of variation of the mean peak force (MPF) for the first minute of measurement compared with the second for all subjects at submaximal work loads was < 4%.

There was no significant difference between the right and left legs in the mean peak force applied for given W in one-leg exercise for a given subject (Figure 10). In two-leg exercise, however, there was a consistent and significant ($p < 0.01$; paired 't') tendency for the right leg to exert a slightly (~ 3%) greater peak force than the left.

The relationship of mean peak force (MPF) and work load $\dot{W}$ were linear (Figure 10) in both one and two leg exercise and are given by the following equations:

(a) 1-leg : MPF = 11.23 + 0.065 ($\dot{W}$), r = 0.98, cv = 12%

(b) 2-legs: MPF = 10.74 + 0.032 ($\dot{W}$), r = 0.98, cv = 10%

If account is taken of the doubled work output in 2-leg cycling, there is no significant difference between the MPF/$\dot{W}$ relationships in one and two leg work, although in both cases there are inter-subject differences reflecting slight variations in the pattern of force exerted in cycling.

Work performed on the cranks ($\dot{W}_{CR}$)

Preliminary analysis of both one and two leg pedalling showed that during the first 180° of the cycle (from top dead centre) positive force was applied to the crank and that during the second 180° a negative force was applied in all but the highest work loads (Tables 2 and 3, Figure 8).

$\dot{W}_{CR}$ (positive or negative) from these two phases which coincide approximately with leg extension and flexion were therefore measured separately and then added to give a total value. The net total work ($\dot{W}_{CR}$net) was obtained by subtracting the work performed pedalling at zero load (see methods). Net total work was highly correlated ($r = 0.98$, $P < 0.001$, $n = 48$) in both one and two leg cycling with the work load ($\dot{W}$) set on the bicycle ergometer (Figure 11). Total $\dot{W}_{CR}$net is on average ~ [illegible]% higher than $\dot{W}$ and the regression relationship for the combined data is given by the equation:

$$\text{Total } \dot{W}_{CR}\text{net} = 1.127\ \dot{W} - 51.43 \quad cv = 9\%.$$

The relative contribution of the extension and flexion phases of cycling to the total $\dot{W}_{CR}$net is shown in Figure 12. There are no significant differences in this relationship either between legs or between 1- and 2-leg exercise. Under all conditions and work loads studied ~ 80% of $\dot{W}_{CE}$ net was performed in the leg extension and ~ 20% in leg flexion phases of cycling. The relationships are given by the equations:

(a) $\dot{W}_{CE}$ net (extension) = [illegible] + [illegible] (Total $\dot{W}_{CE}$ net)

(b) $\dot{W}_{CE}$ net (flexion) = 10.5 + 0.2 (Total $\dot{W}_{CE}$ net).

Crank Rotation Speed

In one leg work deceleration occurs over at least half the cycle whilst in two leg work this effect is mitigated by the alternating leg action.

Figure 13 illustrates the variation in speed in one compared with two leg exercise over a range of work loads for subject D. At 900 kpm/min the effect is such that whilst the variation in two leg exercise is approximately ± 10% of the mean speed (50 rpm) in one leg exercise this increases to +20% and −30% of the mean speed.

Table 2. Principal indices of responses to 2-leg exercise in 4 normal subjects. Means (± SD) are given for total work performed on the wheel of the bicycle ($\dot{W}$), oxygen uptake ($\dot{V}O_2$), cardiac frequency (f_H), mean peak force (MPF), and work performed on the cranks of the bicycle calculated separately for the right and left legs and for the extension and flexion phases of cycling . * n = 3

$\dot{W}$ kpm/min		0	297 ±8	597 ±38	888 ±31	1184* ±37	1515* ±235
$\dot{V}O_2$ l/min		0.60 ±0.04	1.06 ±0.06	1.49 ±0.08	1.98 ±0.14	2.43 ±0.21	3.11 ±0.58
f_H beats/min		88 ±18	102 ±20	126 ±31	147 ±32	149 ±13	167 ±17
MPF Kg	left	10.9 ±1.2	18.9 ±1.7	28.0 ±2.8	38.5 ±3.6	52.2 ±4.4	62.1 ±10.4
	right	12.1 ±1.9	21.0 ±2.7	29.2 ±2.7	40.4 ±1.4	52.2 ±3.9	61.1 ±10.1
Work performed - Kpm/min							
Left leg	extension	178 ±39	294 ±21	414 ±21	574 ±39	729 ±17	853 ±89
	flexion	-138 ±25	-88 ±14	-86 ±37	-40 ±33	-37 ±33	+1 ±16
	Total	39 ±17	205 ±27	327 ±42	534 ±50	691 ±51	854 ±104
Right leg	extension	188 ±30	307 ±17	432 ±28	582 ±31	733 ±24	870 ±54
	flexion	-147 ±33	-126 ±38	-111 ±54	-81 ±35	-46 ±11	29 ±47
	Total	40 ±33	182 ±29	320 ±73	501 ±54	687 ±29	900 ±102

Table 3. Principal indices of responses to 1-leg [illegible]
Parameters as for Table 1. ± n = [illegible].

(a) Left Leg	$\dot{W}$ kpm/min	0	300 ±11	[illegible] ±8
	$\dot{V}O_2$ l/min	0.59 ±0.07	1.08 ±0.06	1.33 ±0.[illegible]
	f_H beats/min	94 ±25	112 ±27	132 ±34
	MPT – kg	12.7 ±1.9	27.3 ±4.1	42.2 ±4.8
	Work performed kpm/min			
	Extension	192 ±20	440 ±42	574 ±44
	Flexion	-120 ±39	-73 ±52	-54 ±44
	Total	72 ±28	368 ±21	521 ±45
(b) Right Leg	$\dot{W}$ kpm/min	[illegible]	[illegible] ±18	[illegible] ±30
	$\dot{V}O_2$ l/min	0.59 ±0.07	1.09 ±0.09	1.44 ±0.12
	f_H beats/min	81 ±17	109 ±32	128 ±35
	MPT – kg	[illegible] ±2.2	30.3 ±4.8	38.5 ±4.3
	Work performed – kpm/min			
	Extension	187 ±21	454 ±73	603 ±61
	Flexion	-138 ±32	-88 ±75	-71 ±47
	Total	50 ±14	367 ±57	532 ±5[illegible]

for (a) the left and (b) the right legs.

606 ±40	868* ±172
1.78 ±0.17	2.50 ±0.69
150 ±33	161 ±13
50.4 ±5.0	66.4 ±5.7
709 ±89	923 ±180
-24 ±46	+54 ±54
685 ±55	977 ±232
609 ±33	872* ±170
1.82 ±0.18	2.55 ±0.64
145 ±37	161 ±10
52.8 ±5.0	68.5 ±5.0
732 ±104	938 ±184
-33 ±43	+74 ±71
698 ± 74	1012 ±248

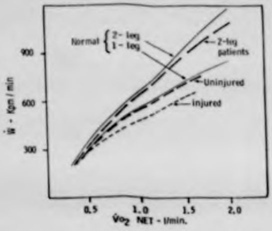


Figure 9. Work output ($\dot{W}$) in relation to oxygen uptake ($\dot{V}O_2$) in normal subjects and patients.

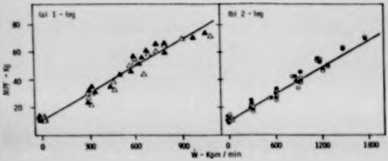


Figure 10. Mean peak force (MPF) exerted at varying work loads (W) in (a) 1-leg and (b) 2-leg cycling.
1-leg cycling: Right ▲ , Left △
2-leg cycling: Right ● , Left ○

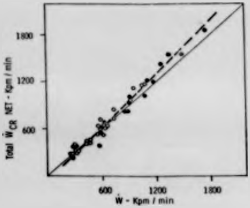


Figure 11. The relationship of the total net work performed on the cranks (total $\dot{W}_{CR}$ net) compared with the work load set on the ergometer wheel ($\dot{W}$).
1-leg cycling ○ , 2-leg cycling ●.

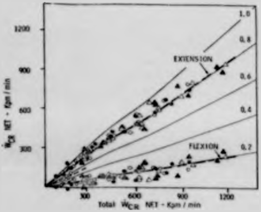


Figure 12. Relative contribution to the total net work performed on each crank (Total $\dot{W}_{CR}$net) of the extension (top dead centre to 180°) and flexion (180° to top dead centre), phases of cycling.
One leg exercise: right ▲, left △
Two leg exercise: right ●, left ○
Regression lines are given (see text) against a background indicating the proportional contribution.

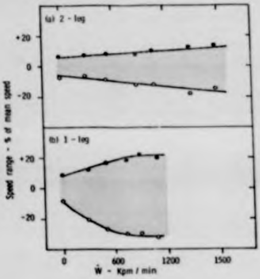


Figure 13. The maximum (●) and minimum (○) speeds (mean over 15°) of crank rotation expressed as a percentage of the mean speed for varying work loads during 1 and 2-leg exercise: Subject D.

RESULTS - PATIENTS

Table 1b gives the physical characteristics and maximal exercise responses for the six patients. The leg (muscle plus bone) volume of the injured leg is 11% smaller than the uninjured and this is associated with a reduction in the maximum oxygen uptake achieved in 1-leg cycling with the injured (1.13 ± 0.19 l/min) compared with the uninjured leg (2.42 ± 0.30 l/min).

The principal indices of the progressive 1- and 2-leg exercise tests are given in Tables 4 and 5.

Cardiac frequency for a given oxygen uptake was higher in one-leg exercise with the injured compared with the uninjured leg and higher in both of these compared with two-leg exercise.

Workload ($\dot{W}$) for a given net oxygen uptake is consistently higher in two-compared with one-leg exercise and higher in one-leg exercise with the uninjured compared with the injured leg (Figure 9).

Peak Force

The coefficient of variation of the mean peak force (MPF) for the first compared with the second minute of recording for all patients, legs and workloads in 1- and 2-leg exercise was <4%, although the cycle by cycle variation during the recording results in a coefficient of variation (cv) of from 5-10% in a given subject and leg at a given $\dot{W}$. These values are similar to those found for normal subjects.

Reproducibility of the level of MPF exerted with the injured and uninjured legs in 2-leg cycling was examined in two subjects over a range of work loads (n = 20). There was no systematic difference between the first (x) and second measurements (y). The relationship is given by:

$y = 1.73 + 0.93x, \quad r = 0.99, \quad cv = 7\%$ (Figure 14)

The relationship of MPF to $\dot{W}$ is not significantly different between one-leg exercise performed with either the injured or the uninjured leg (Figure 15a). The combined data can therefore be described by the regression equation

$MPF = 11.29 + 0.056\dot{W}; \quad r = 0.97; \quad cv = 11\%.$

When the patients performed two leg cycling the MPF generated at a given work load was consistently higher in the uninjured compared with the injured leg (Figure 15b). The relationship in the two cases is linear and given by:

(a) Injured leg : $MPF = 10.98 + 0.0215\dot{W}; \quad r = 0.92; \quad cv = 17\%$

(b) Uninjured leg : $MPF = 11.73 + 0.0353\dot{W}; \quad r = 0.95; \quad cv = 14\%.$

Work performed on the crank ($\dot{W}_{CR}$)

The total net work performed on the crank(s) (Total $\dot{W}_{CR}$net) was highly correlated ($r = 0.97$, $P < 0.001$ $n = 59$) in both one and two-leg cycling with the work load ($\dot{W}$) set on the bicycle (Figure 16).

However, in two-leg exercise there was a large and significant difference ($P < 0.001$) between $\dot{W}_{CR}$net performed with the injured compared with the uninjured leg (Figure 17). The injured leg contributing on average only 38% of the total $\dot{W}_{CR}$net of two-leg cycling over the range of work loads studied; the disproportionately larger share (62%) being contributed by the uninjured leg.

$\dot{W}_{CR}$ of extension and flexion

The relative contribution of the extension and flexion phases of cycling to the 'total' $\dot{W}_{CR}$net performed by a given leg is shown in Figure 18. There is no significant difference between the injured and uninjured legs in the proportional contribution of the two phases in either one-leg or two-leg cycling and the combined data can be described by the following equations:

Extension $\dot{W}_{CR}$net = 0.76 (Total $\dot{W}_{CR}$net) −16.2

Flexion $\dot{W}_{CR}$net = 0.24 (Total $\dot{W}_{CR}$net) +15.8

Analysed in this way the greater proportion of the total $\dot{W}_{CR}$net is performed in leg extension (~ 75%) whilst only ~ 25% is performed in leg flexion.

Table 4. Principal indices of responses to 2-leg exercise in 6 patients. Means (± SD) are given for total work performed on the wheel of the bicycle ($\dot{W}$), oxygen uptake ($\dot{V}O_2$), cardiac frequency (f_H), mean peak force (MPF) and work performed on the cranks of the bicycle calculated separately for the injured (inj) and uninjured (uninj) legs and for the extension and flexion phases of cycling.

$\dot{W}$ kpm/min		0	300 ±23	590 ±57	808 ±107	968 ±113
$\dot{V}O_2$ l/min		0.59 ±0.05	1.06 ±0.09	1.55 ±0.17	1.87 ±0.25	2.22 ±0.45
f_H beats/min		104 ±16	118 ±13	142 ±14	168 ±13	176 ±12
MPF kg	inj.	11.0 ±2.7	17.0 ±3.5	22.5 ±3.2	29.5 ±4.6	35.0 ±6.9
	uninj.	12.4 ±3.1	20.6 ±2.4	30.1 ±3.0	43.6 ±5.4	46.7 ±4.5
Work performed – kpm/min						
Injured leg	extension	190 ±54	265 ±60	364 ±84	408 ±82	455 ±122
	flexion	-154 ±47	-105 ±35	-65 ±44	-41 ±34	-27 ±32
	Total	45 ±51	160 ±57	298 ±80	367 ±84	428 ±129
Uninjured leg	extension	195 ±62	324 ±45	481 ±83	576 ±77	656 ±67
	flexion	-157 ±27	-104 ±25	-60 ±34	-20 ±29	+9 ±48
	Total	37 ±46	220 ±32	421 ±85	555 ±88	575 ±83

Table 5. Principal indices of responses to 1-leg exercise for (a) the injured and (b) the uninjured legs. Parameters as for Table 4.

(a) Injured Leg	$\dot{W}$ kpm/min	0	277 ±27	390 ±42	569 ±102	
	$\dot{V}O_2$ l/min	0.55 ±0.02	1.06 ±0.12	1.32 ±0.13	[illegible] ±0.25	
	f_H beats/min	103 ±17	128 ±10	149 ±8	168 ±8	
	MPF – kg	10.5 ±2.3	24.9 ±2.9	35.4 ±[illegible]	42.9 ±4.2	
	<u>Work performed kpm/min</u>					
	Extension	177 ±45	369 ±50	459 ±84	590 ±130	
	Flexion	–115 ±18	–31 ±53	32 ±36	35 ±51	
	Total	62 ±45	338 ±75	490 ±93	624 ±155	
(b) Uninjured Leg	$\dot{W}$ kpm/min	0	305 ±14	454 ±30	573 ±23	733 ±70
	$\dot{V}O_2$ l/min	0.54 ±0.03	1.08 ±0.09	[illegible] ±0.11	1.64 ±0.21	[illegible] ±[illegible]
	f_H beats/min	100 ±13	122 ±13	143 ±13	158 ±12	176 ±13
	MPF – kg	12.2 ±2.0	26.5 ±2.6	36.5 ±3.8	45.8 ±5.2	54.6 ±4.9
	<u>Work performed kpm/min</u>					
	Extension	202 ±29	406 ±46	527 ±47	646 ±59	747 ±21
	Flexion	–110 ±48	–15 ±37	+11 ±37	41 ±38	94 ±19
	Total	92 ±[illegible]	392 ±[illegible]	538 ±[illegible]	686 ±[illegible]	841 ±[illegible]

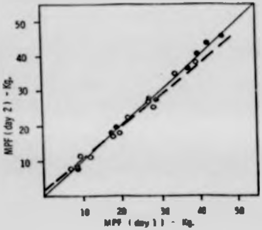


Figure 14. The relationship between measurements made on successive days of the mean peak force (MPF) exerted in 2-leg cycling by patients (P & Q) with their injured (O) and uninjured legs (●).

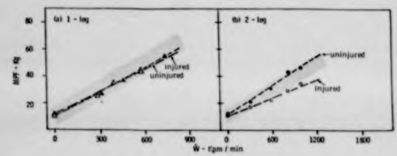


Figure 15. The relationship of mean peak force (MPF) and work load (Ẇ) in (a) 1-leg and (b) 2-leg exercise. Regressions (see text) are based on full data but only mean values (Tables 4 & 5) at each work load are shown. The shaded area represents the 95% confidence limits of the relationship (at the mean of y) found in normal subjects (Figure 10).

1-leg cycling: injured △ , uninjured ▲

2-leg cycling: injured ○ , uninjured ● .

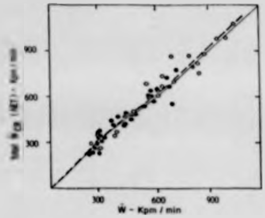


Figure 16. The relationship in patients of the total net work performed on the cranks (total $\dot{W}_{CR}$ net) to the work load set on the ergometer ($\dot{W}$).

1-leg cycling ●

2-leg cycling ○

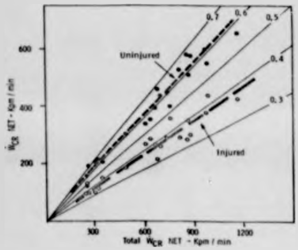


Figure 17. The contribution ($\dot{W}_{CR}$ net) of the injured (o——o) and uninjured (● – – – ●) legs to the total net work (Total $\dot{W}_{CR}$ net) during 2-leg cycling.
The regression lines are given (see text) against a background indicating the proportional contribution.

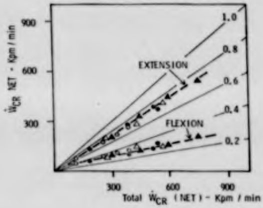


Figure 18. Net work performed on the crank in the extension and flexion phases of cycling. The symbols (as in Figure 15) represent mean values for each work load.
1-leg cycling: injured ▵ , uninjured ▴ .
2-leg cycling: injured ○ , uninjured ● .
The regression lines are given (see text) against a background indicating the proportional contribution.

DISCUSSION

In considering the data presented in this chapter a number of important qualifications should be borne in mind:

Although the subjects had all cycled as children and still did so occasionally, they had never received any specific training in cycling technique or taken part in competitive sport. Thus although they may be typical of the "normal" population, their pattern of cycling may differ significantly from that shown by competitive cyclists (see e.g. Hoes et al 1968).

One-leg cycling was measured using a friction braked bicycle of the van Dobeln type with a fixed wheel. With the active foot attached to the pedal (see methods) this allowed the subject to rely on the momentum of the heavy flywheel to carry the leg through the inactive phase of the cycle. Other investigators, however, have adopted different strategies: Glaser (1973) for example, had two subjects standing one either side of a bicycle sharing the work between them; Freyschuss and Strandell (1968) used an ergometer which free wheeled and found it necessary to use a spring mechanism to return the pedal to the top of the cycle in order to ensure a smooth cycling movement. Obviously, there may be important differences between these approaches.

All of the experiments reported here were carried out at a nominal pedal speed of 50 rpm in both one and two leg exercise. Large variations in this speed will certainly modify the efficiency of cycling (Dickinson 1929) and will probably influence the pattern of force application.

Measurement of the peak force of each cycle over a full two minute period (i.e. [illegible] cycles) was made after three minutes at each work load. This in contrast to the relatively brief measurement periods, often immediately at the commencement of exercise used in studies of 2-leg cycling by other investigators (Cavanagh et al 1974, Hoes et al 1968). As a consequence the present subjects had ample opportunity to accustom themselves to the work load and this is reflected in a coefficient of variation for both patients and normal subjects of ~ [illegible] for a given subject, leg and work load. This was attributable to cycle by cycle variation rather than periodic changes over the measurement period in (a) the pattern of cycling or (b) in the case of 2-leg pedalling, work sharing between the two legs. Consequently the coefficient of variation of the mean peak force for the first minute of measurement compared with the second was < [illegible].

The changes in leg volume (muscle plus bone) and $\dot{V}O_{2\,max}$ of the patients injured compared with their uninjured leg are similar to those reported in Chapter 4 for a larger group and it is not proposed to discuss them in detail here, beyond establishing the magnitude of the functional and structural asymmetry of the patients legs. Neither is it proposed to discuss variations in the cardio-respiratory responses to submaximal one and two-leg exercise in either patients or normal subjects for the same reason. Readers should refer to Chapter 4.

1- and 2-leg pedalling performed by normal subjects

The normal subjects showed no significant difference between the right and left legs in the MPF/$\dot{W}$ relationship of 1-leg exercise (Figure 10). In two leg exercise, however, a slightly though significantly greater force is exerted by the right leg (t = [illegible]). In this context it is interesting to note that all subjects identified the right leg as being their strongest and preferred leg when kicking, jumping or hopping, although the effect of this preference was not reflected by any significant differences in the leg volume or $\dot{V}O_{2\ max}$ measurements (Table 1a).

The range over which force can be effectively applied to the cranks in leg extension and flexion will obviously depend upon the saddle position relative to the crank (Carlsöö and Molbech 1966, Moss et al 1968) as well as the length of leg segments of individual subjects. However, visual inspection of the force records (Figure 8) reveals that very little force is being effectively applied to the crank for a few degrees, either at the top or the bottom of the cycle. Therefore, the analysis has been standardised by calculating $\dot{W}_{CR}$ separately for the first and second 180° of each cycle as measured from top dead centre in order to indicate the work done in leg extension and flexion respectively.

Analysed in this way it becomes clear that over almost the whole range of submaximal work loads positive work performed on the crank in leg extension is used both to carry out work on the bicycle and also to lift the leg during the flexion phase when a negative force is applied to the crank (Tables 2 and 3). Total work ($\dot{W}_{CR}$)

which is the sum of the extension (+ve) and flexion (-ve at all but the highest loads) phases indicates the work done on the bicycle. At zero load total $\dot{W}_{CR}$ is ~ 70 kpm/min reflecting the work necessary to overcome the frictional resistance in the bicycle transmission as well as in the slip ring assemblies. In order to compare the work load ($\dot{W}$) as set with the calculated values of work performed on the cranks ($\dot{W}_{CR}$) it is necessary to subtract from the latter value the $\dot{W}_{CR}$ of pedalling at zero load to give $\dot{W}_{CR}$net. When comparison is made in this way $\dot{W}$ and $\dot{W}_{CR}$ are highly correlated (r = 0.98) although $\dot{W}_{CR}$ is on average ~ 5% higher than $\dot{W}$ (Figure 11); this may be due to frictional losses increasing with work load due to imposed stresses on the bearings.

When $\dot{W}_{CR}$net is calculated separately for the extension and flexion phases of cycling it is clear that there is a progressive increase in active lifting of the leg in flexion during both one and two-leg work. Thus $\dot{W}_{CR}$net of flexion increases, although it is not until the highest work loads (> 90% $\dot{V}O_{2\,max}$) that the absolute value of $\dot{W}_{CR}$ in flexion becomes positive and assists the forward rotation of the crank.

The proportional contribution of extension and flexion phases to total $\dot{W}_{CR}$net remains constant at ~ 80 and 20% respectively throughout the range of work loads studied in both 1- and 2-leg cycling (Figure 12). Thus in this respect 1- and 2-leg cycling are comparable activities.

Whilst the proportional contribution of extension and flexion phases does not change in 1- compared with 2-leg work the conditions under which they perform this work notably in terms of crank rotation speed and thus muscle contraction speed clearly do. Hence in one leg work at for example 300 kpm/min work load the rotation speed of the crank at the start of leg extension is equivalent to a pedal speed of ~35 rpm, by the end of leg extension the speed has risen to ~61 rpm. In contrast the speed fluctuation in 2-leg exercise is much less marked being the equivalent to ~45 rpm minimum rising to ~55 rpm maximum (Figure 13). It has been shown by many investigators (see e.g. Dickinson 1929, Banister and Jackson 1967) studying 2-leg cycling, that marked variation in pedal frequency from optimum levels of 50-60 rpm results in reduced mechanical efficiency. In one leg exercise the fact that the muscles are contracting and applying force at least for part of each cycle at greater extremes of crank rotation speed than is the case in 2-leg pedalling may contribute to the reduced mechanical efficiency noted in this (Figure 9) and other investigations (Dumer 1959, Freyschuss and Strandell 1968, Fernow and Saltin 1971). Although other factors may be at least if not more important; for example a relatively greater increase with $\dot{W}$ of the postural work required to stabilise the body position in one compared with two-leg exercise.

1 and 2-leg cycling performed by the patients

1-leg cycling:

In 1-leg exercise there is no significant difference between the injured and uninjured legs in the relationship of mean peak force (MPF) to work load ($\dot{W}$). The regression line for the combined data lies within although towards the lower margin of the confidence limits observed in the normal subjects (Figure [illegible]).

When $\dot{W}_{CR}$net is considered separately for the leg extension and flexion phases in 1-leg cycling, no significant differences are revealed between the legs: the largest proportion (~ 75%) of $\dot{W}_{CR}$net being generated by leg extension both with the injured and uninjured legs throughout the range of work loads studied (Figure 18). This is slightly (~ [illegible]) but significantly less than the proportion of work done in leg extension by the normal subjects. However, it should be remembered that both the patients injured and uninjured legs show the same proportional contribution in the extension and flexion phases. It therefore seems reasonable to suppose that rather than being an intrinsic difference resulting from muscle disuse the difference between the patients and normal subjects is most likely attributable to normal intersubject variation in the pattern of cycling coincidentally emphasised by the small number in each group.

Comparison of the relationship between oxygen uptake and work load in 1-leg exercise indicates that the injured leg is performing at a reduced level of mechanical efficiency (Figure 9). This difference cannot be accounted for in terms of gross changes in the pattern of cycling (e.g. by the injured leg doing more or less work in the extension or flexion phases of cycling), since on the present analysis the injured and uninjured legs appear to behave in an identical fashion. Obviously the difference in efficiency may be accounted for by more subtle biomechanical changes than could be identified by this investigation (e.g. by the pattern of force application on the crank being generated by different muscle groups). It does however seem unlikely that significant changes of this nature would not produce some variation in the pattern of force application between the injured and uninjured leg.

The increased oxygen cost of one-leg cycling with the injured leg may be due to an increase in postural work as suggested to explain the difference in efficiency between 2- and 1-leg cycling. This explanation is not entirely convincing however since it is difficult to see why the same work load (although admittedly 'relatively' greater for the injured leg) should require an increased postural effort at the low levels of $\dot{W}$ at which the $\dot{W}/\dot{V}O_2$ relationship begins to diverge.

Alternatively, the difference may reflect genuine variation in the metabolic efficiency of the atrophied muscle in the injured leg dependent upon for example the velocity of contraction and the relative contribution of type I or type II muscle fibres (Goldspink, Larson and Davies 1970, Bolstad and Ersland 1976).

2-leg cycling:

In 2-leg cycling the relationship of mean peak force (MPF) to work load ($\dot{W}$) is significantly different for each leg (Figure 15). In net terms MPF is ~ 40% lower in the injured compared with the uninjured leg for a given work load. This striking difference is also reflected in the $\dot{W}_{CM}$net calculated separately for each leg so that the injured leg is contributing ~ 40% less work than the uninjured leg towards the total (Figure 17). However, the proportional contribution of extension and flexion to $\dot{W}_{CM}$net remains the same for each leg and is not significantly different to that found in 1-leg exercise (Tables 4 & 5, Figure 18).

Thus it appears that the 'pattern' of cycling with the injured leg whether used in one or two leg exercise remains the same as with the uninjured leg, but in 2-leg exercise the injured leg operates at a relatively lower overall level compared with the uninjured leg. The difference in work performed ($\dot{W}_{CM}$net) by the legs during 2-leg exercise is in marked contrast to a loss in maximal aerobic function ($\dot{V}O_{2\,max}$) and leg volume of only ~ 11%.

Explanation of this apparent anomaly may lie in a simple "resting" or "protecting" of the injured leg. However, if so, it was an apparently unconscious effort on the part of the patients who were not aware that work sharing was being assessed during the exercise and who in addition when subsequently questioned, said without exception that they were not consciously aware of using one leg more than the other. Furthermore, although there was some inter-subject variation, the ratio of work sharing between the legs in any one patient was remarkably consistent throughout a range of work loads. MPF also, whether examined on a test re-test basis over a wide range of work loads (Figure 14) or on a minute to minute basis (cv < 4%) is highly correlated in any one patient and leg during 2-leg cycling.

The consistency of these latter findings suggests that there may be a genuine physiological basis for the disproportionate work sharing between the legs, although it is not clear what this may be. One possibility may be that the ratio of work sharing is related to optimal mechanical efficiency as illustrated in Figure 19.

In this theoretical calculation work loads from 600–900 kpm/min have been divided in different proportions between the legs and the oxygen cost calculated from the known relationship between $\dot{W}$ and $\dot{V}O_2$ (Figure 9) for each leg as though each were acting independently (i.e. performing 1-leg exercise). If it could be assumed that the same relative difference in efficiency exists between the legs in 2 as in 1-leg exercise, it can be seen from this analysis that the ratio of work sharing between legs as observed in our patients falls within the optimum range for efficiency. It is not clear how this optimal work sharing could be achieved. It may be that the same number and type of motor units representing the optimum for efficiency are innervated in both legs but that those in the injured leg produce less tension as a result of atrophy.

In conclusion, disproportionate work sharing in 2-leg cycling, whether it is simply due to "protecting" the injured leg or whether it reflects a real physiological difference has important practical and, or, theoretical implications. In the former case it means that 2-leg exercise may not produce the maximal desired effect when used as part of a programme of rehabilitation therapy unless carefully monitored; in the second case it suggests that, following immobilisation there is a physiological difference of considerable magnitude between the limbs which is not adequately reflected by measurement of maximal function ($\dot{V}O_{2\ max}$) or gross structure (LV), but which may reflect changes occurring at a cellular level in the atrophied muscle. Clearly this is an area requiring further investigation to elucidate the functional significance.

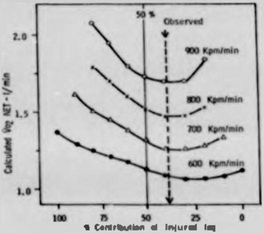


Figure 19. Theoretical calculation of the effect of varying the percentage contribution of the injured leg towards the performance of 4 work loads using both legs.
The calculation is based on the relationships for 1-leg exercise with the injured and uninjured legs (Figure 9).
Total work load, 900 (o), 800 (x), 700 (▲) and 600 (●) kpm/min.

CONCLUSIONS

The pattern of force applied in 1- and 2-leg exercise by normal subjects

The pattern of force application, as characterised by mean peak force and the pattern of work performed in the leg extension and flexion phases, was the same in 1- and 2-leg exercise in normal subjects. The investigation therefore supports the assumption that the same muscle groups (and thus muscle mass) are used to produce the same pattern of force in both forms of exercise. Consequently comparison based on an assumed doubling of the active muscle mass in 2 compared with 1-leg exercise seems justified.

The pattern of force applied by patients with their injured and uninjured legs.

The pattern of force exerted in 1-leg cycling performed by the patients with their injured leg was the same as with their uninjured leg. Thus direct comparison between the 1-leg exercise performance of the patient's injured and uninjured legs seems justified.

Work sharing between legs in 2-leg exercise

Normal subjects showed a tendency in 2-leg cycling towards doing more work (~ 3%) with their right ('preferred') rather than left legs.

This difference was however relatively insignificant in comparison with the patients who showed a large and consistent difference between the work performed by the injured compared with the uninjured leg throughout the range of work loads studied. Hence the injured leg contributed on average 40% less than the uninjured leg to the total net work. This large difference is not reflected in the difference ($\sim$11%) between $\dot{V}O_{2\ max}$ or leg (muscle plus bone) volume of the legs. Whether the phenomenon is simply an unconscious resting of the injured leg or whether it has some genuine physiological basis is not clear.

<u>Differences in apparent mechanical efficiency.</u>

The differences in mechanical efficiency between 1- and 2-leg cycling and between 1-leg cycling performed with the patients injured and uninjured leg cannot be accounted for in terms of the pattern of force application as characterised by mean peak force or the proportional contribution of the leg extension and flexion phases of the cycling action.

At high work loads there is a greater variation in crank rotation speed in 1- and 2-leg exercise and this may contribute to the differences in efficiency between these two forms of exercise. However, a simpler explanation based on an increase in the postural component of one-leg work cannot be discounted, and this could also account for the difference between one-leg exercise performed by the patients injured and uninjured legs. Further evidence is needed on this point.

CHAPTER 4

Physiological responses to exercise.

INTRODUCTION

The development of the anthropometric techniques described in Chapter 2 enabled the degree of disuse muscular atrophy to be assessed in patients injured legs following prolonged disuse. In this chapter measurements are reported of the physiological responses to 1 and 2-leg exercise combined with anthropometric estimates of muscular atrophy. Some of the data is included in detailed form in Appendix 2 (Davies and Sargeant 1975b) and reference will be made to this to avoid unnecessary repetition.

The patients examined were 25 young servicemen who had suffered fracture of one leg as a consequence of which they had had that leg immobilized in a plaster cast for a mean period of 105 days (range 32-205). They were seen on average 50 days after the plaster cast was removed and 18 days after arriving at a residential rehabilitation unit. They could all pedal a bicycle ergometer at least during sub-maximal exercise without discomfort or pain at the time of the measurements. Data was also collected for comparative purposes on 9 normal subjects. The physical characteristics of both groups are given in Table 1 of Appendix 2.

Cardiorespiratory and anthropometric measurements were made using the methods already described in detail in Chapters 2 and 3.

SUBMAXIMAL EXERCISE

The responses to submaximal exercise are summarised in Table 2 of Appendix 2. Mean and standard deviations are given of the values, (predicted from linear regression) for pulmonary ventilation ($\dot{V}_E$) at a carbon dioxide output of 1.5 l/min ($\dot{V}_{E\ 1.5}$); tidal volume at a $\dot{V}_E$ of 30 l/min ($V_{T\ 30}$); oxygen uptake ($\dot{V}O_2$) at a work load of 450 kpm/min for 1-leg work ($\dot{V}O_{2\ 450}$) and 900 kpm/min for 2-leg work ($\dot{V}O_{2\ 900}$); cardiac frequency (f_H) at a $\dot{V}O_2$ of 1.5 l/min ($f_{H\ 1.5}$); and $\dot{V}O_2$ at a f_H of 175 beats/min for 1-leg work ($\dot{V}O_{2\ 175}$) and 195 beats/min for 2-leg work ($\dot{V}O_{2\ 195}$).

Pulmonary ventilation at a given CO_2 output ($\dot{V}_{E\ 1.5}$) was almost identical in 1-leg exercise performed by the patients with their injured and uninjured legs (50.5 ± 7.2 and 50.5 ± 9.0 l/min respectively) and not significantly different to that of normal subjects exercising with their right and left legs (46.9 ± 4.1 and 47.9 ± 3.8 l/min). Neither was there a significant difference in $\dot{V}_{E\ 1.5}$ between patients and normals performing 2-leg exercise (44.6 ± 4.8 and 42.6 ± 7.1 l/min). V_T at a given ventilation ($V_{T\ 30}$) was significantly smaller ($P < 0.001$) in patients compared with normals in both 1 and 2-leg exercise, although there was no difference between injured and uninjured leg exercise performed by patients or between right or left leg exercise in the normal subjects.

In both patients and normal subjects it was found that there was a significant increase in the oxygen cost of performing one compared with two leg work. This observation is in agreement with previous studies in normal subjects (Dunér 1959, Freyschuss and Strandell 1968, Pernow and Saltin 1971, Davies and Sargeant 1974a).

However, in addition it was found that there was a significantly higher ($P < 0.001$) oxygen cost of performing one-leg work with the patients injured compared with uninjured legs. Hence oxygen uptake at a given work load of 450 kpm/min ($\dot{V}O_{2\ 450}$) was 1.40 ± 0.11 l/min compared with 1.51 ± 0.11 l/min in the uninjured and injured legs respectively. The possible reasons for these observed differences in mechanical efficiency have been examined and discussed in Chapter 3 of this thesis.

When the patients performed two leg exercise the cardiac frequency for a given oxygen uptake ($f_{H\ 1.5}$) was significantly higher ($P < 0.01$) than in a group of normal subjects (140 ± 18 cf. 121 ± 12 beats/min respectively).

That there is an increase in cardiac frequency for a given oxygen uptake in submaximal exercise following immobilisation or simply reduced activity levels is well recognised (see e.g. Saltin et al 1968, Åstrand and Rodahl 1970). It is not however clear how these changes in circulatory responses are mediated: one suggestion has been that they are brought about by the effect of reduced activity on the myocardium, (Saltin et al 1968). It was interesting therefore to find that when the patients performed one-leg cycling $f_{H\ 1.5}$ was significantly higher ($P < 0.001$) in exercise with the injured as compared with the uninjured leg (153 ± 19 and 142 ± 15 beats/min respectively) since both legs are dependent on the same central cardiovascular system. Further examination of the cardiovascular response was therefore undertaken and this is presented in the next section of this chapter.

The difference in the submaximal cardiac frequency response ($f_{H\ 1.5}$) was reflected in oxygen uptake predicted at the maximal cardiac frequencies previously reported for normal subjects performing 1- and 2-leg exercise (respectively 175 beats/min, Davies and Sargeant 1974a; and 195 beats/min, Davies 1968). The mean values of $\dot{V}O_{2\ 175}$ and $\dot{V}O_{2\ 195}$ also reflect the differences, although not the absolute values, of $\dot{V}O_{2\ max}$ in the different groups and exercises where maximal measurements were made.

In three patients blood for the determination of lactic acid concentration was sampled at the end of each work load from an antecubital vein. Lactic acid concentration measured by an enzymatic method (Boehringer GmbH) was higher for a given oxygen uptake in one-leg exercise with patients injured compared with their uninjured legs (Figure 20). This difference was an indication of the greater 'relative' stress imposed on the injured leg at a given oxygen uptake, thus if $\dot{V}O_2$ is expressed as a percentage of the $\dot{V}O_{2\ max}$ of the exercising leg the differences between the legs disappear.

Cardiovascular response to exercise

The implications of the observed difference in cardiac frequency at a given submaximal oxygen uptake ($f_{H\ 1.5}$) during exercise with the injured and uninjured legs was further examined in a group of five subjects. In these subjects cardiac output was estimated using a carbon dioxide rebreathing method, (Jones et al 1967), arterial PCO_2 being estimated from the end tidal CO_2 (Godfrey and Davies 1970). Cardiac output ($\dot{Q}$) at a given $\dot{V}O_2$ of 1.5 l/min ($\dot{Q}_{1.5}$) was not significantly different in exercise with the injured and uninjured legs

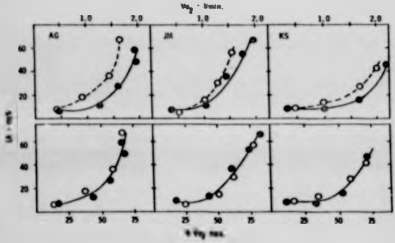


Figure 21. Lactic acid (LA) concentration in the blood in relation to $\dot{V}O_2$ expressed in absolute (l/min) and below this relative (% $\dot{V}O_{2\ max}$) terms.
Data is given for 3 subjects performing 1-leg exercise with their injured (o- - -o) and uninjured (●—●) legs.

[[illegible] ± [illegible] and [illegible] ± [illegible] l/min respectively] but as in the larger group $f_{H\,1.5}$ was significantly ($P < 0.001$) different ([illegible] ± [illegible] and [illegible] ± [illegible] beats/min). Thus by direct implication stroke volume must have been smaller in exercise with the injured leg and there is indeed a consistent trend so that the mean $SV_{1.5}$ is reduced by 10 ml ([illegible] ± [illegible] cf. [illegible] ± [illegible] ml in the uninjured leg). However due to the variance of the cardiac output data and the small numbers involved this just fails to reach conventional levels of significance (in fact 't' = 2.70, with [illegible] degrees of freedom, $P > 0.10 < 0.05$).

Oxygen uptake of 1.5 l/min represents 68 and 59% of the total $\dot{V}O_{2\,max}$ of the injured and uninjured legs respectively. If cardiac frequency is predicted instead at a $\dot{V}O_2$ equivalent to 65% in each leg ($f_{H\,65}$) the differences observed between the legs disappear. Hence $f_{H\,65}$ is 148 ± 9 and 148 ± 11 beats/min respectively in the injured and uninjured legs.

This finding is comparable to Saltin et al's (1968) observation of an increase in submaximal cardiac frequency response to 2-leg exercise following bed rest. These latter authors also found that expressing $\dot{V}O_2$ in relative terms (i.e. % $\dot{V}O_{2\,max}$) removed the significant differences they observed but went on to suggest as a possible major factor changes in the myocardium. This however cannot be a factor in the present study where both legs are dependent upon the same myocardium; rather it is peripheral factors which are implicated since the differences appear to accurately reflect the relative stress imposed upon a given leg. A similar asymmetrical response related to "peripheral stress" has recently been noted by Saltin et al (1976) following one leg training and by Saltin and Landin (1975) in hemiparetic patients.

It must be admitted however that there is no evidence of a causal link between relative work load and f_H. It may be that the differences found in the latter merely reflect impairment, resulting from immobilisation, in the control of the capacitance vessels, this impairment being coincidentally related to the magnitude of the reduction in function in the injured limb.

However although no supine exercise was undertaken in this study, Saltin et al (1968) found that the changes in circulatory adaptation to exercise following bed rest were similar in both upright and supine exercise. The latter type of exercise facilitates venous return by reducing peripheral pooling and it is suggested that the persistence of the circulatory differences in Saltin's bed rest patients (in contrast to patients with central nervous system damage resulting in postural hypotension) rules out the impairment of control of the capacitance vessels as a major factor although it may be contributory

Studies of indocyanine green clearance in relation to heart rate (Rowell et al 1964, Clausen et al 1973) indicate a common neural activation governing increase in heart rate and reinforced vasoconstriction in non-active tissues (Rowell 1974). In the training study of Clausen et al (1973) it is suggested that there is a reduction in this neural activity when trained muscle is used for exercise, and as with the data presented in this chapter and in accord with Saltin's data, this reduction is related to the relative stress. Thus it appears that the cardiovascular response to submaximal exercise may be significantly influenced by feedback, which is proportional to the relative stress involved, emanating from the active muscle (e.g. Coote et al 1971, McCloskey and Mitchell, 1972). However, it may equally be that this control is due to impulses arising centrally (see e.g. Folkow and Neil 1971, Freyschuss 1970) possibly related to the degree of cortical activity necessary to perform a given work load with atrophied and normal muscle. No definite conclusions can be drawn regarding these possibilities from the present data.

MAXIMAL EXERCISE

It was possible to obtain satisfactory measurements of maximal performance in only fifteen out of the twenty-five patients studied during 1-leg exercise. To achieve even this required considerable patience, encouragement and careful explanation of the purpose of the tests in order to elicit the patient's cooperation. These results are summarised in Table 3 of Appendix 2.

Maximal ventilation ($\dot{V}_{E\ max}$) was consistently and significantly higher ($P < 0.001$) in both 1- and 2-leg exercise performed by the normal subjects compared with the patients. There were however no significant differences between the $\dot{V}_{E\ max}$ achieved in 1-leg exercise with patients injured and uninjured legs or between that achieved with normal subjects' right and left legs.

Maximal cardiac frequency ($f_{H\ max}$) was not significantly different between the patients and normals in either 1- or 2-leg exercise although as previously reported (Pernow and Saltin 1971, Davies and Sargeant 1974b) $f_{H\ max}$ was higher ($\sim$ 10 beats/min) in 2- compared with 1-leg exercise.

The $\dot{V}O_{2\ max}$ net of the injured and uninjured legs were smaller by 26% and 19% respectively when compared with the right and left legs of normal subjects. However, these differences were reflected by concomitant variation in the size of leg muscle (plus bone) volume (LV). Thus for a given LV there were no significant differences in the 1-leg $\dot{V}O_{2\ max}$ of the patients injured or uninjured legs or normal subjects right or left legs (Figure 21) and nearly all data points fall within the 95% confidence limits of the relationship previously

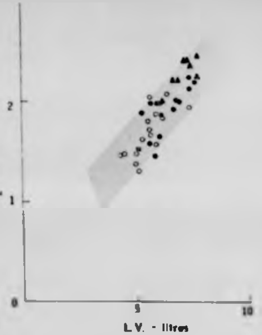


Figure 21. Relationship of one-leg maximal aerobic power output ($\dot{V}O_{2\ max}$ net) to leg volume (LV - muscle plus bone). Data points are shown for patients uninjured legs (●); injured legs (○); and normal subjects right and left legs (▲). The shaded area represents the 95% confidence limits of the relationship previously found for normal subjects (Davies and Sargeant 1974a, b).

found in normal healthy subjects (Davies and Sargeant, 1974a,b). This close association was emphasized by an examination of techniques for predicting one leg $\dot{V}O_{2\ max}$ in this group of patients (Davies and Sargeant 1975e). It was found that prediction of one leg $\dot{V}O_{2\ max}$ based solely on limb size was at least as accurate as conventional prediction techniques based on the submaximal relationship of $\dot{V}O_2$ and f_H adapted to one leg exercise (Davies and Sargeant 1974c).

The related changes of LV and $\dot{V}O_{2\ max}$ indicate that in these patients and in the normal subjects the maximum aerobic power output of 1-leg exercise is limited by the size of the effective muscle mass. This is in agreement with previous observations of 1-limb exercise in normal subjects (Davies and Sargeant 1974a, b) but in contrast to the situation in 2-leg exercise where it has often been argued that the limitations to maximal exercise are imposed by cardiac output and the resulting arterial desaturation (see e.g. Bevegård and Shepherd 1967, Hermansen 1973, Davies and Sargeant 1974b): It should be pointed out that this latter view has recently been challenged (Kaijser 1970, Pirnay et al 1972) although not as yet conclusively.

In two leg exercise performed by the present group of patients there is a deterioration of $\dot{V}O_{2\ max}$ of 18% (0.51 l/min) which results in a reduction for a given LV when comparison is made with normal subjects, (Figure 22). Thus the deterioration in 1-leg exercise performance associated with the decrease of LV is probably combined in 2-leg work with a further factor resulting from general cardio-vascular deconditioning as might be expected from the enforced period of relative inactivity (Saltin et al 1968).

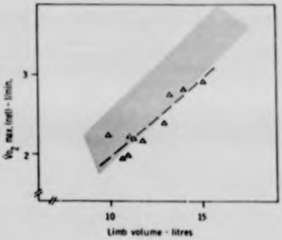


Figure 22. 2-leg $\dot{V}O_{2\ max}$net in relation to leg volume (muscle plus bone). Data points for the patients are given against the 95% confidence limits of the relationship found in normal subjects (Davies et al 1973).
The regression line is given by the equation

$$\dot{V}O_{2\ max}net = 0.38 + 0.163\ LV$$

PERCEIVED EXERTION

An important factor affecting the motivation and hence successful rehabilitation of limb injury patients is how they perceive their own level of exertion. Using a numerical rating scale (Borg 1962, Borg and Linderholm 1967, Skinner et al 1969, Borg 1970, Bar-Or et al 1972) I sought to quantify the level of perceived exertion during the 1- and 2-leg exercise tests performed by the patients and normal subjects. The scale used (Borg 1970) gives values from 6 - 20 each odd number on the scale chart being accompanied by a brief verbal description as given below:

6
7 very very light
8
9 very light
10
11 fairly light
12
13 somewhat hard
14
15 hard
16
17 very hard
18
19 very very hard
20

Subjects were shown the chart at the end of each work load and asked to indicate a number on the scale corresponding to the degree of exertion perceived.

The results showed that work load ($\dot{W}$), minute ventialtion ($\dot{V}_E$), cardiac frequency (f_H) and oxygen uptake ($\dot{V}O_2$) were lower at given levels of perceived exertion in 1-leg exercise with the injured compared to the uninjured leg and lower in both of these compared to normal subjects (Table 6, figure 23). Similarly in 2-leg exercise the levels achieved by patients were lower than those of normal subjects. In nearly all cases comparison of the regression equations indicated statistically significant differences ($P < 0.05$ - Table 6).[1] In addition there were consistent differences between 1-leg and 2-leg exercise response in both patients and normals (Table 6).

When the net $\dot{V}O_2$ was expressed as a percentage of the net $\dot{V}O_{2\ max}$ the differences shown in absolute (1/min) terms between the responses of the injured and uninjured legs of the patients, and those of the normal subjects performing 1-leg exercise were removed (Figure 24, Table 6). Expression of the $\dot{V}O_2$ in relative terms also removed the differences between the 2-leg responses of the patients and normals, although significant differences in the slope of RPE/%$\dot{V}O_{2\ max}$ lines for 1-leg and 2-leg responses remained.

Predictions of the $\dot{V}O_2$ at RPE_{20}($\dot{V}O_{2\ R20}$) from the linear regression of 3 or 4 submaximal ($<$ 80% $\dot{V}O_{2\ max}$) measurements of $\dot{V}O_2$ and RPE, reflected the observed difference in $\dot{V}O_{2\ max}$ between the injured and uninjured legs of the patients although in absolute

1 The two exceptions were in the relationship $\dot{V}_E$/RPE in 2-leg exercise (patients vs normals) and 1-leg exercise (normals vs patients uninjured leg).

Table 6. Relationship of y (Dependent variable) to RPE (x) in patients performing 2-leg and 1-leg exercise with the injured (inj) and uninjured (uninj) legs and normal subjects performing 2- or 1-leg exercise. Significant differences between regressions are shown for 2 leg exercise - patients vs. normals (A) and 1-leg exercise normals vs. uninjured (B); normals vs. injured (C); injured vs. uninjured (D).
*** $P < 0.001$; ** $P < 0.01$; * $P < 0.05$; ns not significantly different.

Exercise	Group	y	intercept	regression coefficient	SEy	correlation coefficient	n	Significance A	B	C	D
2-legs	Normals	[illegible] ml/kg/min	-523	7.95	240	[illegible].76	32	ns			
	Patients		-372	6.48	202	[illegible]	[illegible]				
1-leg	Normals		[illegible]	[illegible]	162	[illegible]	105		ns	*	
	Patients inj		-565	65.6	174	0.71	59				*
	Patients uninj		[illegible]	[illegible]	[illegible]	[illegible]	[illegible]				
2-legs	Normals	[illegible] kpm/min	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**			
	Patients		[illegible]	33.[illegible]	[illegible]	[illegible]	37				
1-leg	Normals		-33[illegible]	[illegible]	[illegible]	[illegible]	104		**	**	
	Patients inj		- 94	29.8	[illegible]	[illegible]	[illegible]				ns
	Patients uninj		- [illegible]	[illegible]	140	[illegible]	[illegible]				
2-legs	Normals	f_H beats/min	+ [illegible]	[illegible]	16.9	[illegible]	[illegible]	*			
	Patients		+ [illegible]	5.85	16.6	[illegible]	37				
1-leg	Normals		+ [illegible]	7.74	13.3	[illegible]	105		**	*	
	Patients inj		+ [illegible]	5.86	15.7	[illegible]	[illegible]				*
	Patients uninj		+ [illegible]	5.86	17.9	[illegible]	[illegible]				
2-legs	Normals	[illegible] l/min	- 0.[illegible]	[illegible]	0.51	[illegible]	[illegible]	**			
	Patients		+ 0.94	[illegible]	0.57	[illegible]	[illegible]				
1-leg	Normals		- 0.[illegible]	[illegible]	0.33	[illegible]	[illegible]		**	**	
	Patients inj		- 0.08	0.09	[illegible]	0.60	43				**
	Patients uninj		- [illegible]	[illegible].11	[illegible]	[illegible]	41				
2-legs	Normals	% $\dot{V}O_2$ max (BET)	- [illegible]	[illegible]	14.3	[illegible]	[illegible]	ns			
	Patients		- [illegible]	[illegible]	16.2	[illegible]	35				
1-leg	Normals		- [illegible]	[illegible]	10.4	[illegible]	100		ns	ns	
	Patients inj		-44.4	6.32	16.3	[illegible]	43				ns
	Patients inj		[illegible]	6.42	12.1	[illegible]	[illegible]				

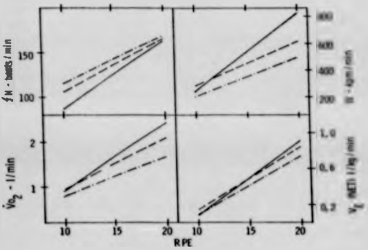


Figure 23. The relationship in one-leg exercise of work load ($\dot{W}$) minute ventilation ($\dot{V}_E$), cardiac frequency (f_H) and oxygen uptake ($\dot{V}O_2$) to rated perceived exertion (RPE). Regression lines are given for exercise involving the patients injured (-.-) and uninjured (---) legs and for the one-leg exercise performed by the normal control subjects (————)

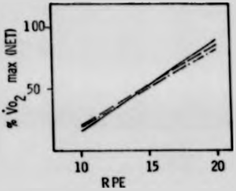


Figure 24. The relationship in one-leg exercise of relative work load (% $\dot{V}O_{2\ max}$) to rated perceived exertion. Regression lines are given for the exercise involving the patients injured (-·-) and uninjured (- - -) legs and for the one leg exercise performed by the normal control subjects (——).

[illegible] $\dot{V}O_{2\,RDO}$ underestimates the observed values [illegible] ~ 15% in both cases. The relationship in the patients between $\dot{V}O_{2\,max}$ (observed) and $\dot{V}O_{2\,RDO}$ (predicted) in both injured, uninjured and two-leg exercise is shown in Figure 25.

In interpreting these findings it should be remembered that the numerical scale for rating perceived exertion (RPE) developed and validated by Borg and his co-workers was structured to give a linear response of RPE with heart rate during exercise performed on a stationary bicycle ergometer. If however, there are differences in the heart rate response to exercise due for example to age (Borg and Linderholm, 1967); environmental conditions (Skinner et al 1973); training (Ekblom and Goldbarg 1971); illness (Borg and Linderholm 1970, Sanne, 1973), or the size of the muscle mass utilized in exercise (Sargeant and Davies 1973) then significant differences in the RPE/f_H relationship become apparent between groups.

The heart rate response as indicated by maximal levels attained and/or submaximal levels for a given oxygen intake has been shown to differ in one compared with two leg exercise and in one leg exercise involving patients injured and uninjured compared with normal subjects right or left legs. It was not therefore surprising that in the present study clear differences were indicated in the RPE/f_H relationship between these groups and types of exercise, although a linear relationship was maintained (Table 6 - Figure 23).

It was previously shown (Sargeant and Davies 1973) that under dynamic exercise conditions involving different muscle masses such differences could be resolved by relating RPE to the relative work

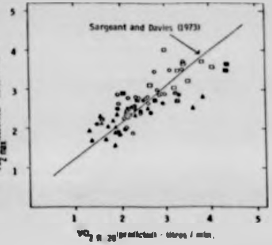


Figure 25. The relationship of observed $\dot{V}O_{2\,max}$ to $\dot{V}O_2$ predicted at RPE_{20} ($\dot{V}O_{2\,R20}$). The regression line shown is from Sargeant and Davies (1973), where $y = 0.284 + 0.929\,\dot{V}O_{2\,R20}$.
Data points are given for: 1-leg exercise performed by normals subjects (○) and by the patients with their injured (▲) and uninjured (●) legs; and for 2-leg exercise by the normal subjects (□) and patients (■).

load (i.e. net $\dot{V}O_2$ expressed as a percentage of the net $\dot{V}O_{2\,max}$). The present data extended that work and confirmed that in patients who had suffered a loss of function in one leg due to immobilization following fracture, the perception of exertion was accurately related to the new reduced functional level so that RPE for a given relative work load remained the same in 1-leg exercise in either leg of the patients or normals (Figure 24). This implies that the accurate perception of exertion is not dependent on long term memory and experience of exercise situations since the patients had not previously exercised at maximal levels with their injured legs and therefore had no direct experience of the limbs functional capacity. Furthermore, if the limitation to maximal one leg exercise is peripheral rather than central, the present data may be interpreted as indicating that the accurate perception of exertion is predominantly dependent on feedback emanating from the active limb itself, such feedback being proportional to the physiological stress imposed.

The relationship of RPE/$\dot{V}O_2$ at submaximal exercise levels ($<80\%$ $\dot{V}O_{2\,max}$) can be used to estimate $\dot{V}O_{2\,max}$ in these patients in the same way as previously developed in normal subjects (Sargeant and Davies 1973) (Figure 25). Although even when correction is made for the systematic underestimation of $\dot{V}O_{2\,max}$ at RPE_{20} by the application of the appropriate regression equation, the method remains a relatively crude guide in the individual case and whilst it may prove a useful adjunct to the therapist in gaining insight into a patients capability and relative level of exertion in a given exercise situation it is clearly a poor substitute for the direct measurement of maximum oxygen intake.

The present data confirms the slight though significant differences previously noted (Sargeant and Davies 1973) between one and two leg exercise in the RPE/%$\dot{V}O_{2\,max}$ relationship in both patients and normal subjects (Table 2). It seems reasonable to speculate that this may result from the fact that whilst in one-leg exercise the limitations to maximal performance are largely peripheral, in two-leg exercise, where there is normally a close integration of the component parts of the oxygen transporting system, there may be a summation of inputs from a number of these component parts both peripheral and central with increasing stress leading to a relatively elevated sense of exertion. However, as before the differences are slight and related to the slope of the regression lines so that they intersect at ~ RPE 15 and even when extrapolated to RPE_{20} the difference indicated is only ~ 10%.

In conclusion it should be noted that the patients studied although still suffering a loss of function as a result of fracture and immobilisation were fully mobile, had good union at the fracture site and were able to pedal a bicycle ergometer up to maximal levels without pain. However, in patients who are anxious regarding their exercise capability, following for example myocardial infarction (see for example Hanne 1973) the relationship of RPE/%$\dot{V}O_{2\,max}$ may be considerably modified depending on the level of anxiety, amount of reassurance or therapy received, etc. Such modification of the RPE response may in itself prove to be a useful tool in assessing the current level of anxiety regarding functional capability. Furthermore, the RPE scale administered to individual patients performing exercise as part of their clinical assessment may prove a useful key for advising patients on desirable exercise levels when they return to a normal work/domestic routine. These are areas of practical application of the RPE scale which deserve further investigation.

CHAPTER [illegible]

Changes in the Physiological Responses to Exercise following Rehabilitation therapy.

Introduction

In the previous chapter the effects of disuse muscular atrophy on the physiological responses to exercise were described in a group of patients at the commencement of a residential course of rehabilitation therapy. The course included exercises specifically (but empirically) designed to improve not only the injured limb function but also general cardiovascular fitness. The present chapter describes and discusses the changes in physiological performance in eight of these patients following an average period of seven weeks of therapy. This data is compared with the effects of a training programme based on 1-leg exercise undertaken by seven normal subjects. Full details of the patient and normal data are included in Appendices 3 and 4 respectively and reference will be made to these where necessary.

The physical characteristics of the patients are summarised in Table 1 of Appendix 3 and those of the normal subjects in Table 1 of Appendix 4. The methods used in studying both the normal subjects and patients are the same as previously described (Chapters 2, 3 and 4).

Changes in physiological responses to submaximal exercise

The submaximal responses to exercise have been characterised as in Chapter 4 and the changes following rehabilitation are summarised in Table 2 of Appendix 3.

Following therapy there were significant reductions ($P < 0.001$ and $P < 0.05$) in cardiac frequency at a given $\dot{V}O_2$ ($f_{H\ 1.5}$) during

1-leg exercise performed by the patients with their injured and uninjured legs (-15 and -12 beats/min respectively). In 2-leg exercise there was a similar reduction in $f_{H\,1.5}$ of 6 beats/min following rehabilitation although this latter change was not statistically significant. Thus at the end of rehabilitation therapy cardiac frequency response in the patients approached that observed in normal subjects (Table II of Appendix 2). These changes were reflected in significant increases ($P < 0.001$) in $\dot{V}O_2$ predicted at a given cardiac frequency ($\dot{V}O_{2\ f_H}$) in exercise with each leg (+0.49 l/min).

At the commencement of therapy $\dot{V}O_2$ for given work output of 450 kpm/min ($\dot{V}O_{2\ 450}$) was higher in exercise with the injured than the uninjured leg (respectively 1.50 ± 0.12 and 1.37 ± 0.09 l/min ; $P < 0.001$). The effect of rehabilitation was to reduce the oxygen cost of work with either leg producing a small rise in mechanical efficiency, (Figure 1 of Appendix 3). In contrast the mechanical efficiency of two-leg work was unaffected by rehabilitation and throughout the investigation was closely in accord with previous results found for normal healthy subjects (Davies and Sargeant 1974b). The differences between 1-leg work in both patients and normals has already been discussed in detail in Chapter 3. However the present observation of an increase in mechanical efficiency in 1-leg exercise following training adds a new aspect to the problem. It could be argued that the effect of training may be to reduce the strain on the body during 1-leg cycling leading to a reduction in the postural component of work and hence an increase in mechanical efficiency. However in the present study measurement of mechanical efficiency has been made from a baseline of zero load, and although it is true that there may be additional postural cost at maximal levels of exercise (see Davies and Sargeant 1974b) it is difficult to see why there should be an increase at the submaximal levels of work as noted in this and other investigations (Chapter 3).

A more convincing argument may be found in the possibility of changes in the metabolic cost of producing tension related to the optimum number and type of muscle fibres. The maximal tension produced by muscle fibres is related to their cross-sectional area and since this is reduced in atrophied muscle (Chapter 2) more fibres may have to be recruited to produce a given tension when compared with a 'normal' muscle. The effect of training in these patients is to reverse the atrophy i.e. increase the cross sectional area of the muscle fibres, and hence reduce the number of fibres that it is necessary to recruit to produce a given tension. The reduction in the number of fibres necessarily recruited may in itself lead to a reduction in the metabolic cost of the work as suggested in another context by Abbott, Bigland and Ritchie (1952). However if this were the only factor it might be expected that training in normal subjects would result in improved mechanical efficiency of two-leg cycling, but there is no evidence to suggest that it does (see e.g. Åstrand and Rodahl, 1970 for a general review). A slightly more elaborate explanation may be that due to the atrophy of the fibres which would normally be recruited at a given tension other fibres of different type (and efficiency for a given contraction velocity; Goldspink, Larson and Davies 1970) are necessarily recruited which operate at a lower metabolic efficiency for the prevailing conditions.

Changes in physiological responses to maximal exercise

The changes in response to maximal exercise following rehabilitation in the patients, and training in the normal subjects, are summarised in Table 3 (Appendix 3) and Table 2 (Appendix 4) respectively.

The effect of rehabilitation was to increase the $\dot{V}O_{2\ max}$ achieved in exercise with the injured and uninjured legs of the patients by 17% and 9% respectively, thus abolishing the significant difference found between them at the start of therapy. At the same time there was in both the patients injured and uninjured legs an increase in leg muscle (plus bone) volume (LV). However, whilst in the injured legs the latter changes tended to be proportional to the increase in $\dot{V}O_{2\ max}$, in the uninjured leg there was proportionally a greater increase in the $\dot{V}O_{2\ max}$ compared with LV, and in normal subjects undergoing a training programme of 1-leg exercise there was virtually no change in LV but a highly significant increase in $\dot{V}O_{2\ max}$ (Figure 26). Thus it may be hypothesised that in the patients injured leg there is a close association between aerobic potential and the size of the active muscle mass, whereas in normal subjects where the LV is already 'optimal' any increase of aerobic potential occurs independently of muscle size being dependent upon

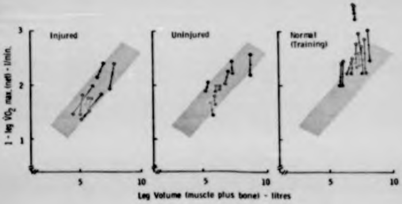


Figure 26. Relationship of 1-leg $\dot{V}O_{2\ max}$ net to leg muscle (plus bone)volume in the patients injured and uninjured legs before and after rehabilitation and in normal subjects before and after 1-leg training. The arrows indicate the direction of change. The shaded area represents the 95% confidence limits for the relationship previously found in normal subjects (Davies and Sargeant 1974b).

[illegible] in the muscle. The uninjured leg of the patients represents some intermediate stage between these two contrasting extremes.

The improvement in 1-leg $\dot{V}O_{2\ max}$ following training in the normal subjects was closely associated with the initial level. This was an inverse relationship so that those cases with the highest $\dot{V}O_{2\ max}$ (standardised for LV) showed the least improvement (Figure 2 of Appendix 4). A similar relationship was demonstrated in the case of the patients uninjured and injured legs following rehabilitation although all of the data points except one were displaced to the left of the regression line for normal subjects (Figure 2 of Appendix 3). That the patients show somewhat smaller improvements than the normal subjects over a similar period of time may have been due to the less specific nature of the rehabilitation therapy compared with 1-leg training since the rehabilitation programme included elements to improve all aspects of general fitness. Notwithstanding the difference in absolute level between patients and normal subjects the inverse nature of the relationship between improvement and initial level is well recognised, (see Ekblom 1969). It is presumably due to a progressive reduction in the margin of possible improvement the higher the initial level becomes.

The sum of the increases in net $\dot{V}O_{2\ max}$ of the patients legs measured independently are approximately equal to the increase of 0.43 l/min found in the 2-leg $\dot{V}O_{2\ max}$ net. This is in marked contrast to the situation observed in normal subjects undergoing one-leg training where an average increase of 0.3[illegible] l/min in the $\dot{V}O_{2\ max}$ of each leg measured independently was not reflected in the 2-leg $\dot{V}O_{2\ max}$ which only increased by 0.14 l/min (Table 8).

It could be argued that the present findings in normal subjects following 1-leg training support the view that whereas in one-leg exercise the limiting factor to maximal performance is peripheral (i.e. related to the state of the exercising muscle) in 2-leg exercise it is more likely to be central (cardiovascular). Thus 1-leg training increased the aerobic potential of each leg by 14% ($P < 0.001$) but no significant improvement was elicited in central cardiovascular function. The body was therefore unable to take full advantage of this increased potential in 2-leg exercise where the limiting factor may be cardiac output. Hence the improvement in 2-leg $\dot{V}O_{2\ max}$ was only 4.7% and not statistically significant.

These findings in normal subjects were similar to those reported by Gleser (1973) but at variance with a recent study by Saltin et al (1976). These latter authors showed a significant increase in two-leg $\dot{V}O_{2\ max}$ in groups of subjects following different one leg training programmes although in, for example, the group showing the most striking increase in one leg $\dot{V}O_{2\ max}$ of 0.58 l/min (24%) the improvement in two leg $\dot{V}O_{2\ max}$ is only 0.34 l/min (11%). Clearly not all of the increase in aerobic potential of the muscle is being utilised in two leg work. Furthermore the improvement of one leg $\dot{V}O_{2\ max}$ shown as a result of endurance training by Saltin et al is of a greater magnitude than in the present or Gleser's studies and this may reflect litres/minute

	Increase in Uninjured or Right leg $\dot{V}O_{2\ max}$ net	Increase in Injured or Left leg $\dot{V}O_{2\ max}$ net	Combined Increase in aerobic potential	Observed Increase in 2-leg $\dot{V}O_{2\ max}$ net
Patients	0.17^{ns}	0.29^{***}	0.46 cf.	0.43^{***}
Normals	0.39^{**}	0.29^{**}	0.68 cf.	0.14^{ns}

Table 8. Changes in 1-leg and 2-leg $\dot{V}O_{2\ max}$ net resulting from rehabilitation in patients and training in normal subjects.

Significance *** $P < 0.001$; ** $P < 0.01$;

* $P < 0.05$; ^{ns} not significant

a more severe training programme. (In the present study the total training time for each leg was ≈ [illegible] minutes cf. Saltin's study where subjects may have trained for up to a maximum of 1000 minutes per leg.) If training of one leg is sufficiently severe, bearing in mind that it can achieve ≈ 70 to 80% of two leg $\dot{V}O_{2\ max}$ it will result in training of the central cardiovascular system, which will be reflected in improvement of the $\dot{V}O_{2\ max}$ achieved in 2-leg exercise when central factors are in fact limiting.

Despite these qualifications regarding the comparability of Saltin et al's and the present normal data the changes in patients 1- and 2-leg $\dot{V}O_{2\ max}$ appear to support the former rather than the latter. Hence the combined increases in 1-leg $\dot{V}O_{2\ max}$ are reflected by an almost exactly equal rise in the 2-leg $\dot{V}O_{2\ max}$. The rehabilitation programme included however not only exercises designed to improve injured limb function but also the patients general cardiovascular condition. It seems likely therefore that the close association between the changes in 1- and 2-leg $\dot{V}O_{2\ max}$ are coincidental rather than causal.

Finally, the effect of the general cardiovascular fitness aspect of the rehabilitation programme may be seen in the improvement of the 2-leg $\dot{V}O_{2\ max}$ for a given leg volume (Figure 27). Thus at the end of rehabilitation there is no significant difference between the patients and a previous large scale study of service personnel (Davies 1972).

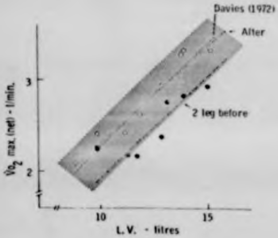


Figure 27. Relationship of 2-leg $\dot{V}O_{2\ max}$(net) to leg (muscle plus bone) volume (LV) before (• – – •) and after (o – – o) rehabilitation.
The solid line is the relationship found in a previous study of service personnel (Davies 1972).
The shaded area represents the 95% confidence limits for normal data (Davies et al 1973).

CHAPTER 6

Limb volume, composition, and maximum oxygen uptake, associated with habitual "preference" in young male subjects.

INTRODUCTION

One criticism which could be raised against the analysis of the patient uninjured and injured leg data as presented in this thesis is that it has been interpreted in the light of normal subjects right and left legs. At the time this seemed justified since in none of the groups of normal subjects studied was a significant difference found between the right and left legs either in terms of LV or $\dot{V}O_{2\,max}$.

However, there is the possibility that real differences exist between the functional and structural status of contralateral limbs in normal subjects. In particular it might be argued that habitual "preference" of one limb in exercise situations might result in significant differences occurring in these parameters and that this effect might have been obscured by merely comparing right and left legs and also by the relatively small numbers involved.

I have therefore collected together all available normal subject data where limb volume and 1-limb $\dot{V}O_{2\,max}$ determinations have been made for both legs and in some cases both arms. This data I have analysed in order to examine the possible variation in limb size and function associated with habitual "preference" of one limb in exercise situations.

SUBJECTS

The subjects were twenty healthy active males. Their mean age was 29 years; weight 73.9 kg; and height 1[illegible]4.9 cm. Inclusion in this analysis was dependent upon them being able to identify their "preferred" limb. This presented no problem in the case of arms but some subjects found it difficult to identify a preferred leg. Subjects were therefore only included in the analysis if they consistently identified one leg as being (a) the strongest; (b) the preferred leg for kicking and (c) the leg that was used to "take off" from when jumping or hopping. Subjects who gave mixed responses to these questions or who had no identifiable preference in a given situation were not included in the analysis. Thus the data presented may represent the larger differences found within the normal population, especially in relation to the legs, since some subjects are unable to identify a preferred leg or have some mixture of preference depending on the activity.

None of the subjects included in the analysis took a 'professionally' intensive part in sports likely to result in extreme asymmetrical development although like most healthy active males in this age group they all had at some time or still did play recreational football and racquet games. None of the subjects had any history of serious or recent limb injury.

METHODS

Leg volume and composition

Estimates of total and muscle plus bone limb volume were made using anthropometric techniques (after the methods of Jones and Pearson 1969). Leg bone volume was estimated from X-rays (Jones 1970a).

One Limb $\dot{V}O_2$ max

One leg exercise was performed as described in Chapter 3 . To briefly summarise this involved pedalling a fixed wheel stationary bicycle ergometer with the active foot attached to the pedal by means of a shoe which was bolted to the pedal.

One arm exercise was performed on a modified bicycle ergometer (Monark) which had a crank constructed vertically above the flywheel at shoulder height. The saddle of the bicycle was removed and was replaced with a seat incorporating a shoulder board and harness which allowed the trunk and upper body to be restrained and remain stationary, hence confining the exercise to the active arm. The pedals of the cranks were replaced with hand grips (see Davies and Sargeant 1974a).

Maximum determinations of $\dot{V}O_2$ in both one arm and one leg work were made at the end of a progressive exercise test designed to span the subject's capacity.

Criteria of maximal performance

It was not always possible in progressive exercise tests using one limb to establish the "$\dot{V}O_2$ plateau" criterion for $\dot{V}O_2$ max.

To overcome this difficulty when it arose, duplicate measurements were made on separate occasions at different supramaximal loads.

Full details of the methods used in measuring the cardio-respiratory response to maximal exercise are given in Chapter [illegible]. Arm exercise measurements were made using the same methods as described for one-leg exercise.

[illegible]

Limb Volume and Composition

(i) Legs: The total leg volume of the preferred leg (18 right 2 left) was on average 160 ml larger than the non-preferred leg, and whilst this difference is small (2%) it is nevertheless consistent so that it is statistically singificant ($P < 0.01$; Table 1). When correction is made for the fat content of the legs this difference is maintained and although the percentage difference between the volume of fat in the two legs is of the same magnitude (1.6%) as the total volume, it fails to reach conventional levels of significance. Bone volume estimated from X-rays after the method of Jones (1970a) shows no measureable difference although it is in any case only a small proportion (~ 11%) of the muscle plus bone volume. Hence the difference in total leg volume can be largely attributed to differences in the muscle component (Table 1).

(ii) Arms: Arm volume was measured in eleven of the twenty subjects by adaptation of the anthropometric methods described for the legs by Jones and Pearson (1969). In this the arm measured in the horizontal extended position was treated as a series of truncated cones defined by circumferences at (i) the minimum wrist, (ii) maximum forearm, (iii) olecranon process at the elbow, (iv) minimum upper arm below the biceps, (v) mid upper arm, (vi) minimum upper arm above the biceps, (vii) the angle of the axilla.

A correction for fat based on skinfold thicknesses measured at the dorsal and ventral forearm surfaces and the biceps and triceps was made using equations developed by Jones (1970b).

Correlation between total arm volume measured in this way and by water displacement in nine subjects was + 0.973, there was no systematic bias shown by a paired t-test. The relationship is given by the equation:

Arm volume (water displacement) =

0.15 + 0.955 (arm volume - anthropometry); cv = 4%

The total volume of the non-preferred arm (2.72 litres) was ~ 5% ($P < 0.01$) smaller in comparison with the preferred arm (2.85 litres) and as with the legs this difference was maintained when allowance was made for subcutaneous fat leaving muscle plus bone volumes of 2.15 and 2.30 litres respectively (Table 9). No radiographic assessment was made of bone size in the arm but assuming that this represents a fairly small and constant proportion of the total volume (see e.g. Cooper, Edholm and Mottram, 1953), as in the legs (i.e. ~ 11%) it can be seen that the differences in total arm volumes must be largely due to differences in the volume of the muscle component.

Table 9. Volumes (estimated from anthropometry) of the total leg, muscle plus bone, fat, bone (from X-ray), and muscle in the preferred and non-preferred limbs of healthy male subjects. The difference (d%) is expressed as a percentage of the preferred limb. Means ± SD are given.

VOLUME – Litres

		Total	Muscle + Bone	Fat	Bone	Muscle
LEG (n = 20)	Preferred	8.75 ±0.92	7.47 ±0.84	1.25 ±0.29	0.80 ±0.10	6.66 ±0.76
	Non-preferred	8.59 ±0.88	7.33 ±0.82	1.26 ±0.27	0.80 ±0.10	6.53 ±0.75
	d%	−1.8**	−1.9*	[illegible]	0	−2.0*
ARM (n = 11)	Preferred	2.85 ±0.57	2.30 ±0.43	0.55 ±0.18	0.24[a]	2.06
	Non-preferred	2.72 ±0.63	2.15 ±0.47	0.56 ±0.19	0.24[a]	1.91
	d%	−4.6**	−6.5**	+1.8	0	−7.3**

Significance (paired 't' test): ** = $P < 0.01$; * = $P < 0.05$

[a] – assumed values – see text

<u>Maximal exercise [illegible]</u>

(i) <u>Legs</u>: Maximal work ($\dot{W}_{max}$) and ventilation ($\dot{V}_{E\ max}$) were slightly lower (1.[illegible] and [illegible]% respectively) in the non-preferred compared with the preferred leg. These differences are not however significant (Table [illegible]). The difference in $\dot{V}O_{2\ max}$, [illegible] in the non-preferred compared with 2.84 l/min in the preferred leg, was however significant ($P < 0.01$) and this difference of ~ 4% was maintained when expressed in net terms ($\dot{V}O_2$ of exercise minus the $\dot{V}O_2$ of zero load pedalling - Fig.[illegible]). There was no difference in the maximal heart rates.

(ii) <u>Arms</u>: One arm: As with the legs $\dot{W}_{max}$ and $\dot{V}_{E\ max}$ were lower though not significantly so in the non-preferred compared with the preferred arm by 53 kpm/min and 7.4 l/min respectively (Table 10). Also the absolute and net $\dot{V}O_{2\ max}$ showed a similar difference to the legs of ~ 4% in favour of the preferred arm. This was not however statistically significant. $f_{H\ max}$ is virtually identical in both arms being 143 and 141 beats/min for the preferred and non - preferred arms respectively.

Table 10 Maximal work ($\dot{W}_{max}$), ventilation ($\dot{V}_{E\,max}$), absolute and net oxygen intake ($\dot{V}O_{2\,max}$) and heart rate ($f_{H\,max}$) in the preferred and non-preferred legs and arms of healthy male subjects (mean ± SD). The difference (d %) is expressed as a percentage of the preferred limb.

		$\dot{W}_{max}$ kpm/min	$\dot{V}_{E\,max}$ l/min	$\dot{V}O_{2\,max}$ l/min	$\dot{V}O_{2\,max\,net}$ l/min	$f_{H\,max}$ beats/min
Leg (n = 15)	Preferred	1045 ±207	120.1 ±19.9	2.84 ±0.42	2.39 ±0.37	173 ±11
	Non-preferred	1032 ±181	114.3 ±21.3	2.74 ±0.39	2.29 ±0.34	173 ±11
	d%	1.2	4.8	3.5**	1.2*	0
Arm (n = 7)	Preferred	263 ±58	51.8 ±18.9	1.10 ±0.32	0.72 ±0.31	143 ±24
	Non-preferred	210 ±81	45.4 ±18.5	1.[illegible] ±[illegible].39	0.69 ±0.35	141 ±22
	d%	20.0	14.0	4.5	4.2	1.4

Significance: ** $P < 0.01$; * $P < .$[illegible]

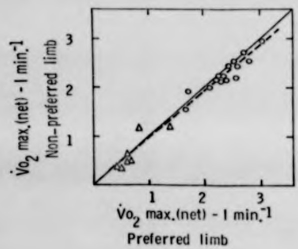


Figure 28. Maximum aerobic power ($\dot{V}O_{2\ max}$) of the preferred in relation to the non-preferred arm (Δ) and leg (O). The regression equation is of the form $y = 0.025 + 0.947x$, ($r = 0.98$) and is shown with the line of identity.

$\dot{V}O_{2\ max}$ in relation to limb volume

$\dot{V}O_{2\ max}$ standardised in terms of the limb volume (LV - muscle plus bone) involved in the exercise gives values of 330 $\pm$ 59 and 323 $\pm$ 60 $ml.l_{(LV)}^{-1}min^{-1}$ in the preferred and non-preferred legs and 304 $\pm$ 87 and 314 $\pm$ 126 $ml.l_{(LV)}^{-1}min^{-1}$ in the preferred and non-preferred arms.

If standardisation is made in this way, the differences noted in $\dot{V}O_{2\ max}$ expressed in litres per minute (Table 10) are reduced and are no longer statistically significant (analysis of variance) either between preferred and non-preferred limbs or between arms and legs.

DISCUSSION

In this analysis an examination has been made of the possible variation in limb size and function associated with habitual "preference" of one limb in exercise situations. Because of this I have been concerned only to identify in a pragmatic way the limb that is and has been habitually preferred by these young male subjects for a number of years (i.e. disregarding any early predisposition which may have been overridden by training).

The results indicate that the total volume of the non-preferred leg was slightly but significantly smaller when compared with the preferred leg and that most of this difference was attributable to changes in muscle volume. The arms show a more marked difference between the total volume of the preferred and non-preferred limbs as compared with the legs representing 4.6% (cf. 1.8% in the legs) of the preferred limb volume. When correction is made for the subcutaneous fat component which shows no significant difference between the arms and an assumed constant value for bone the difference in the size of the muscle component is increased to 7.3% (cf. 2% in the legs).

That the arms should show greater differences than the legs is not perhaps surprising when one considers that whereas the legs are both used fairly continuously in walking, running etc. albeit with more emphasis on the preferred leg in certain situations, (e.g. kicking, jumping) the preferred arm by contrast is used alone for a much greater proportion of the time as in racquet games, tool handling, writing etc.

The maximum oxygen uptake was significantly ($P < 0.05$) reduced by ~4% in the non-preferred compared with the preferred leg (Table 2), Figure 29. The non-preferred arms showed a similar reduction in $\dot{V}O_{2\ max}$ although this difference failed to reach conventional levels of statistical significance due to the reduced number of subjects measured ($n = 7$). Also there are greater difficulties in accurately measuring maximal responses to dynamic exercise involving a very small muscle mass where the changes in $\dot{V}O_2$ represent a relatively small increase over the resting level and where the exercise can only be sustained for relatively brief periods.

If the net $\dot{V}O_{2\ max}$ is standardised for the size of the active mass (LV - muscle plus bone) as previously suggested (Davies 1974) the significant difference between the preferred and non-preferred legs and between the legs and arms disappears. This suggests that in normal subjects there is little qualitative difference in the capacity of the muscles of contralateral limbs for aerobic function and that such differences as there are, are most closely associated with the size of the muscle mass involved.

It is clear that there is a significant association between limb volume and $\dot{V}O_{2\ max}$ and habitual limb preference, although discussion of the role of genetic, developmental and environmental factors in determining this preference must be speculative. Furthermore it should be remembered that the association between limb volume and $\dot{V}O_{2\ max}$ is not necessarily causal since the two parameters can be varied independently (See Chapter 5). Thus it seems possible that in these subjects the habitual preference of a limb for short term strength limited activity results in slight and relative (to the contralateral limb) hypertrophy of the muscle and that associated with this was a concomitant increase in endurance activity and capacity as represented by $\dot{V}O_{2\ max}$, so that the association of LV and $\dot{V}O_{2\ max}$ remains the same in both limbs. In this context the investigation described in Chapter 3 illustrates how in two-leg cycling which is an exercise apparently involving both legs on an equal basis the preferred leg may perform more work than the non-preferred leg of normal subjects.

The finding in normal subjects of a significant association between LV, $\dot{V}O_{2\ max}$, and limb preference has important implications for studies of patients where an injured leg is compared with the uninjured "normal" leg. Firstly, the size (LV) and function ($\dot{V}O_{2\ max}$) of the muscles in the injured and uninjured legs following prolonged immobilization will be unrelated to limb preference before fracture; rather these parameters will depend on the metabolic activity of the legs during the period of immobilization (Roux 1905). Thus the uninjured leg will reflect a relatively normal though possibly sedentary state whilst the injured leg will reflect the effect of the total immobilization of knee and ankle joints preventing dynamic movements and reducing metabolic activity to a minimum.

Equally, however, the ultimate levels of $\dot{V}O_{2\ max}$ and LV attained by the injured and uninjured legs and the differences between them will reflect their prevailing level of activity at the end of the recovery process, and this will depend upon the effect of limb preference. It may therefore be necessary to take into account whether there is a consistent preference for one leg in order to assess the normality of any inter-limb differences found at the end of the recovery process.

CONCLUSIONS

1) Whilst the use of the one limb model to study peripheral physiological phenomena is most attractive enabling the contralateral limb to be used as a matched control, careful measurements must be made of the baseline conditions of both limbs, since clearly it cannot be assumed even in normal healthy subjects that the limbs are structurally or functionally identical. However, provided these precautions are observed and standardisation is made fo. the size of the effective muscle mass then the one limb model can prove a potent and valuable tool in exercise physiology.

2) The normal subjects, including as they did only individuals who could consistently identify a preferred leg, probably represent the larger inter-leg differences to be found in the population. Even so, although statistically significant the differences in LV and $\dot{V}O_{2\ max}$ are relatively small in comparison with those in the patient groups and do not materially affect the findings of the present thesis.

3) The effect of limb preference needs to be taken into account in assessing the significance in patients of inter-limb differences found at the end of treatment designed to restore limb structure and function. Once recovery is complete significant differences may still be found as a result of the prevailing activity patterns as determined by limb preference.

CHAPTER 7

Summary and Conclusions.

SUMMARY AND CONCLUSIONS

The aims of this thesis were to study the effects of disuse muscular atrophy on the physiological responses to exercise.

The experimental model adopted for this purpose was based on patients who, following prolonged immobilization of one leg, showed atrophy of the muscles in that leg and a loss of function. The injured leg could thus be compared with the uninjured leg which acted as a 'normal' control within the same subject.

It was necessary to establish the comparability of one and two leg cycling as well as one-leg cycling performed by the patients with their injured and uninjured legs. This was done by developing a system for recording the force applied to the cranks of a stationary ergometer. The pattern of force exterted in one leg cycling performed by the patients with their injured legs was the same as with the uninjured leg, thus justifying direct comparison. In 2-leg cycling the patients showed a disproportionate sharing of total work between the legs but the actual pattern of force remained the same in both legs and the same as in one-leg cycling.

Physiological responses to submaximal exercise in the patients indicate that as with normal subjects there was a significant increase in the oxygen cost of performing a given work load in one compared with two leg exercise. However, in addition it was found that there was a significantly higher oxygen cost of performing one leg work with the patients injured compared with their uninjured legs. Since as differences between the legs had been identified in the pattern of force application during 1-leg cycling it is difficult to explain these variations in mechanical efficiency. Cardiac frequency for a given oxygen uptake ($\dot{V}O_2$) in submaximal exercise was also higher in the injured compared with the uninjured leg and this may have reflected the relatively greater stress imposed on the injured leg at a given $\dot{V}O_2$.

Maximal aerobic power output ($\dot{V}O_{2\ max}$) was significantly reduced in the injured leg and this was associated with a concomitant decrease in leg (muscle plus bone) volume (LV). Thus the relationship between LV and $\dot{V}O_{2\ max}$ remained essentially the same in one leg exercise whether it was performed with the patients injured or uninjured or normal subjects right and left legs. In two leg exercise the loss of function associated with a reduction in muscle mass was combined with a further deterioration in performance due to general cardiovascular deconditioning.

The effect of rehabilitation was to reverse the changes in one and two leg exercise performance and to increase leg volume. The findings indicate that in patients who have suffered disuse atrophy of muscle in one leg the limitation to aerobic power output of that leg may be the size of the effective muscle mass. Hence recovery of aerobic function is closely associated with increase in leg volume. In fact the data suggests that there are two phases of the recovery process: In the first phase improvement of $\dot{V}O_{2\ max}$ and LV are interdependent. However, once an 'optimum' LV is attained any further rise in $\dot{V}O_{2\ max}$ may be independent of the size of the muscle mass, and may be attributable mainly to qualitative changes in the muscle itself. This latter phase is clearly shown in normal subjects undergoing training and is suggested by the small changes occurring in the uninjured leg of patients during rehabilitation.

In normal subjects increasing the $\dot{V}O_{2\ max}$ of each leg separately by one-leg training did not significantly increase the $\dot{V}O_{2\ max}$ achieved in two leg exercise.

This observation was interpreted as supporting the view that in two-leg exercise which involves a relatively large muscle mass the limitation to aerobic power output was most likely imposed by central (cardiovascular) factors as suggested by Bevegård and Shepherd (1967). In contrast the limitation to one leg exercise was presumed to be peripheral, that is dependent upon the size and intrinsic state of the active muscle mass (Davies and Sargeant 1974a, b). However in the patients the combined improvement shown in the one-leg $\dot{V}O_{2\ max}$ of the injured and uninjured legs was reflected in an equivalent rise in the $\dot{V}O_{2\ max}$ of two leg exercise.

This contradictory finding seems to be explained by the fact that the rehabilitation programme undertaken by these patients included elements intended to improve general cardiovascular fitness as well as injured leg function. Thus it is not perhaps surprising that simultaneous improvements occur in both one and two-leg exercise performance.

Therefore the data on this group of patients cannot be interpreted as supporting the view recently revived in the literature (see [illegible]

[illegible] the [illegible]tion to aerobic power output is peripheral rather than central. What the present data both on patients and normals does indicate however is that in an integrated system such as that involved in the transport and utilization of oxygen it may be unwise to argue purely in terms of peripheral and central events. Rather the improvement of $\dot{V}O_{2\ max}$ will depend upon a balance between peripheral (skeletal muscle) and central events. Where the muscle mass is limiting the balance will swing towards dependence on improving peripheral function but in work demanding larger muscle groups it will move towards the delivery of oxygen from the central circulation and the limits imposed by cardiac output. The integration of transport and utilization of oxygen will thus depend upon the type of exercise and the state of training of the subject.

From a practical point of view in terms of rehabilitation procedures there are a number of interesting conclusions to be drawn from the thesis.

The muscle volumes of the patients injured and uninjured legs will under most circumstances accurately reflect the relative functional sta'es of the two limbs. In this context however it needs to be borne in mind that the data suggests that there is some decrement in the uninjured limb size and aerobic function as a result of the enforced reduction of activity levels consequent upon having the contralateral limb in plaster.

It would appear that the course of rehabilitation therapy undertaken by these patients restores maximum aerobic power output of the injured leg to 95% of that achieved with the uninjured leg.

Furthermore the two-leg $\dot{V}O_{2\ max}$ for a given LV is at the end of rehabilitation not significantly different when compared with normal subjects. However, it is not possible to accurately assess the efficacy of the rehabilitation course in the absence of data on spontaneous recovery which occurs without the benefit of specific therapy.

The ultimate levels of $\dot{V}O_{2\ max}$ and LV attained at the end of the recovery process by the injured and uninjured legs will reflect their prevailing level of activity. It may therefore be necessary to take into account whether there is a consistent preference for one leg in order to assess the normality of any inter-limb differences found at that time.

Measurement of the forces exerted and work performed during submaximal two-leg exercise indicates a large disproportionate sharing of work between the legs and this was not attributable to conscious effort on the part of the patients. The net force exerted by the injured leg is ~ 40% less than that exerted by the uninjured leg and clearly this will mean that 2-leg exercises may not produce the desired maximal effect when used as part of a programme of rehabilitation therapy unless carefully monitored.

Finally, to return to more theoretical considerations, the present thesis underlines the potential of the asymmetrical one-leg model. Its particular merit is that it permits the dissociation of central and peripheral factors and may therefore prove a most useful tool in the study of physiological control mechanisms during exercise.

REFERENCES

REFERENCES

[illegible] The physiological cost of negative work. J. Physiol. Lond., 117, 380.

Armitage, P., [illegible] Statistical methods in medical research. Blackwell Scientific: Oxford.

Åstrand, P-O., and Rodahl, K., (1970) Textbook of work physiology. McGraw-Hill, New York.

Banister, E.W., and Jackson, R.C., (1967) The effect of speed and load changes on oxygen intake for equivalent power outputs [illegible]

Bar-Or, O., Skinner, J.S., Buskirk, E.R., and Borg, G., (1972) Physiological and perceptual indicators of physical stress in 41–60 year-old men who vary in conditioning level and in body fatness. Med.Sci. Sports. 4, 96.

Bergstrom, J. and Hultman, E., (1966) Muscle glycogen synthesis after exercise: An enhancing factor localized to the muscle cells in man. Nature, 210, 309.

Bevegård, B.S., and Shepherd, J.T. (1967) Regulation of Circulation during exercise. Physiol. Rev. 47, 178.

[illegible] Energy metabolism in different human skeletal muscles during voluntary isometric contraction. Acta physiol. Scand. 95, 73A.

Borg, G., (1962) Physical performance and perceived exertion. Lund: Studia Psykolog. et Pedagog. Invest XI.

Borg, G., (1970). Perceived exertion as an indicator of somatic stress. Scand. J. Rehab. Med. 2, 92.

Borg, G. and Linderholm, H., (1967) Perceived exertion and pulse rate during graded exercise in various age groups. Acta med. scand. 187, 17.

Carlson, L.A. and Pernow, B., (1959). Oxygen utilisation and lactic acid formation in the legs at rest and during exercise in normal subjects and in patients with arteriosclerosis obliterans. Acta med. Scand. 164, 39.

Carlson, L.A. and Pernow, B., ([illegible]) Studies on the peripheral circulation and metabolism in man. I Oxygen utilisation and lactate-pyruvate formation in the legs at rest and during exercise in healthy subjects. Acta physiol. scand. 52, 328.

Carlson, L.A. and Pernow, B. (1962) Studies on the peripheral circulation and metabolism in man. II Oxygen utilisation and lactate-pyruvate formation in the legs at rest and during exercise in patients with atherosclerosis obliterans. Acta med. scand. 171, 311.

Carlson, L.A., Pernow, B., and Zetterquist, S., (1962). Studies on the peripheral circulation and metabolism in man. III Oxygen utilisation and lactate-pyruvate formation in the legs at rest and during exercise in subjects with hyperkinetic circulation and low physical working capacity (vasoregulatory asthenia) and in healthy females. Acta med. scand. [illegible], [illegible].

Carlsoo, S., and Molbech, S., (1966) The functions of certain two joint muscles in a closed muscular chain. Acta morph. neerl. scand. 6, 377.

Carns, M.L., and Glassow, R.B., (1957) Changes in body volume accompanying weight reduction in college women. Hum. Biol. 29, 305.

Cavanagh, P.R., Petak, K.L., Shapiro, R., and Daly, D. Jnr., (1974) Bilateral asymmetry in work output during cycle ergometer pedalling. Med. Sci. Sports 6, 80.

Clausen, J.P., Klausen, K., Rasmussen, B., and Trap-Jensen, J. (1973) Central and peripheral circulatory changes after training of the arms or legs. Am. J. Physiol. 225, 675.

Clausen, J.P., Trap-Jensen, J. and Lassen, N.A., (1970) The effects of training on the heart rate during arm and leg exercise. Scand. J. clin. Lab. Invest. 26 : 3, 295.

Cooper, K.E., Edholm, O.G., and Mottram, R.F. (1953) The partition of the blood flow between skin and muscle in the human forearm. J. Physiol., Lond. 123, 33P.

Coote, J.H., Hilton, S.M., and Perez-Gonzalez, J.F., (1971). The reflex nature of the pressor response to muscular exercise. J. Physiol. Lond., 215, 789.

Cotes, J.E., Berry, G., Burkinshaw, L., Davies, C.T.M., Hall, A.M., Jones, P.R.M., and Knibbs, A.V., (1973). Cardiac frequency during submaximal exercise in young adults; relation to lean body mass, total body potassium and amount of leg muscle. Quart. Jl. exp. Physiol. 58, 239.

Cuddingham, [illegible], (1973). Qudariceps femoris strength. Rheumat. Rehabil. 12, 77.

Cuthbertson, D.P., (1929) Influence of prolonged muscular rest on metabolism. Biochem. J. 23, 1328.

Davies, C.T.M., (1968). Limitations to the prediction of maximum oxygen intake from cardiac frequency measurements. J. appl. Physiol. 24, 700.

Davies, C.T.M., (1972) The oxygen transporting system in relation to age. Clin. Sci. 42, 1.

Davies, C.T.M., (1974) The relationship of leg volume muscle (plus bone) to maximal aerobic power output on a bicycle ergometer: The effects of anaemia, malnutrition, and physical activity. Ann. Hum. Biol. 1, 47.

Davies, C.T.M., and Barnes, C.A., (1972) Negative (eccentric) work. I : Effects of repeated exercise. Ergonomics 15, 3.

Davies, C.T.M., Barnes, C.A., and Godfrey, S., (1972). Body composition and maximal exercise performance in children. Hum. Biol. 44, 195.

Davies, C.T.M., Barnes, C.A., Edholm, O.G., Fox, R.H., Ojikutu R. Ola, Samueloff, A.S., (1972), Ethnic differences in physical working capacity. J. appl. Physiol. 33, 726.

Davies, C.T.M., Mbelwa, D., Crockford, G.W., and Weiner, J.S. (19[illegible]3) Exercise tolerance and body composition of male and female Africans, aged 18-30 years. Hum. Biol. 45, 31.

Davies, C.T.M., and Sargeant, A.J., (19[illegible]a) Physiological responses to standardised arm work. Ergonomics 17, 41.

Davies, C.T.M. and Sargeant, A.J., (19[illegible]b) Physiological responses to one- and two-leg exercise breathing air and 45% oxygen. J. appl. Physiol. [illegible], 14[illegible].

Davies, C.T.M., and Sargeant, A.J., [illegible] determination of maximal aerobic power output during work with one or two limbs. Europ. J. appl. Physiol. 32, 207.

Davies, C.T.M., and Sargeant, A.J., (1975a) Effects of exercise therapy on total and component tissue leg volumes of patients [illegible] 2, 327.

Davies, C.T.M., and Sargeant, A.J. (1975b) Physiological responses to exercise in patients following fracture of the lower limb. Scand. J. Rehab. Med. 7, 45.

Davies, C.T.M., and Sargeant, A.J., (1975c) Chang[illegible] performance of the lower limb after fracture and subsequent rehabilitation. Clin. Sci. Mol. Med. 48, 10[illegible].

Davies, C.T.M., and Sargeant, A.J., (1975d) Effects of training on the physiological responses to one- and two-leg work. J. appl. Physiol. 38, 377.

Davies, C.T.M. and Sargeant, A.J., [illegible]ion in patients recovering from limb injury. Archs. phys. med. Rehabil. 56, 340.

Davies, C.T.M., and Shirling, D.S., (1967) The rapid sampling, storage and analysis of expired air. Ergonomics 10, 349.

Davies, C.T.M., Tuxworth, W., and Young, J.M., (1970). Physiological effects of repeated exercise. Clin. Sci. 39, 247.

Deitrick, J.E., Whedon, G.D., and Shorr, E., (1948) Effects of immobilization upon various metabolic and physiologic functions of normal men. Am. J. Med. 4, 3.

Dempsey, J.A., (1974) Exercise and Obesity; in Sports Medicine, eds. Ryan, A.J. and Allman, F.L. Academic Press, New York.

Dempster, W.T., [illegible] anthropometry of body action. Ann. N.Y. Acad. Sci. 63, 559.

Dickinson, S., (1929) The efficiency of bicycle pedalling as affected [illegible]

[illegible] segment parameters. USAF WADC Tech. Report No. 116.03 Wright-Patterson Air Force Base, Ohio.

Dunér, H., (1959) Oxygen uptake and working capacity in man during work on the bicycle ergometer with one and both legs. Acta. physiol. scand. 46, 55.

Durnin, J.V.G.A., and Rahaman, M.M., (1967) The assessment of the amount of fat in the human body from measurements of skinfold thickness. Br. J. Nutr. 21, 681.

Edwards, R.H.T., (1971) Percutaneous needle biopsy of skeletal muscle in diagnosis and research. Lancet [illegible]

Ekblom, B., (1969) Effect of physical training on oxygen transporting system in man. Acta. physiol. scand. suppl. 328.

Ekblom, B., and Goldbarg, A.N., (1971) The influence of physical training and other factors on the subjective rating of perceived exertion. Acta physiol. scand. 83, 399.

Folkow, B., and Neil, E., (1971) Circulation. Oxford Univ. Press. Oxford.

Freyschuss, U., (1970) Cardiovascular adjustment to somatomotor activation. Acta physiol. scand. suppl. 342.

Freyschuss, U, and Strandell, T., (1968) Circulatory adaptation to one- and two-leg exercise in supine position. J. appl. Physiol. 25, 511.

Fried, T., and Shephard, R.J., (19[illegible]). Assessment of a lower extremity training program. Can. Med. Ass. J. 103, 260.

Gleser, M.A., (1973) Effects of hypoxia and physical training on haemodynamic adjustments to one-legged exercise. J. appl. Physiol. 34, 655.

Godfrey, S., and Davies, C.T.M., (1970) Estimates of arterial PCO_2 and their effect on the calculated values of cardiac output and dead space on exercise. Clin. Sci. 39, 529.

Goldspink, G., Larson, R.E., and Davies, R.E., (1970) The immediate energy supply and the cost of maintenance of isometric tension from different muscles in the hamster. Z. vergl. Physiol. 66, 389.

[illegible] Local xenon
133 clearance from the quadriceps muscle during exercise in man. J. appl. Physiol. 22, 305.

Helander, E., (1958) Adaptive muscular "allomorphism". Nature 182, 1035.

Hermansen, L., [illegible]
subjects. Acta physiol. scand. Suppl. 399.

Hill, A.V., (1965) Trails and Trials in Physiology. Arnold, London

Hills, W.L., and Byrd, R.J., (1973) Effects of Immobilization in the human forearm. Archs. phys. med. Rehabil. 54, 87.

Hoes, M.J.A.J.M., Binkhorst, R.A., Smeekes-Kuyl, A.E.M.C., Vissers, A.C.A., (1968) Measurement of forces exerted on pedal and [illegible]
Int. Z. angew. Physiol. 26, 33.

Jones, N.L., Campbell, E.J.M., McHardy, G.J.R., Higgs, B.E., and Clode, B., (1967) The estimation of carbon dioxide pressure of mixed venous blood during exercise. Clin. Sci. 32, 311.

Jones, P.R.M. (1970a) Radiographic determination of leg fat muscle and bone volumes in male and female young adults. J. Physiol. Lond. 207. 1P.

Jones, P.R.M. (1970b) An application of physiological anthropometry. Ph.D. Thesis University of Technology, Loughborough.

Jones, P.R.M. and Pearson, J., (1969) Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. J. Physiol. Lond. 204, 63P.

Kaijser, L., (1970). Limiting factors for aerobic muscle performance. Acta physiol. scand. Suppl. 346.

Katch, V.L., Amuchie, F., and Michael, E.D., (1973) The use of body weight and girth measurements in predicting segmental leg volume of females. Hum. Biol. 45, 293.

Klausen, K., Clausen, J.A., Rasmussen, B., and Trap-Jensen, J., (1971) Effect of strenuous arm and leg training on pulmonary ventilation, metabolism and blood pH during submaximal exercise. Acta physiol. scand. 82, 8A.

[illegible], [illegible]. and Mitchell, J.H., (1972) Reflex cardiovascular and respiratory [illegible]. J. Physiol. Lond. 224, 173.

McMorris, R.O., and Elkins, E.C. (1954) A study of production and evaluation of muscular [illegible]. phys.med. Rehabil. 35, 420.

Patel, A.N., Razzak, Z.A., and Dastur, D.K., (1969) Disuse Atrophy of human skeletal muscle. Archs. Neurol. 20, 413.

Pernow, B. and Saltin, B. (1971). Availability of substrates and [illegible] J. appl. Physiol. 31, 416.

[illegible] (19[illegible]) [illegible] peripheral circulation and metabolism in man IV Oxygen utilization and lactate formation in the legs of healthy young men during strenuous exercise. Acta physiol. scand. [illegible]4, 289.

Pirnay, F., Lamy, M., Dujardin J, Deroanne, R. and Petit, J.M. (1972) Analysis of femoral venous blood during maximum muscular exercise. J. appl. Physiol. 33, 289.

Rasch, P.J., Morehouse, L.E., (19[illegible]) Effect of static and dynamic exercises on muscular strength and hypertrophy. J. appl. Physiol. 11, 29.

Rose, D.L., Radzyminski, S.F. and Beatty, R.R., (1957) Effect of brief maximal exercise on the strength of the quadriceps femoris. Archs. phys. med. Rehabil.. 38, 157.

Roux, W., (1905) Die [illegible]klungsmechanik. Engelmann, Leipzig.

Rowell, L.B., (19[illegible]4) Human cardiovascular adjustments to exercise and thermal stress. Physiol. Rev. 54, 75.

Rowell, L.B., Blackm[illegible], J.[illegible], [illegible]ce, R.A., ([illegible]). [illegible] green clearance and estimated hepatic blood flow during mild to maximal exercise in upright man. J. clin. Invest. 43, 1677.

Saltin, B., Blomqvist, G., Mitchell, J.H., Johnson, R.L. [illegible], Wildenthal, K., and Chapman, C.B., (1968). Response to exercise after bed rest and after training. Am. Heart Assoc. Monograph No. 23.

Saltin, B., and Grimby, G., (1968) Physiological analysis of middle aged and old former athletes: comparison with still [illegible]

Saltin, B., and Landin, S., (1975) Work capacity, muscle strength and SDH activity in both legs of hemiparetic patients and patients with Parkinson's disease. Scand. J. clin. Lab. Invest. 35, 531.

Saltin, B., Nazar, K., Costill, D.L., Stein, E., Jansson, E., Essén, B. and [illegible] adaptations to one-legged exercise. Acta physiol. scand. 96, 289.

Sanne, H., (1973) Exercise tolerance and physical training of non-selected patients after myocardial infarction. Acta. med. scand. Suppl. 551.

Sargeant, A.J., and Davies, C.T.M. (1973) Perceived exertion during rhythmic exercise involving different muscle masses. J. Human Ergol. 2, 3.

Skinner, J.S., Borg, G. and Buskirk, E.R., (1969) Physiological and perceptual characteristics of young men differing in activity and body composition. In: Exercise and fitness, ed. D. Franks, The Athletic Institute, Chicago.

Skinner, J.S., Hutsler, R., Bergsteinova, V., and Buskirk, E.R. (1973) Perception of effort during different types of exercise and under different environmental conditions. Med. Sci. Sports. 5, 110.

Stoboy, H., Friedebold, G., and Strand, F.L., (1954) Evaluation of the effect of isometric training in functional and organic muscle atrophy. Archs. phys. med. Rehabil. 49, 508.

Taylor, H.L., Erickson, L., Henschel, A., and Keys, A., (1945) Effect of bed rest on the blood volume of normal young men. Am. J. Physiol. 144, 227.

Weiner, J.S., and Lourie, J.A., (1969) Human Biology, A guide to field methods. I.B.P. Handbook No. 9. Blackwell Scientific, Oxford.

Whipp, B.J., and Wasserman, K., (1968) The efficiency of muscular work. J. appl. Physiol. 26, 644.

[illegible] Isometric and Isotonic exercises of the quadriceps after injuries to the knee. Archs. phys. med. Rehabil. 45, 571.

Zook, D.E., (1932) The physical growth of boys. Am. J. Dis. Child. 43, 1134.

List of Abbreviations used in the text
and Notes on Statistical treatment.

LIST OF ABBREVIATIONS

Physiological Parameters

f_H	cardiac frequency
F_IO_2	fractional concentration of inspired oxygen
LA	lactic acid
MPF	mean of the peak force exerted in each cyle over a 1 or 2 minute period
$\dot{Q}$	cardiac output
SV	stroke volume
RPE	rated perceived exertion
$\dot{V}CO_2$	carbon dioxide output
$\dot{V}_E$	pulmonary expired ventilation
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_{2\,max}$	maximum oxygen uptake
$\% \dot{V}O_{2\,max}$	oxygen uptake expressed as a percentage of $\dot{V}O_{2\,max}$ measured under the same conditions.
V_T	mean tidal volume
$\dot{W}$	work load standardised per unit time
$\dot{W}_{CR}$	work performed on the cranks of the ergometer (calculated from force records) standardised per unit time.

Submaximal responses to exercise are characterised from linear regression of the data as follows:

$f_{H\,1.5}$	cardiac frequency at $\dot{V}O_2$ of 1.5 l/min.
$f_{H\,65}$	cardiac frequency at 65% of $\dot{V}O_{2\,max}$
$\dot{Q}_{1.5}$	cardiac output at $\dot{V}O_2$ of 1.5 l/min
$SV_{1.5}$	stroke volume at $\dot{V}O_2$ of 1.5 l/min
$\dot{V}_{E\,1.5}$	pulmonary ventilation at $\dot{V}CO_2$ of 1.5 l/min

$\dot{V}O_{2\ 175}$	oxygen uptake in 1-leg exercise at f_H of 175 beats/min
$\dot{V}O_{2\ 195}$	oxygen uptake in 2-leg exercise at f_H of 195 beats/min
$\dot{V}O_{2\ 450\ (or\ 73)}$	oxygen uptake in 1-leg exercise at work load of 450 kpm/min (73 watts).
$\dot{V}O_{2\ 900\ (or\ 147)}$	oxygen uptake in 2-leg exercise at work load of 900 kpm/min (147 watts)
$\dot{V}O_{2\ R20}$	oxygen uptake at RPE 20.
$V_{T\ 30}$	mean tidal volume at $\dot{V}_E$ of 30 l/min

Physical characteristics

i	injured leg
ui	uninjured leg
p	preferred limb
np	non-preferred limb
r	right leg
l	left leg
LBM	lean body mass calculated from Σ4sf (Durnin and Rahaman 1967)
LV	leg volume
Σ 4sf	sum of 4 skinfolds (triceps, biceps, subscapular, suprailiac)

Statistical

cv	coefficient of variation
d	difference
r	correlation coefficient
SD	standard deviation
SEy	standard error of the estimate of y
t	Student's 't' value.
Δ	change (e.g. before cf. after training)

STATISTICAL TREATMENT

Conventional methods were used in the statistical treatment of the data (Armitage 1970).

Summarised data is given in the form of means and standard deviations throughout the text.

Comparison of data was made using Student's 't' test. Where these comparisons were between different groups of patients and/or normal subjects a grouped 't' test was used. A paired 't' test was used when comparisons were made within the same individual (e.g. before vs. after treatment/training; or right leg exercise response vs. left leg).

APPENDIX 1

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Effects of exercise therapy on total and component tissue leg volumes of patients undergoing rehabilitation from lower limb injury

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Summary. Anthropometric and X-ray data were collected on 20 young male patients undergoing a systematic programme of exercise therapy following fracture of the leg and consequent immobilization for 25–254 (mean 117) days. Estimates of total leg volume, calculated from X-ray or from anthropometric measurements, were essentially interchangeable in both the injured and uninjured legs. A procedure for estimating muscle volume from total leg volume is given.

At the start of rehabilitation, muscle volume was significantly smaller (860 ml, 16 per cent) in the injured than in the uninjured leg. By the end of rehabilitation (mean 50 days) the injured leg had significantly increased by 360 ml (8 per cent) over its initial volume, and the uninjured one had increased but not significantly (120 ml, 2 per cent), so that the injured leg was still ~11 per cent (620 ml) smaller than the uninjured.

The initial degree of atrophy and the period of immobilization were not significantly correlated, although the latter showed a negative relationship ($P > 0.05$) with the rate of increase of muscle volume in the injured leg. No significant correlation was found between the ratio of injured: uninjured leg volumes and muscle width measurements at ⅓ subischial, at 12.7 cm above the knee joint space or at the maximum calf. In systematic studies involving atrophy muscle volume must therefore be estimated either by anthropometry or by X-ray measurements.

1. Introduction

The importance of the relationship of limb size and structure to physiological function has been shown in a number of papers from this laboratory (see Davies, 1974, for general review and Davies and Sargeant, 1974 a, b) but no comparable data exist for patients who suffer limb injury.

The present paper is concerned with anthropometric studies on patients undergoing a systematic programme of exercise therapy following fracture of the leg and consequent immobilization for 25–254 days (mean 117 days) at the Joint Services Medical Rehabilitation Unit, Chessington.

A cross-sectional study was made of 20 patients from 1 to 79 (mean 28) days following the end of immobilization; sixteen of these patients were studied at both the beginning and end of a period of exercise therapy (mean length 50, range 20–89 days).

2. Subjects

The subjects were young service personnel who had suffered leg fracture. The fractures were divided as follows: fractures of femur, 2 left; fractures of tibia and fibula, 7 left and 9 right; and two cases, both left legs, where fractures of both upper and lower leg were sustained. Of these 20 cases, 8 had some form of internal fixation. Patients included in the longitudinal study were either seen within one week of arrival at Chessington, or as soon as satisfactory union had occurred and the injured limb was weight-bearing and active exercise therapy began.

Data were also collected on 12 normal subjects, 7 of whom underwent an intensive training programme (see Davies and Sargeant, 1975, for further details).

The mean age, height, weight and lean body mass (LBM) of the subjects were respectively: Patients—22·4 years, 172·5 cm, 69·7 kg and 58·7 kg LBM; Normals—31·0 years, 175·5 cm, 73·7 kg and 63·3 kg LBM.

3. Methods

Height and weight of subjects were measured and lean body mass estimated from the sum of four skinfold measurements (Durnin and Rahaman, 1967). Leg volumes were obtained by anthropometry, after the method of Jones and Pearson (1969), and from soft-tissue X-rays (Jones, 1970).

The X-rays were taken at an anode–film distance of 2 m with the subject standing erect, but relaxed. Thigh X-rays were taken in the medio-lateral plane whilst the lower leg X-rays were taken in the anterior–posterior plane. The subjects wore appropriate lead-lined shielding to protect the gonads during this procedure (Weiner and Lourie, 1969).

4. Results

The patients were on average ~8 years younger ($P<0·001$) than the normals and tended to be somewhat shorter and lighter in terms of both total body weight and lean body mass (LBM); these latter differences are not, however, statistically significant. The effect of exercise therapy on 16 patients and a training programme on the seven normal subjects produced no significant changes of whole body characteristics.

Comparison of X-ray and anthropometry

The estimates of total leg volume calculated from direct anthropometry and from soft tissue X-ray measurements (table 1) are highly correlated ($P<0·001$; coefficient of variation 4·6 per cent). The X-ray estimates appear to exceed the anthropometrically derived volumes in the patients (~1·5 per cent) and the reverse is seen in the normal subjects (~0·8 per cent) but these differences are not statistically significant.

In order to convert the total leg volumes estimated by anthropometry to muscle plus bone volumes it is necessary to make allowance for the thickness of the subcutaneous fat. The relationships of skinfold caliper with X-ray measurements of subcutaneous fat at each of the four measurement sites were linear and highly

		Uninjured leg					Injured leg				
		Total leg volume (litres)					Total leg volume (litres)				
		A	X-ray	d %	r	c.v. %	A	X-ray	d %	r	c.v. %
Patients	Before (n = 20)	8.07 ± 1.48	8.19 ± 1.51	−1.6 ± 6.7	0.9[illegible]	4.2	7.57 ± 1.02	7.68 ± 1.23	−1.4 ± 6.1	0.91	4.3
	After (n = 8)	8.04 ± 1.40	8.04 ± 1.40	−1.1 ± 7.8	0.95	4.1	8.15 ± 1.19	8.27 ± 1.10	−1.5 ± 5.7	[illegible]	[illegible]
		Right leg					Left leg				
Normals	(n = 12)	8.07 ± 0.96	8.62 ± 0.88	−[illegible] ± 5.2	0.9[illegible]	5.4	[illegible]	8.6 ± [illegible]	+0.0 ± 6.5	0.9[illegible]	4.6

Table 1. Comparison of direct anthropometric (A) and X-ray determinations of total leg volume, mean ± s.d., for the patients' injured and uninjured legs before and after rehabilitation and for 12 normal subjects. d is the % difference (A − X-ray), r correlation coefficient and c.v. coefficient of variation. None of the differences reach statistical significance when compared with a paired t test.

Subcutaneous fat site	Group	a	b	P	SEy	r	n	$\bar{x}$
Anterior thigh	Patients (injured)	0·07	0·69	<0·001	1·70	0·89	20	14·3
	Patients (uninjured)	2·75	0·45	<0·001	1·26	0·84	20	13·8
	Normals	0·70	0·61	<0·001	1·22	0·84	24	9·9
Posterior thigh	Patients (injured)	1·55	0·60	<0·001	1·64	0·76	20	13·5
	Patients (uninjured)	3·48	0·42	<0·001	1·43	0·70	20	12·2
	Normals	1·48	0·49	<0·001	1·42	0·66	24	9·6
Medial calf	Patients (injured)	1·26	0·53	<0·001	1·06	0·88	20	11·6
	Patients (uninjured)	0·29	0·56	<0·001	0·91	0·90	20	9·4
	Normals	1·12	0·51	<0·001	0·75	0·88	24	6·6
Lateral calf	Patients (injured)	3·03	0·21	<0·002	1·05	0·52	20	11·7
	Patients (uninjured)	2·36	0·26	<0·005	0·96	0·60	20	9·5
	Normals	2·05	0·27	<0·001	0·69	0·75	24	7·3

Table 2. The relationship of X-ray (y) to skinfold caliper measurements (x) of subcutaneous fat at 4 leg sites in the patients' injured and uninjured legs and in normals. a=intercept, b=regression coefficient, SEy=standard error of estimate of y, r=correlation coefficient, P=significance, n=number, $\bar{x}$=mean value of x.

significant in all cases, allowing caliper measurements to be converted to true fat thickness by application of the appropriate regression equation given in table 2. The 2 thigh and the 2 calf fat widths thus obtained were then summed and deducted from the diameters obtained from the respective circumference measurements of the upper and lower legs. The segments of the legs were then computed as though they were truncated cones representing a muscle plus bone volume (Jones and Pearson, 1969).

The possibility of using an assumed value of bone volume in order to obtain an estimate of the muscle volume alone using anthropometry was examined. Calculating bone volumes from X-ray measurements of bone dimensions after the method suggested by Jones (1970) no significant difference was seen in absolute terms between the bone volumes of the injured and uninjured legs of the patients or between the right and left legs of the normals. Furthermore, in normal subjects and in the uninjured legs of the patients the bone volume is a fairly constant and rather small proportion (~11 ± 1 per cent) of the muscle plus bone volume. The proportion of bone to muscle plus bone volume of the injured compared with the uninjured leg is however somewhat higher, particularly before rehabilitation (13·1 per cent) due to a reduction in the muscle component, although the proportion of bone decreases (1·4 per cent) as a result of an increase in the muscle component following exercise therapy. However, none of the differences or changes attain conventional levels of significance.

Thus if the bone volume is assumed to be 11 per cent of the uninjured leg muscle plus bone volume, the error involved in using this to derive muscle volume alone of the injured leg as compared with using an estimate of bone volume based on direct X-ray measurements is very small indeed (c.v. ~1 per cent representing ~ ± 60 ml of muscle volume).

		Uninjured leg (litres)				Injured leg (litres)			
		Total	Fat	Muscle + Bone	Muscle	Total	Fat	Muscle + Bone	Muscle
Patients (n=16)	Before	7·88** ±1·19	1·68* ±0·42	6·20** ±0·86	5·51** ±0·77	7·19 ±1·06	1·85 ±0·55	5·34 ±0·72	4·65 ±0·63
	After	8·00** ±1·31	1·67 ±0·44	6·32** ±0·97	5·63** ±0·86	7·47 ±1·20	1·77 ±0·54	5·70 ±0·82	5·01 ±0·72
	Δ	+0·12 (1%)	−0·01 (1%)	+0·12 (2%)	+0·12 (2%)	+0·28†† (4%)	−0·08 (4%)	+0·36†† (7%)	+0·36†† (8%)
		Right leg (litres)				Left leg (litres)			
Normals (n=7)	Before	8·87 ±0·80	1·54 ±0·40	7·33‡ ±0·76	6·46‡ ±0·67	8·56‡ ±0·58	1·50 ±0·37	7·05‡‡ ±0·53	6·26‡‡ ±0·45
	After	8·76 ±0·91	1·50 ±0·39	7·27‡ ±0·73	6·47‡ ±0·65	8·52‡ ±0·71	1·48 ±0·38	7·04‡‡ ±0·61	6·24‡‡ ±0·54
	Δ	−0·11 (1%)	−0·04 (2%)	+0·06 (<1%)	+0·01 (<1%)	−0·04 (<1%)	−0·02 (1%)	−0·01 (<1%)	−0·02 (<1%)

Significance: Patients, injured vs. uninjured **$P<0·001$, *$P<0·05$
Δ Change, before vs. after ††$P<0·001$, †$P<0·05$
Normals vs. patients ‡‡$P<0·001$, ‡$P<0·05$

Table 3. Changes in total leg and component tissue volumes determined by physical anthropometry in 16 patients undergoing therapy and in 7 normal subjects undergoing an intensive training programme (see Davies and Sargeant, 1975).

Total and component leg tissue volumes

Table 3 summarizes the total and component tissue volumes for 16 patients before and after rehabilitation and 7 normal subjects before and after an intensive training programme (Davies and Sargeant, 1975).

The normal subjects demonstrate no significant differences either between right and left legs or as a result of training. However, before rehabilitation in the patients, the data indicate that the mean total volume of the injured leg is reduced ($P<0{\cdot}001$) by 690 ml (9 per cent) compared with the uninjured leg. When the muscle volume alone is considered the difference between the injured and uninjured legs rises to 860 ml (16 per cent; $P<0{\cdot}001$). In contrast the estimated fat volume is slightly but significantly larger (+170 ml; $P<0{\cdot}05$) in the injured than in the uninjured leg, while the bone volume estimated by direct X-ray measurement is identical.

During rehabilitation, the muscle volume of the injured leg significantly ($P<0{\cdot}001$) increases by 360 ml (8 per cent), while the muscle volume of the uninjured leg shows a non-significant increase of 120 ml (2 per cent). As a result, there still remain after rehabilitation significantly ($P<0{\cdot}001$) smaller total (530 ml; 7 per cent), muscle plus bone (620 ml; 10 per cent) and muscle (620 ml; 11 per cent) volumes in the injured compared with the uninjured legs. The previous difference between fat volumes disappears, however, as the measured injured-leg fat decreases by 80 ml.

Rehabilitation rate

The time course of the increase in muscle volume during the period of study is illustrated in figure 1, where changes in the patients' injured and uninjured legs are considered as percentages of the initial measurement, and where the time course is given as a percentage of the rehabilitation period.

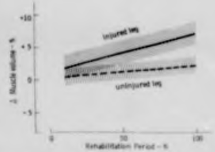

Figure 1. The time course during rehabilitation of the per cent change in muscle volume of the injured (——) and uninjured legs (- - -) expressed in terms of the initial measurement for each leg. In each case the total duration of the rehabilitation period is taken as 100 per cent, the hatched area represents the standard error of the regression lines.

There is a small but significant ($P<0{\cdot}05$) negative association between the original length of time spent immobilized and the overall rate of increase in the muscle volume of the injured leg (calculated from table 3) expressed as percentage change per 10 days as indicated in figure 2.

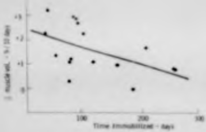

Figure 2. The relationship between the overall rate of increase in muscle volume of the injured leg (expressed as per cent improvement over the starting value over a 10-day period) and the time spent immobilized. $y=2{\cdot}39-0{\cdot}007x$, $r=-0{\cdot}53$

Simple indices for gauging muscle loss

We also investigated the possibility of using single muscle width measurements (from X-ray) in lieu of the more extended muscle volume estimations in order to gauge the relative loss of muscle volume from the injured compared with the uninjured legs of patients. Comparison of the ratios of injured : uninjured leg muscle volumes with the ratios of muscle width at each of 3 sites showed no significant correlation. The widths were measured at one third the subischial height above the knee joint space (Cotes, Berry, Burkinshaw, Davies, Hall, Jones and Knibbs, 1973), at 12·7 cm (5 inches) above the knee joint space, and at the maximum calf. The highest correlation coefficient was for the first of these width measurements ($r = +0{\cdot}33$) but even this fails to reach conventional levels of significance.

5. Discussion

The atrophy and hypertrophy of muscle in response to changing activity patterns first found scientific generalization in the "aktivitätshypertrophie" and "inaktivitätatrophie" theories of Rou[illegible]) and it is a common observation that [illegible] limb is immobi[illegible] and Davies and Sargeant, 1974 a, b). Such studies as there are have relied on limb circumference measurements (e.g. Rose, Radzyminski and Beatty, 1957; Zohn, Leach and Stryker, 1964; Rasch and Morehouse, 1957; Stoboy, Friedebold and Strand, 1968; Patel, Razzak and Dastur, 1969), or muscle width measurements from X-rays (Fried and Shephard, 1970); the former measurement will include the subcutaneous fat component which may obscure changes in muscle volume, while both measurements are usually taken at a single site on a limb segment which may not be truly representative and may inadequately reflect the changes in actual muscle volume.

We have set out to examine the effects of immobilization and subsequent rehabilitation on total and component tissue leg volumes on a group of young male patients recovering from leg fracture. Total leg volume was estimated by treating the leg as a series of truncated cones extending from the minimum ankle circumference to the gluteal furrow (Jones and Pearson, 1969). This mathematical treatment has previously been shown, using both measurements taken from X-ray and direct anthropometry, to correlate highly with limb volume determinations by water displacement (Jones and Pearson, 1969; Davies, Barnes and Godfrey, 1972; Davies, 1974). In the present study we independently assessed limb volume by anthropometry and X-ray, and found a high correlation (table 1, $P<0{\cdot}001$; coefficient of variation 4·6 per cent) between these techniques with only a slight and non-significant bias towards underestimation ($\sim$1·5 per cent) by anthropometry in the patients, indicating that they are essentially interchangeable and that where it is considered desirable, simple anthropometry using a steel tape and rule may be used in lieu of X-ray measurements.

Determination of component tissue changes from anthropometry is, however, more problematical since it is not possible to take direct measurements of muscle or bone dimensions. However, an estimate of the muscle plus bone volume may be derived from the total leg volume by subtracting the thickness of the subcutaneous fat layer measured with skinfold calipers from the total diameter of the respective truncated cones. In order to do this it is necessary to convert the caliper reading into a single thickness. We have compared the caliper with X-ray measurements of the subcutaneous fat layer at the four sites measured both in patients' injured and uninjured legs and in normal subjects (table 2). The relationship was highly significant and linear in all cases, thus enabling the subcutaneous fat thickness to be estimated from caliper measurements alone by application of the appropriate regression equation.

The partitioning of the muscle and bone volumes without resorting to radiography may seem a more intractable problem. However, the bone volume as estimated after the technique of Jones (1970) from X-ray measurements is a rather small and constant proportion of the muscle plus bone volume in uninjured legs. Therefore, if the bone volume is calculated at 11 per cent of the uninjured leg muscle plus bone volume and then subtracted from the latter volumes of injured and uninjured legs, then in comparison with volumes derived after precise X-ray measurement of the bone dimensions, the error involved in the estimation of the much larger muscle component is very small indeed (c.v. <1 per cent) and thus for most practical purposes the use of radiography in this connection seems hard to justify.

The effects of immobilization and subsequent rehabilitation on the total, fat, muscle plus bone and muscle volumes as derived from anthropometry according to the techniques described are summarized in table 3. The volume changes which occur in these patients are largely attributable to changes in the muscle volume alone, since bone volumes remain constant, although the fat volume measured in the injured leg is slightly (170 ml) but significantly ($P<0.05$) larger than in the uninjured leg at the start of rehabilitation. The effect of rehabilitation is to reduce the measured fat volume in the injured leg by 80 ml and in the uninjured leg by 10 ml. It would be most interesting if these differences in the amount of subcutaneous fat reflected genuine changes resulting from the effects of immobilization and subsequent exercise therapy. However, the changes are admittedly small and the possibility that they are artifacts of the method of measurement cannot be discounted.

Thus although the difference between the injured and uninjured legs at the start of rehabilitation is only 9 per cent in terms of total volume, when allowance is made for the fat and bone volumes, the difference in muscle volume rises to 16 per cent. As was expected, the muscle volume increased significantly ($P<0.001$) in the injured leg as a result of rehabilitation by 360 ml (8 per cent). Rather more surprisingly it was found that the uninjured leg muscle volume also showed a slight though non-significant increase representing 2 per cent of the initial volume, thus off-setting some of the apparent improvement in the injured leg, so that the difference at the end of rehabilitation between injured and uninjured leg was still 11 per cent (cf. 16 per cent before). This finding would seem to indicate that the immobilization of one leg with consequent restriction of normal activities is sufficient to result in muscle atrophy in the uninjured limb. It is possible, however, though less likely, that the rehabilitation programme, including as it does elements of strength training for both limbs, may may result in a hypertrophy of the uninjured leg muscle above the level prior to injury, and certainly this view is not inconsistent with the finding of a ~6 per cent increase in cross-sectional area in normal subjects (McMorris and Elkins, 1954) as a result of 12 weeks intensive training (cf. 7 weeks in the present study).

Considering the rate of increase in the leg muscle volume as a percentage of the initial pre-rehabilitation measurement (figure 1) the mean rate of improvement of the injured leg is ~1.2 per cent per 10 days. This rate seems largely independent of the stage of rehabilitation and the increase in volume appears to be linear with time. Despite a great deal of intersubject variability there is a slight but significant ($P<0.05$) negative association between the rate of muscle volume increase and the time spent immobilized (figure 2). The possible reasons for this association are complex and may be more psychological rather than physiological arising from loss of motivation and increasing apathy with the length of time taken for the fracture to achieve satisfactory union, in addition to restricted joint mobility and muscle adhesions which limit full participation in the exercise therapy programme.

Like Patel *et al.* (1969) we could find no correlation between the initial degree of atrophy (whether taken as the first measurement or predicted by backward extrapolation at the end of immobilization) and the length of time spent immobilized, although this period ranged from 25 to 254 days. This suggests that the atrophic response to disuse in man is a rapid phenomenon occurring within the first few weeks of immobilization.

The nature of the muscle atrophy is not clear although it is interesting to note

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References

Cotes, J. E., Berry, G., Burkinshaw, L., Davies, C. T. M., Hall, A. M., Jones, P. R. M., and Knibbs, A. V. (1973). Cardiac frequency during submaximal exercise in young adults: relation to lean body mass, total body potassium and amount of leg muscle. *Quarterly Journal of Experimental Physiology*, **58**, 239–250.

Davies, C. T. M. (1974). The relationship of leg volume (muscle plus bone) to maximal aerobic power output on a bicycle ergometer: the effects of anaemia, malnutrition and physical activity. *Annals of Human Biology*, **1**, 47–55.

Davies, C. T. M., Barnes, Carolyn A., and Godfrey, S. (1972). Body composition and maximal exercise performance in children. *Human Biology*, **44**, 195–214.

Davies, C. T. M., and Sargeant, A. J. (1974 a). Physiological responses to standardised arm work. *Ergonomics*, **17**, 41–49.

Davies, C. T. M., and Sargeant, A. J. (1974 b). Physiological responses to one- and two-leg exercise breathing air and 45% oxygen. *Journal of Applied Physiology*, **36**, 142–148.

Davies, C. T. M., and Sargeant, A. J. (1975). Effects of habituation and training on the physiological responses to 1- and 2-leg work. *Journal of Applied Physiology*. (In the press.)

Durnin, J. V. G. A., and Rahaman, M. M. (1967). The assessment of the amount of fat in the human body from measurements of skinfold thickness. *British Journal of Nutrition*, **21**, 681–689.

Fried, T., and Shephard, R. J. (1970). Assessment of a lower extremity training program. *Canadian Medical Association Journal*, **103**, 260–266.

Helander, E. (1958). Adaptive muscular "allomorphism". *Nature*, **182**, 1035–1036.

Jones, P. R. M. (1970). Radiographic determination of leg fat, muscle and bone volumes in male and female young adults. *Journal of Physiology*, **207**, 1–3P.

Jones, P. R. M., and Pearson, J. (1969). Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. *Journal of Physiology*, **204**, 63–66P.

McMorris, R. O., and Elkins, E. C. (1954). A study of production and evaluation of muscular hypertrophy. *Archives of Physical Medicine*, **35**, 420–426.

Patel, A. N., Razzak, Z. A., and Dastur, D. K. (1969). Disuse atrophy of human skeletal muscle. *Archives of Neurology*, **20**, 413–421.

Rasch, P. J., and Morehouse, L. E. (1957). Effect of static and dynamic exercise on muscular strength and hypertrophy. *Journal of Applied Physiology*, **11**, 29–34.

Rose, D. L., Radzyminski, S. F., and Beatty, R. R. (1957). Effect of brief maximal exercise on the strength of the quadriceps femoris. *Archives of Physical Medicine*, **38**, 157–164.

Roux, W. (1905). *Die Entwicklungsmechanik*. Leipzig: Engelmann.

Stoboy, H., Friedebold, F., and Strand, F. L. (1968). Evaluation of the effect of isometric training in functional and organic muscle atrophy. *Archives of Physical Medicine*, **49**, 508–514.

that our patients had a predicted loss of muscle volume at the end of immobilization (table 3, figure 1) of ~20 per cent which is similar to the 21 per cent muscle weight loss found in the immobilized limbs of rabbits (Helander, 1958) and in the latter case this loss was found to be almost entirely due to a decrease in myofibrillar protein.

Finally, we considered the usefulness of a single measurement taken as a clinical gauge as to the degree of atrophy. Of the three muscle widths examined that taken at one third the subischial height above the knee joint space correlated most highly with the degree of atrophy but even this fails to reach convential levels of significance. Thus it is in our view essential if any systematic study of immobilization and subsequent rehabilitation is to be undertaken that leg muscle volumes should be assessed either by X-ray or anthropometric techniques.

Weiner, J. S., and Lourie, J. S. (1969). *Human Biology. A Guide to Field Methods.* **I.B.P. Handbook.** No. 9. Oxford and Edinburgh: **Blackwell** Scientific Publications.

Zohn, D. A., Leach, R. E., and Stryker, W. S. (1964). A comparison of isometric and isotonic exercises of the quadriceps after injuries to the knee. *Archives of Physical Medicine,* **45,** 571–574.

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Zusammenfassung. Anthropometrische und Röntgen-Daten wurden von 20 jungen männlichen Patienten gesammelt, die sich einem systematischen therapeutischen Übungs-Programm unterzogen nach einem Beinbruch und darauffolgender Unbeweglichkeit von 25 254 (Durchschnitt 117) Tagen. Schätzungen des gesamten Beinvolumens, entweder berechnet aus Röntgenaufnahmen oder anthropometrischen Massen, waren im wesentlichen sowohl beim verletzten als auch beim gesunden Bein austauschbar. Ein Verfahren zur Schätzung des Muskelvolumens aus dem Gesamtvolumen wird angegeben. Zu Beginn der Rehabilitation war das Muskelvolumen im verletzten Bein bedeutend kleiner (860 ml, 16 prozent) als im gesunden. Am Ende der Rehabilitation (Durchschnitt 50 Tage) hatte das verletzte Bein mit 360 ml (18 prozent) bedeutend gegenüber dem vorherigen Volumen zugenommen. Auch das gesunde hatte zugenommen, aber nicht bedeutend (120 ml, 2 prozent), sodass das verletzte Bein noch immer um ca. 11 prozent (620 ml) kleiner war als das gesunde. Der ursprüngliche Grad der Atrophie und die Dauer der Unbeweglichkeit waren nicht signifikant miteinander korreliert, obwohl die Dauer eine negative Beziehung ($P > 0{,}05$) zur Zunahme des Muskelvolumens im verwundeten Bein zeigte. Es wurde keine signifikante Korrelation gefunden zwischen dem Verhältnis des Volumens bei verletztem und gesundem Bein und den Muskeldickemassen bei 1/3 subischial, bei 12,7 cm über dem Kniegelenkraum oder bei dem grössten Wadendurchmesser. In systematischen Untersuchungen zur Muskelatrophie müssen daher Masse durch anthropometrische Messungen oder durch Röntgenaufnahmen geschätzt werden.

Résumé. Des données anthropométriques et radiologiques ont été relevées sur 20 jeunes patients masculins soumis à une kinésithérapie systématique après fracture de la jambe et immobilisation consécutive de 25 à 254 jours (117 en moyenne). Les estimations du volume total de la jambe, faites d'après les mesures radiologiques et anthropométriques, étaient semblables pour les jambes fracturées et non fracturées. Une méthode d'estimation du volume musculaire à partir du volume total est donnée.

Au début de la rééducation le volume musculaire est significativement inférieur pour la jambe atteinte (860 ml, 16 pour cent). A la fin de la rééducation (50 jours en moyenne), la jambe atteinte a augmenté significativement de 360 ml (8 pour cent), et le membre non atteint a augmenté aussi mais non significativement (120 ml, 2 pour cent) de sorte que la jambe atteinte est encore inférieure à l'autre de 620 ml (11 pour cent).

La corrélation entre le degré d'atrophie initiale et la durée d'immobilisation n'est pas significative, bien que cette dernière soit en corrélation négative ($P > 0{,}05$) avec le taux d'accroissement du volume musculaire dans le membre atteint. Il n'a pas été trouvé de corrélation significative entre le rapport des volumes musculaires des membres atteint et non-atteint et les mesures d'épaisseur musculaire au tiers sous-iliaque, à 12,7 cm au dessus de l'espace articulaire du genou, ou au maximum du mollet. Dans les études systématiques, l'atrophie musculaire doit donc être estimée par des mesures soit anthropométriques soit radiologiques.

APPENDIX 2

Reprint of: Davies, C.T.M. and Sargeant A.J. (1975b) Physiological responses to exercise in patients following fracture of the lower limb. Scandinavian Journal of Rehabilitation Medicine [illegible]

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PHYSIOLOGICAL RESPONSES TO EXERCISE IN PATIENTS FOLLOWING FRACTURE OF THE LOWER LIMB

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ABSTRACT. Twenty-five patients with healed fractures of the lower limb and nine normal control subjects were measured anthropometrically and during maximal and submaximal one- and two-leg bicycle exercise. Oxygen intake at a given submaximal work level of 450 kmp min^{-1} and cardiac frequency at an oxygen intake of 1.5 l min^{-1} were significantly higher ($p<0.001$) in the injured compared with the uninjured limbs of the patients and normal subjects. The maximum aerobic power of the injured and uninjured limbs of the patients were 18.8% (0.44 l min^{-1}) and 25.6% (0.61 l min^{-1}) respectively lower than the right and left legs of the control subjects. The corresponding value for 2-leg work was 17.6% (0.51 l min^{-1}). The deterioration in 1-leg performance of the patients was associated with a concomitant decrease in leg muscle (plus bone) volume. In 2-leg work this factor was also probably combined with a deterioration in performance due to general cardiovascular deconditioning.

INTRODUCTION

In previous work from this laboratory we have shown that during cranking the stationary bicycle ergometer with the arms (4) or with one- (5) or two-leg(s), (3) a close association exists between maximal exercise performance and the effective muscle (plus bone) volume used to perform the work. The data were collected on normal healthy subjects but to our knowledge no systematic studies of this type have been applied to patients undergoing rehabilitation from limb injury.

Following a bone fracture, there is loss of muscular power and atrophy of the affected limb. This loss of function may be partially due to hospitalization of the patient and the immobilization of the limb in post-operative plaster. Courses of rehabilitation are designed to reverse these changes and aim to return the patient as soon as possible to a normally active life. However, few scientific data are available on these points, and indeed, little is known of the combined effects of limb fracture and immobilization on the subsequent performance and aerobic power output of the muscle.

In the present paper we have examined 25 patients with healed fracture(s) of the lower limb, 50 days following removal of plaster together with a small group of 9 healthy normal male subjects. Submaximal (and in some cases maximal) one-leg and two-leg exercise were performed; the uninjured limb measurements of each patient were used for control purposes.

MATERIAL

The patients were 25 male servicemen with leg fracture: they were studied at the beginning of a full time course of rehabilitation at the Joint Services Medical Rehabilitation Unit, Chessington. All patients had suffered fractures of one leg only and these were divided as follows: fractures of femur, 2 left and 3 right; fractures of tibia (and fibula), 6 left and 12 right; and finally in two cases, (both left legs) combined fractures of the femur and tibia. Of these 25 cases, 10 had some form of internal fixation. The causes of fracture were sport (10 cases), motor accidents (6), accidental falls (5), parachuting accidents (3) and gunshot wound (1). The average period spent immobilized was 105 days (range 35–205) and patients were seen when they first entered Chessington or as soon as they were fully weight bearing and had sufficient joint mobility to pedal a bicycle without discomfort or pain. Thus the patients were seen on average 50 days after the end of immobilization and 18 days after commencing therapy at Chessington.

For comparison data on 4 of the patients' instructors and 5 laboratory assistants were collected. The instructors and laboratory workers were on average 7 years older than the patients, their physical details together with those of the patients are included in Table I.

METHODS

During the first visit to the laboratory, subjects were measured for height and weight. Skinfold measurements were taken at four sites according to the method of Durnin & Rahaman (9) to enable lean body mass to be estimated. The volume of both legs (muscle plus bone) was measured after the anthropometric technique developed by Jones & Pearson (12). The validity of this technique as applied to limbs which have undergone muscle atrophy due to immobilization is discussed in detail elsewhere (6).

In order to reduce the effects of learning and habituation to the task (8) the subjects were allowed to exercise on the first visit to the laboratory; the definitive measurements were taken during the second visit.

During the definitive measurements both patients and normal subjects were required to exercise in three sessions with a rest period of not less than 1 hour between each pedalling a standard Monark stationary bicycle ergometer with each leg separately and then with 2 legs. During 1-leg exercise the foot of the active limb was fitted with a plimsoll which was secured to the bicycle pedal by bolts and two metal plates. The bicycle had a fixed wheel and no attempt was made to return the "passive" pedal during cycling (10). Care was taken to ensure that the saddle height was correctly adjusted to enable the pedalling to be performed with maximal extension of the leg. The subjects were required to pedal the ergometer in a progressive test starting from zero load and increasing up to and sometimes including maximal levels. The submaximal work loads were chosen to give 4 or sometimes 5 work levels. In submaximal experiments, oxygen intake ($\dot{V}O_2$), minute ventilation ($\dot{V}_E$) and respiratory (f_R) and cardiac frequencies (f_H) were measured during the last two minutes of a 5 minute period by the standard open circuit technique (1) using dry gas (Parkinson Cowan Ltd.) paramagnetic (Servomex Ltd.) and infra red (Hilger Watts Ltd.) meters for ventilation volume and O_2 and CO_2 analysis respectively. Mechanical efficiency (defined as the ratio of work performed, W, to aerobic energy expenditure) was calculated from the $\dot{V}O_2$ W data using a baseline of pedalling against zero load (11, 14).

Where the subjects were able to exercise at maximum, the final collection was taken using the standard Douglas Bag technique over the last minute of a 3 minute work load during which the subject was encouraged to pedal at maximal effort. If this could be sustained the load was raised again and a second collection taken.

Criteria for maximal performance

In the normal control subjects performing 2-leg exercise, the "$\dot{V}O_2$ plateau" criterion for the attainment of maximum aerobic power ($\dot{V}O_{2\ max}$) was applied (1). However, in two leg work with the patients and with one leg work in both patients and controls, we found as previously (5) that this criterion was not easy to apply. The patients in particular, although they were "encouraged" to keep going as long as possible, found it possible to sustain maximal or near maximal effort for relatively short periods. In order, in cases of doubt, to overcome this difficulty, we took duplicate measurements of $\dot{V}O_2$ on subsequent days and assessed the results in conjunction with secondary criteria based on our previous observation of a maximum cardiac frequency of 175 beats/min in one leg work (5). If the patient complained of pain either at the fracture site or in the joints, the exercise was discontinued and the results not included.

RESULTS

The responses to submaximal exercise are shown in Table II.

For a given $\dot{V}CO_2$, $\dot{V}_E$ is identical for exercise with the injured and uninjured limb of patients and does not differ significantly from that of normal subjects. The $\dot{V}O_2$ at a W of 450 kpm min^{-1} is significantly higher ($P<0.001$) in the injured limb compared with the uninjured limb of the patients and the normal limbs of the instructors and laboratory workers. The raised $\dot{V}O_2$ for a given W in the injured limb is also associated with a decline in the predicted $\dot{V}O_2$ at an f_H of 175 beats min^{-1}. The $\dot{V}_{E\ 50}$ is similar for both limbs of the patients but significantly lower ($P<0.001$) than that observed for the normal subjects.

In 2-leg exercise the $\dot{V}_E$ and $\dot{V}O_{2\ 1.0}$ are again significantly higher ($P<0.001$) in the normals and $f_{H\ 1.5}$ lower but $\dot{V}O_{2\ max}$ and $\dot{V}_{E\ 1.5}$ are similar in both groups.

Table 1. *Physical characteristics of the 25 patients, 4 normal instructors and 5 laboratory assistants*

Weight (wt); **height** (ht); sum of 4 skinfold thicknesses (Σ sf.), lean body mass (LBM) calculated from Σ sf. after the **method of** Durnin & Rahaman (9); limb (muscle plus bone) volume (LV—see Jones & Pearson (12) and Davies & Sargeant (6) of the uninjured (u) and injured (i) legs.

Subjects	Age (yr)	Wt (kg)	Ht (cm)	Σ sf. (mm)	LBM (kg)	LV (litres) u	LV (litres) i
Patients (n=25)	22*** ±4	69.8 ±11.4	174.2 ±6.5	31.8 ±9.2	59.7 ±8.7	6.49+++*** ±0.92	5.76*** ±0.86
Normals (n=9)	29 ±6	73.3 ±9.2	176.0 ±7.4	29.6 ±6.6	65.2 ±6.9	7.36 ±0.79	7.29 ±0.70

Significance: patients cf. normals ***$P<0.001$; patiens LV (u cf. i) +++$P<0.001$.

Table II. *Submaximal responses to 1- and 2-leg work*

The data have been expressed in terms of pulmonary minute ventilation ($\dot{V}_E$) at a fixed carbon dioxide output of 1.5 l min^{-1} ($\dot{V}_{E\,1.5}$); tidal volume at a $\dot{V}_E$ of 30 l min^{-1} ($V_{T\,30}$); oxygen intake ($\dot{V}O_2$) at a work load of 450 kpm min^{-1} ($\dot{V}O_{2\,450}$) for 1-leg and 900 kpm min for 2-leg work ($\dot{V}O_{2\,900}$), cardiac frequency at a $\dot{V}O_2$ of 1.5 l min^{-1} ($f_{H\,1.5}$) and a $\dot{V}O_2$ at an f_H of 175 beats min ($\dot{V}O_{2\,175}$ 1-leg) and 195 beats min ($\dot{V}O_{2\,195}$ 2-legs)

(a) 1-leg	$\dot{V}_{E\,1.5}$ l min^{-1} B.T.P.S.	$V_{T\,30}$ l B.T.P.S.	$\dot{V}O_{2\,450}$ l min^{-1} S.T.P.D.	$f_{H\,1.5}$ beats min^{-1}	$\dot{V}O_{2\,175}$ l min^{-1} S.T.P.D.
Patients (n = 25)					
Uninjured leg	50.46 ±9.00	1.14 ±0.18	1.40*** ±0.11	142*** ±15	2.16** ±0.37
Injured leg	50.54 ±7.23	1.12 ±0.15	1.51 ±0.11	153 ±19	1.98 ±0.42
Normals (n = 9)					
Right leg	46.87 ±4.07	1.52+++ ±0.94	1.35 ±0.08	123++ ±13	2.66++ ±0.39
Left leg	46.94 ±3.81	1.85+++ ±0.96	1.36+++ ±0.07	124+++ ±9	2.58+++ ±0.32

(b) 2-legs	$\dot{V}_{E\,1.5}$ l min^{-1} B.T.P.S.	$V_{T\,30}$ l B.T.P.S.	$\dot{V}O_{2\,900}$ l min^{-1} S.T.P.D.	$f_{H\,1.5}$ beats min^{-1}	$\dot{V}O_{2\,195}$ l min^{-1} S.T.P.D.
Patients (n = 13)	44.56 ±4.78	1.21 ±0.23	2.13 ±0.15	140 ±18	3.74 ±0.62
Normals (n = 9)	42.63 ±7.15	2.34+++ ±1.07	2.12 ±0.11	121++ ±12	3.55 ±0.40

Significance: Patients uninjured cf. injured leg: $^{**}P<0.01$; $^{***}P<0.001$.
Patients cf. normals (1-leg and 2-leg): $^{++}P<0.01$; $^{+++}P<0.001$.

At maximal exercise (Table III) the $\dot{V}_{E\,max}$ and $\dot{V}O_{2\,max}$ of the patients for both 1-leg and 2-leg exercise are significantly ($P<0.001$) lower than their normal counterparts but the $f_{H\,max}$ if comparable in the two groups. In the normal subjects there is no difference between the $\dot{V}O_{2\,max}$ of the right and left leg but in the patients the net aerobic power of the injured limb is 10.6% lower then the uninjured limb. Comparison of the limbs of the patients with those of the normal subjects shows larger differences: 18.8% (0.44 l min^{-1}) uninjured leg and 25.6% (0.61 l min^{-1}) injured leg. For 2-leg work the reduction of $\dot{V}O_{2\,max}$ in the patients was 17.6% (0.51 l min^{-1}).

The association of net $\dot{V}O_{2\,max}$ with estimate of leg (muscle plus bone) volume is shown in Fig. 1. The reduction in $\dot{V}O_{2\,max\,net}$ of the injured leg of patients is associated with a decline in LV. For a given LV the $\dot{V}O_{2\,max\,net}$ of the uninjured and injured legs of patients and the right and left leg of the control subjects lie within previously found normal limits for young healthy subjects. Though the data for the patients lie below and on average are displaced to the right of their normal counterparts. Thus inpatients, the decline in 1-leg $\dot{V}O_{2\,max\,net}$ is partly a function of the change in leg muscle (plus bone) volume.

The relationship of 1-leg to 2-leg $\dot{V}O_{2\,max}$ of the patients and normal subjects is shown in Fig. 2. It can be seen that whilst the uninjured leg to 2-leg relationship in the patients is similar, though somewhat lower in absolute values, to the normal subjects the injured leg to 2-leg relationship is significantly displaced to the right ($P<0.05$).

DISCUSSION

The submaximal and maximal exercise observations on the patients and normal subjects in this study were made under standardised laboratory conditions.

The normal subjects were 5 laboratory workers and 4 remedial gymnasts. They were somewhat older, heavier, taller, less fat and had larger LV's, than the patients (Table I). However, the LV data for the left and right legs of the normal subjects were not significantly different from those previously pub-

Table III. *Responses to maximal exercise*

Maximal ventilation ($\dot V_{E\,max}$) absolute ($\dot VO_{2\,max}$) and net ($\dot VO_{2\,max\,net}$—see methods), oxygen intake and cardiac frequency ($f_{H\,max}$)

	Patients ($n=15$)				Normals ($n=9$)				
	$\dot V_{E\,max}$ l min^{-1} B.T.P.S.	$\dot VO_{2\,max}$ l min^{-1} S.T.P.D.	$\dot VO_{2\,max\,net}$ l min^{-1} S.T.P.D.	$f_{H\,max}$ beats min^{-1}	$\dot V_{E\,max}$ l min^{-1} B.T.P.S.	$\dot VO_{2\,max}$ l min^{-1} S.T.P.D.	$\dot VO_{2\,max\,net}$ l min^{-1} S.T.P.D.	$f_{H\,max}$ beats min^{-1}	
Uninjured leg	97.6 16.0	2.35*** ±0.29	1.89*** ±0.24	179 ±6	125.7+++ ±10.6	2.81+++ ±0.17	2.33+++ ±0.17	174 ±5	Right leg
Injured leg	92.6 ±15.5	2.14 ±0.32	1.69 ±0.26	178 ±8	121.5+++ ±13.2	2.73+++ ±0.18	2.30+++ ±0.16	177 ±7	Left leg
2 legs*	113.4 ±20.3	2.87 ±0.45	2.36 ±0.36	188 ±6	145.7+++ ±10.6	3.41+++ ±0.23	2.87+++ ±0.21	189 ±8	2 legs

Significance: Patients uninjured cf. injured leg: *** $P<0.001$. Patients with cf. normals (1-leg and 2-leg), +++ $P<0.001$.
* $n=10$.

published (5) for young healthy men, and the mean difference in LV between the injured and uninjured legs of patients was closely similar to that found in a larger cross sectional anthropometric survey of patients entering the Joint Services Medical Rehabilitation Unit at Chessington (6). Theefore in terms of LV the data presented may be considered representative of patients recovering from leg fractures and healthy men so far measured in this laboratory.

In stationary bicycle ergometer tests care was taken to minimise the effects of learning and habituation to cycling (8) by allowing the subjects to practise and perform the complete series of exercise tests before definitive measurements were taken. Complete submaximal data were obtained on all subjects, but maximal experiments, as expected, were more difficult to conduct successfully. During heavy exercise patients often complained of muscle soreness, weakness, joint pain and expressed fears of re-injuring the affected limb. We felt it unwise to try and motivate patients beyond levels of exercise that they were prepared to go to voluntarily. However, of the 25 measurements of maximal performance attempted we did obtain successful observations on 15 patients but the final work load was only maintained for 1 min.

To achieve this a great deal of patience, and encouragement were required to gain the confidence of the patient and an understanding of what we were trying to achieve. To obtain a reliable duplicate measurement of maximal performance the test procedure was often repeated on 4 different occasions in each patient and thus our observations are open to the criticism that we may have been changing (through training) the parameter we were trying to measure. This we accept, though it should be noted that during daily repeated exercise studies on 2-leg work (8) no measurable change in $VO_{2\,max}$ occurred during the first 4 days of observation. It is within the context of these facts that our results must be evaluated and interpreted.

During submaximal work in the patient, the most striking features are the decreased mechanical efficiency, the increased $f_{H\,1.5}$ and lower predicted $VO_{2\,max}$ of the injured compared with uninjured limb. A lower mechanical efficiency and raised f_H at given VO_2 for 1-leg work compared with 2-leg work are in accord with our previous findings on young adults (4, 5) but in all our previous studies of normal cycling we have been unable to demonstrate differences in pedalling efficiency even in most disparate groups of individuals irrespective of whether they have worked on (or seen) a bicycle before (see, e.g. 2). Even in the present study it should be noted that although $f_{H\,1.5}$ is lower and $VO_{2\,max}$ higher in the normal subjects compared with the patients in 2-leg work, the $VO_{2\,max}$ is identical in the two groups (Table II). We have found (Davies and Sargeant, unpublished observations) that the difference in mechanical efficiency between injured and uninjured legs of the patients remains after an extended period of habituation to 1-leg bicycle ergometer exercise, but we now have some evidence that the effect may be due to the state of training of the injured limb (7). The raised VO_2 for given W of the injured limb of patients is not reflected either by a similar change in $V_{E\,1.5}$ or $V_{T\,30}$. Indeed

Fig. 1. Relationship of net maximal aerobic power output ($\dot{V}O_{2\ max\ net}$) of 1-leg to leg (muscle plus bone) volume. Patients: ●, uninjured limb; ○, injured limb; ▲, normal subjects. The shadowed area represents the limits (mean ±2 S.D.) previously found (4, 5) for healthy young subjects, age 18–27 years.

the $\dot{V}_{E\ 1.5}$ remains constant in patients and normal subjects independently of the type of exercise performed (Table II) though $\dot{V}_{E\ 30}$ is higher in the normal subjects.

During maximal 1-leg and 2-leg exercise the patients reached similar $f_{H\ max}$ values to the normal subjects (Table III) but $\dot{V}_{E\ max}$ values in both forms of work were significantly ($P<0.001$) lower. The diminished ventilatory response of the patients is probably a function of the time they were able to endure maximal effort. We have found previously (5) that the "$\dot{V}_{E\ max}$" can be increased by 30% in healthy well motivated subjects, who are prepared to sustain 1-leg exercise for 2–3 min at or above a level of work at which $\dot{V}O_{2\ max}$ occurs. The most surprising (and interesting) feature of the maximal performance study is that the $\dot{V}O_{2\ max\ net}$ of the patients injured leg is only 200 ml min^{-1} (10.6%) below that of their good leg. However, it should be noted that in turn the patients uninjured and injured 1-leg $\dot{V}O_{2\ max}$ and LV are 430 ml min^{-1} (18.8%) and 1.11 litres (15%); and 610 ml min^{-1} (25.6%) and 1.53 litres (21%) respectively lower than the right and left legs of the normal subjects (Table III). This suggests that as a result of leg fracture and subsequent hospitalization and immobilization, both limbs undergo a deterioration of physiological structure and function. It will be remembered that our patients were measured 173 days after sustaining their fractured limb and 70% of this time was spent either immobilized completely in bed or physically inactive because the patient was unable to support his own body weight. Clearly this enforced period of inactivity not only effects a deterioration in limb structure but is also likely to produce a degree of cardiovascular deconditioning (13). This would lend support to current practice in rehabilitation work that there is need for general conditioning exercises as well as those designed specifically to increase muscle strength and joint mobility.

The loss in function of uninjured and injured patients' legs is reflected in a reduced 2-leg $\dot{V}O_{2\ max\ net}$ of 510 ml min^{-1} (17.6%) when compared to their control subjects. The decline in 2-leg $\dot{V}O_{2\ max}$ is associated with the decrease in the uninjured and injured 1-leg $\dot{V}O_{2\ max}$ in patients, and the relationship of the 2-leg/1-leg $\dot{V}O_{2\ max}$ of the uninjured and injured leg lies within the limits expected for normal subjects (Fig. 2). However the regression lines for the injured and uninjured leg are significantly different, the former being displaced to the left (Fig. 2).

Fig. 2. The relationship of 1-leg to 2-leg aerobic power output ($\dot{V}O_{2\ max}$) in patients: ●, uninjured leg; ○, injured leg. ▲ normal subjects.

These changes in 1- and 2-leg performance are undoubtedly, in part, a reflection of the different limitations to maximal effort in the two forms of work. In previous papers (4, 5) we have shown that maximal single limb exercise is mainly limited by the effective muscle mass which can be brought into play whereas when both legs are combined the ultimate limit is more likely $\dot{Q}$ and the ability of the circulation to transport O_2 and perfuse a given muscle mass with blood.

The present data support this concept: in 1-leg work the $\dot{V}O_{2\,max}$ of the patients is associated with a loss of limb muscle (plus bone) volume and in 2-leg work despite the reduced muscle mass of the injured leg the expected relationship (4, 5) of 2- to 1-leg $\dot{V}O_{2\,max}$ is maintained within normal limits (Fig. 2).

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REFERENCES

1. Davies, C. T. M.: Limitations to the prediction of maximum oxygen intake from cardiac frequency measurements. J Appl Physiol 24: 700–706, 1968.
2. Davies, C. T. M., Barnes, Carolyn A., Edholm, O. G., Fox, R. H., Ojikutu, R. Ola. & Samueloff, A. S.: Ethnic differences in physical working capacity. J Appl Physiol 33: 726–732, 1972.
3. Davies, C. T. M., Mbelwa, D., Crockford, G. W. & Weiner, J. S.: Exercise tolerance and body composition of male and female Africans, aged 18–30 years. Human Biol 45: 31–40, 1973.
4. Davies, C. T. M. & Sargeant, A. J.: Physiological responses to standardised arm work. Ergonomics 17: 41–49, 1974.
5. — Physiological responses to one- and two-leg exercise breathing air and 45% oxygen. J Appl Physiol 36: 142–148, 1974.
6. — Effect of exercise therapy on total and component tissue leg volumes of patients undergoing rehabilitation from lower limb injury. Annals of Human Biology, 1975, in press.
7. — Effects of training on the physiological responses for 1- and 2-leg work. J Appl Physiol. 1975, in press.
8. Davies, C. T. M., Tuxworth, W. & Young, J. M.: Physiological effects of repeated exercise. Clin Sci 39: 247–258, 1970.
9. Durnin, J. V. G. A. & Rahaman, M. M.: The assessment of the amount of fat in the human body from measurements of skinfold thickness. Brit J Nutr 21: 681–689, 1967.
10. Freyschuss, U. & Strandell, T.: Circulatory adaptation to one- and two-leg exercise in supine position. J Appl Physiol 25: 511–515, 1968.
11. Hill, A. V.: Trails and Trials in Physiology. E. Arnold, London, 1965.
12. Jones, P. R. M. & Pearson, J.: Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. J Physiol 204: 63–66 P, 1969.
13. Saltin, B., Blomquist, G., Mitchell, J. H., Johnson, R. L. J., Wildenthal, K. & Chapman, C. B.: Response to exercise after bed rest and after training. Amer Heart Assoc Monograph No. 23, 1968.
14. Whipp, B. J., & Wasserman, K.: The efficiency of muscular work. J Appl Physiol 26: 644–648, 1969.

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APPENDIX 3

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Changes in physiological performance of the lower limb after fracture and subsequent rehabilitation

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Summary

1. Eight patients who had suffered a fracture of one leg were studied before and after a 7 weeks period of rehabilitation during work with one leg and both legs on a bicycle ergometer.

2. In submaximal exercise minute ventilation for a given carbon dioxide output and tidal volume at a given minute ventilation remained unchanged throughout the period of therapy for both one- and two-leg exercise: oxygen intake for a given work output and cardiac frequency for a given oxygen intake decreased in both the injured and uninjured limb during one-leg work, although in two-leg exercise there was no significant change.

3. Oxygen intake at zero load was subtracted from the maximum oxygen intake measured during loaded exercise to give net values for each limb exercised separately or both legs exercised together. The net maximum oxygen intake thus calculated increased 8·9% (+0·17 l/min) in the uninjured leg and 17·4% (+0·29 l/min) in the injured leg during one-leg exercise. In two-leg exercise the increase was 17·2% (+0·43 l/min), which approximately equals the increase in the two legs measured separately.

4. In both legs there was an increase in leg muscle (plus bone) volume although this was significant in the injured leg only.

5. The maximum oxygen intake attained in two-leg exercise for a given leg volume in the patients at discharge was not significantly different from that found previously in a cross-sectional survey of young healthy (naval) servicemen. Thus the rehabilitation programme investigated appears to be effective, although the spontaneous recovery without a rehabilitation programme is unknown.

Key words: aerobic power, rehabilitation, fracture, exercise, muscle.

Introduction

In a previous paper (Davies & Sargeant, 1975a) we described the effects of fracture and subsequent immobilization of the leg on the exercise tolerance of twenty-five patients on admission to the Joint Services Medical Rehabilitation Unit at Chessington, Surrey. The present study was designed to follow the changes in physiological performance of the lower limbs of eight of these patients, weekly during an intensive course of rehabilitation therapy. The course included exercises specifically (but empirically) designed to improve the mobility, strength and aerobic capacity of the patients. All the patients were servicemen, the therapy lasted on average 7 weeks and was supervised by trained remedial gymnasts.

Material and methods

All eight patients had suffered fractures of one leg only and these were divided as follows: five fractures of the tibia and fibula (three right and two left); one fracture of the left femur, and two cases where femur and tibia and fibula fractures were sustained (both left legs). The average period spent immobilized was 105 days and exercise tests were first given 25

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TABLE 1. *Physical characteristics of the eight patients before and after a 7 weeks' course of rehabilitation*

Age, height, weight, sum of four skinfold thicknesses (Σsf), lean body mass (LBM) and leg volume (LV) of the injured and uninjured limb are given as mean values ±SD. Significance, before and after therapy: $^{**}P<0{\cdot}01$.

	Age (years)	Height (cm)	Weight (kg)	Σsf (mm)	LBM (kg)	LV (l) Uninjured	LV (l) Injured
Before	21·8 ±3·7	172·9 ±5·8	70·2 ±13·3	35·5 ±11·3	59·21 ±9·38	6·38 ±0·80	5·66 ±0·94
After	21·9 ±3·7	172·8 ±6·0	71·2 ±14·6	33·6 ±13·6	60·48 ±9·42	6·65 ±1·08	6·23** ±1·04

days after the end of immobilization, which was on average 7 days after the commencement of rehabilitation therapy at Chessington. Their physical characteristics before and after the period of rehabilitation are given in Table 1.

The methods used have been described in detail elsewhere (Davies & Sargeant, 1975a), and therefore only a brief outline of the procedure will be given here. The patients were studied at 7–10 day intervals. One- and two-leg exercises were performed on a 'fixed wheel' stationary bicycle ergometer.

Measurements were made on each occasion of the responses to a progressive exercise test of each leg separately and of two legs combined with a rest of at least 1 h between each test, the aim in each test being to span the subject's capacity from zero load up to and, where possible, including maximum in four or five work loads.

At submaximal work levels, oxygen intake ($\dot{V}O_2$), carbon dioxide output ($\dot{V}CO_2$), minute ventilation ($\dot{V}_E$), and cardiac (f_H) and respiratory (f_R) frequencies were measured over the last 2 min of each 5 min work load by a standard open-circuit technique (Davies & Sargeant, 1974). Owing to the difficulty of obtaining maximal measurements in one-leg exercise (particularly in patients) which meet the criteria developed for two-leg exercise, it was sometimes necessary to take duplicate measurements on subsequent days and to assess the results in the light of secondary criteria based on our previous observation of a maximum cardiac frequency of ~175 beats/min in one-leg work. The maximal aerobic power output ($\dot{V}O_{2\,max}$) was expressed in absolute terms (l/min) as directly measured and as a net value ($\dot{V}O_{2\,max,\,net}$) calculated from the $\dot{V}O_{2\,max}$ minus the $\dot{V}O_2$ of pedalling at constant speed against zero load (see Davies & Sargeant, 1974 for further details). In addition, height and weighs were measured on each visit to the laboratory at well as four skinfold thicknesses (suprailiac, subscapular, triceps and biceps) for the estimation of lean body mass (Durnin & Rahaman, 1967). Leg (muscle plus bone) volume (LV) measurements by physical anthropometry were also made after the technique developed by Jones & Pearson (1969) (see Davies & Sargeant, 1975b, for further details and validation of the technique for use with patients undergoing rehabilitation therapy).

To overcome difficulties of habituation to and learning (Davies, Tuxworth & Young, 1970) of the standard one- and two-leg exercise tests, all the patients were required to perform the work test before definitive measurements were taken.

Results

The changes in physical characteristics and responses to submaximal exercise are summarized in Tables 1 and 2.

During the period of rehabilitation, body weight, height and lean body mass (LBM) remained unchanged (Table 1). The major effect of therapy was to increase the mean (±SD) leg muscle (plus bone) volume (LV) of the uninjured (6·38 ± 0·80 litres to 6·65 ± 1·08 litres) and injured (5·66 ± 0·94 litres to 6·23 ± 1·04 litres; $P<0{\cdot}01$) legs, though at the end of rehabilitation there was still a significant difference ($P<0{\cdot}01$) between the two limbs.

In response to submaximal exercise (Table 2) minute ventilation at $\dot{V}CO_2$ 1·5 l/min ($\dot{V}_{E\,1{\cdot}5}$) and tidal volume at $\dot{V}_E$ 30 l/min ($V_{T\,30}$) during exercise with the injured, uninjured and two legs combined were similar at the beginning of therapy and were not significantly different from the values found

TABLE 2. *Changes in submaximal responses to exercise after rehabilitation*

Results shown are: minute ventilation at $\dot{V}CO_2$ 1·5 l/min ($\dot{V}_{E\,1.5}$); tidal volume at $\dot{V}_E$ of 30 l/min ($V_{T\,30}$); oxygen intake at a work load of 73 W in one-leg work ($\dot{V}O_{2\,(73)}$), or 147 W in two-leg work ($\dot{V}O_{2\,(147)}$); cardiac frequency at $\dot{V}O_2$ 1·5 l/min ($f_{H\,1.5}$); oxygen intake at f_H 175 beats/min in one-leg ($\dot{V}O_{2\,(175)}$) and 195 beats/min in two-leg exercise ($\dot{V}O_{2\,(195)}$). Significance: *$P<0·05$; ***$P<0·001$.

Variable	Units	One-leg exercise: Uninjured	One-leg exercise: Injured	Two-leg exercise
$\dot{V}_{E\,1.5}$	l/min	−3·20	+2·29	+2·23
$V_{T\,30}$	l	−0·03	+0·32	−0·05
$\dot{V}O_{2\,(73/147)}$	l/min	−0·01	−0·06	−0·04
$f_{H\,1.5}$	beats/min	−12*	−18***	−6
$\dot{V}O_{2\,(175/195)}$	l/min	+0·49***	+0·49***	+0·16

previously on a larger group of servicemen studied on single occasions at Chessington (Davies & Sargeant, 1975a). Rehabilitation had no effect on the ventilatory responses to work; indeed the relationship of $\dot{V}_E$ to $\dot{V}CO_2$ and V_T to $\dot{V}_E$ before and after therapy for the different forms of exercise could be adequately represented by equations (1) and (2).

$$\dot{V}_E\ (\text{l/min}_{BTPS}) = -0·45 + 32·69\ \dot{V}CO_2\ (\text{l/min}_{STPD}) \quad (r = 0·97;\ SD = 6·93\ \text{l/min}) \qquad (1)$$

$$\dot{V}_E\ (\text{l/min}_{BTPS}) = -20·95 + 46·56\ V_T\ (\text{l}_{BTPS}) \quad (r = 0·89;\ SD = 11·20\ \text{l/min}) \qquad (2)$$

At the onset of therapy $\dot{V}O_2$ for given work output ($\dot{W}$) of 73 W was higher in exercise with the injured (1·50 ± 0·12 l/min) than with the uninjured leg (1·37 ± 0·09 l/min; $P<0·001$). The effect of rehabilitation was to reduce the oxygen cost of work in exercise with either leg producing a small rise in mechanical efficiency (Fig. 1).

The mechanical efficiency of two-leg work was unaffected by rehabilitation and throughout the investigation was closely in accord with previous results found for normal healthy subjects in this laboratory. The cardiac frequency values showed similar changes to those described for $\dot{V}O_2$. At the beginning of the rehabilitation period cardiac frequency at $\dot{V}O_2$ 1·5 l/min ($f_{H\,1.5}$) was 150 ± 21 beats/min in exercise with the injured leg compared with 139 ± 18 beats/min ($P<0·001$) with the uninjured leg. At the end of therapy these values in exercise with the uninjured and injured legs were reduced to 127 ± 9 beats/min and 132 ± 14 beats/min respectively, but the difference between them was still significant ($P<0·05$). The predicted $\dot{V}O_2$ at f_H 175 beats/min changes from 2·22 ± 0·44 l/min to 2·71 ± 0·35 l/min in exercise with the uninjured leg

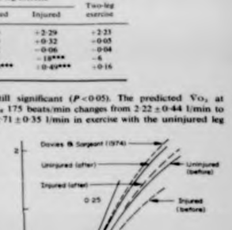


FIG. 1. Relationship of work output ($\dot{W}$) to aerobic energy expenditure ($\dot{E}$) expressed in terms of W/kg body weight for the injured and uninjured limbs of patients before and after rehabilitation. Isopleths for mechanical efficiency and previous one-leg exercise data (Davies & Sargeant, 1974) from normal healthy subjects are also shown.

TABLE 3. *Changes in response to maximal exercise after rehabilitation*

Pulmonary minute ventilation ($\dot{V}_{E\,max.}$), absolute ($\dot{V}O_{2\,max.}$) and net ($\dot{V}O_{2\,max.\,net}$) maximum oxygen intake and cardiac frequency ($f_{H\,max.}$) values are shown as mean values. Significance: ***$P<0·001$; **$P<0·01$; *$P<0·05$.

Variable	Units	One-leg exercise: Uninjured	One-leg exercise: Injured	Two-leg exercise
$\dot{V}_{E\,max.}$	l/min	+9·7	+7·7	+8·8
$\dot{V}O_{2\,max.}$	l/min	+0·17	+0·33***	+0·42**
$\dot{V}O_{2\,max.\,net}$	l/min	+0·17	+0·29***	+0·43***
$f_{H\,max.}$	beats/min	−7*	−6**	−3

and 1·97 ± 0·43 l/min to 2·46 ± 0·38 l/min with the injured leg over the period of therapy. Both these changes were highly significant ($P<0·001$), as were the differences in the values in exercise with the injured compared with the uninjured leg both before ($P<0·001$) and after ($P>0·05$) rehabilitation. In contrast, in two-leg work the f_H [illegible] and $\dot{V}O_2$ [illegible] remained almost constant over the period of the study (Table 2).

The mean changes in responses to maximal exercise are shown in Table 3. Before therapy $\dot{V}_{E\,max.}$ in exercise with the uninjured leg (93·2 ± 18·1 l/min) and injured leg (89·9 ± 17·0 l/min) and $f_{H\,max.}$ (182 ± 6 and 183 ± 4 beats/min) were similar but there were marked differences in absolute $\dot{V}O_{2\,max.}$ (2·35 ± 0·30 l/min compared with 2·11 ± 0·34 l/min; $P<0·001$) and net $\dot{V}O_{2\,max.}$ (1·91 ± 0·27 and 1·67 ± 0·27 l/min; $P<0·001$). The effect of rehabilitation was to increase the $\dot{V}_{E\,max.}$ and $\dot{V}O_{2\,max.}$ and to reduce the $f_{H\,max.}$ in exercise with both the injured and uninjured leg. However, the rise in $\dot{V}_{E\,max.}$ in exercise with the injured and uninjured leg and increase in $\dot{V}O_{2\,max.}$ with the uninjured leg did not reach conventional levels of significance (Table 3). In two-leg work a similar picture emerged; $\dot{V}O_{2\,max.}$ increased significantly ($P<0·001$) but $\dot{V}_{E\,max.}$ and $f_{H\,max.}$ remained unchanged.

The change in $\dot{V}O_{2\,max.\,net}$ in exercise with both the injured and uninjured legs was related to their initial state of aerobic performance (Fig. 2), but only in the case of injured leg exercise was the increase in $\dot{V}O_{2\,max.\,net}$ associated with increase in LV; the improvement in $\dot{V}O_{2\,max.\,net}$ in exercise with the uninjured limb appeared to be largely independent of LV (Fig. 3). The relationship of $\dot{V}O_{2\,max.}$ during one-leg (injured and uninjured) exercise to that during two-leg exercise after rehabilitation was described by the linear regression equation (3).

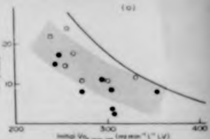


FIG. 2. Relationship of change in $\dot{V}O_{2\,max.}$ ($\Delta\dot{V}O_{2\,max.}$ %) to initial $\dot{V}O_{2\,max.}$ in ml min^{-1} l^{-1} (LV). ——, Data for young healthy male subjects taken from Davies & Sargeant (1975c). The stippled area represents the limits (mean ± SD) of the curve for patients in the present study. ○, Injured leg; ●, uninjured leg. One injured leg value ([illegible]), which appeared to fall outside the normal range for these patients is excluded.

$$\text{Two-leg } \dot{V}O_{2\,max.}\ (\text{l/min}) = 0·191 + 1·23\ \text{one-leg } \dot{V}O_{2\,max.}\ (\text{l/min}) \quad (3)$$

$$(r = 0·90;\ \text{SD} = 0·22\ \text{l/min})$$

This equation did not differ significantly from that found previously (Davies & Sargeant, 1974) for normal healthy adults. The relationship of two-leg $\dot{V}O_{2\,max.}$ to LV is shown in Fig. 4.

Discussion

The results before therapy commenced are in agreement with data previously published by us on a larger anthropometric and exercise cross-sectional study of new entrants to the Rehabilitation Unit at Chessington (Davies & Sargeant, 1975a, b) and therefore require no further discussion. We have also alluded to the main difficulties of measuring maximal aerobic power in patients recovering from

LV (L)

FIG. 3. **Relationship of net maximal aerobic power ($\dot{V}O_{2\ max}$) of the injured (○) limb and the uninjured (●) limb before and after rehabilitation to estimates of leg muscle (plus bone) volume (LV). The arrows indicate the direction of change. The shaded area represents the 95% confidence limits for the relationship previously found in normal subjects (Davies & Sargeant, 1974).**

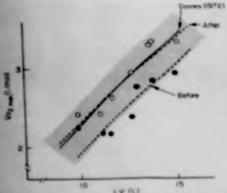
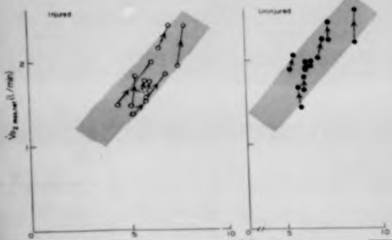


FIG. 4. **Relationship of net $\dot{V}O_{2\ max}$ during two-leg exercise before (●) and after (○) rehabilitation. ——, Regression line for service personnel data previously collected (Davies, 1972). The shaded area represents the 95% confidence limits for normal data (Davies, Mbelwa, Crockford & Weiner, 1973).**

limb injuries in our previous paper (Davies & Sargeant, 1975a) and the same limitations described there apply to the present investigation. However, in studying the effects of a period of therapy on the responses to standard exercise one further difficulty is encountered, that of familiarization with the task. In many investigations where the exercise responses of a patient are measured before and after the administration of physical (or drug) therapy, it is often tacitly assumed that the differences observed are due to the treatment. In two-leg work this assumption has been shown to be open to question (Davies, Tuxworth & Young, 1970); on exposure to repeated tests, patients habituate to the given exercise and their physiological responses change.

In the present study we found it impractical to subject the patients to a comprehensive habituation programme as both the patients and their instructors were anxious to commence (or to continue if the subjects were weight-bearing) the programme of rehabilitation. The instructors thought (rightly) that they could not afford a break of 2 weeks in the already condensed programme whilst we subjected


Injured
Uninjured
$\dot{V}O_{2\,max,net}$ (l./min)
0
1
2
5
10
0
5
10

the patients to repeated exercise on the bicycle ergometer. To partially overcome this difficulty, observations were made on two successive occasions at the onset of therapy and our first day's results were discarded.

The important effects of rehabilitation on the responses to submaximal work are a significant decrease in $f_{H\,1.5}$ in exercise with both the injured and uninjured leg, with a consequent rise ($P < 0.001$) in the predicted $\dot{V}O_{2\,max.}$ and a small increase in mechanical efficiency (Fig. 1). For a given $\dot{V}CO_2$, $\dot{V}_E$ is the same in one-leg (injured and uninjured) and two-leg work before and after rehabilitation. This is also true for $V_{T\,30}$. The changes in $f_{H\,1.5}$ for two-leg work are less marked; the increase in $\dot{V}O_{2\,(1.5)}$ (0·16 l/min) is small and non-significant.

A change in mechanical efficiency as a result of training has not (to our knowledge) been reported for conventional two-leg work (see Åstrand & Rodahl, 1970, for general review). At present we have no completely satisfactory explanation for its occurrence in single-limb exercise. It may have been due to a decrease in the postural component of work, but in the present study we were careful to measure changes of mechanical efficiency from a baseline of zero load (see the Material and Methods section). The postural component of one-limb work has previously been found (Davies & Sargeant, 1974) to be a factor only at the highest levels of work and it will be noted (Fig. 1) that the shape of the relationship between work output and aerobic energy expenditure does not change before and after rehabilitation. The only marked decline in $\dot{V}O_2$ for given $\dot{W}$ we have observed previously is for subjects performing repeated negative (eccentric) work on a motor-driven treadmill (Davies & Barnes, 1972). In this study we postulated that the effect may be due to the decrease in the number of active muscle fibres required to perform the work (see Abbott, Bigland & Ritchie, 1952). It may be that a similar effect is occurring in one-leg work. To pedal a fixed-wheel cycle ergometer with one limb requires a high degree of muscular strength, particularly in the quadriceps, in order to return the pedal to upright position with each revolution. Normal subjects as well as patients often complain of local (rather than general cardiovascular) fatigue and muscular soreness as limiting factors to one-limb exercise. Undoubtedly the lower limbs of patients recovering from injury are relatively weak (see e.g. Zohn, Leach & Stryker, 1964; Cuddingham, 1973) and it is entirely conceivable that as rehabilitation progresses and dynamic muscular strength improves, the recruitment of fewer muscle fibres are necessary to perform a given work output and thus $\dot{V}O_2$ diminishes. It is interesting to note in this context that at the end of rehabilitation the patients reached 98% of their work output (but not aerobic energy expenditure; see Table 3) with injured compared with uninjured leg as opposed to 85% at the onset.

During maximal work, the $\dot{V}O_{2\,max.\,obs}$ in exercise with the injured leg increases by 290 ml/min (17·4%) compared with 170 ml/min (8·9%) in the uninjured leg (Table 3). In both legs there is an increase in leg muscle (plus bone) volume (LV). However, the relationship of the changes in $\dot{V}O_{2\,max.}$ with LV shows some important differences in the injured and uninjured limbs. In six of the eight patients (Fig. 3) the rise in $\dot{V}O_{2\,max.\,obs}$ of the injured leg is approximately proportional to the change in LV whereas in the uninjured limb two patients show a disproportionate rise in $\dot{V}O_{2\,max.\,obs}$ and in the remainder the rise in $\dot{V}O_{2\,max.\,obs}$ is independent of LV. The change in $\dot{V}O_{2\,max.\,obs}$ in relation to LV for the injured limb is very similar to that previously observed for malnourished children (Davies, 1974). In this latter study the $\dot{V}O_{2\,max.}$ during cycling decreased *pari passu* with the loss of leg muscle (plus bone) volume. Further it was possible to show that improved diet in a different group of rehabilitated children resulted in an improvement in growth and development and an associated rise in physiological performance with an increase in LV. This suggests that in patients recovering from limb injury, as in malnourished children, the limiting factor in maximal aerobic performance during work on a stationary bicycle ergometer is the reduction of muscle (plus bone) mass of the leg. The major effect of rehabilitation in limb injury patients is to reverse the muscle atrophy due to immobilization plaster and the consequent inactivity and thus produce a concomitant rise in aerobic power output. The maximal data for the patient's uninjured limb are consistent with those we have found for normal limbs after a period of systematic training (Davies & Sargeant, 1975c), though in absolute terms the changes are smaller. This is not surprising as in our training study the exercise was specific (it was performed on the bicycle ergometer) and of high intensity and controlled daily under laboratory conditions. However, it is noteworthy that, with these patients, although the changes in $\dot{V}O_{2\,max.\,obs}$ when related to their initial $\dot{V}O_{2\,max.\,obs}$

values are, with one exception, displaced to the left of the curve previously reported for normal subjects, the relationship is nevertheless of similar form (Fig. 2). It is therefore possible that there may be two essential processes governing the physiological improvement of performance in patients recovering from leg injury and that both are related to the initial level of aerobic power output of the lower limbs: first, an increase in $\dot{V}O_{2\,max}$ due to change in LV, which presumably will be self-limiting once the original LV has been achieved, and, secondly, a rise in $\dot{V}O_{2\,max}$ *per se* independently of LV. If therapy is prolonged or the initial level of muscle atrophy in the injured limb is small, both these processes will be observed, giving rise to a change in slope and intercept of the $\dot{V}O_{2\,max}$/LV relationship for a given individual. Clearly the two patients in Fig. 3 may fall into this category.

The increase in the aerobic power output of the patients' injured and uninjured legs is almost exactly paralleled by the observed rise in the combined (two-leg) $\dot{V}O_{2\,max}$ (Table 3). This again is in direct contrast to findings on normal subjects where training (and improving) the $\dot{V}O_{2\,max}$ of each limb individually had minimal effect on the $\dot{V}O_{2\,max}$ of the two limbs combined during work on the bicycle ergometer (Davies & Sargeant, 1975c). However, for reasons mentioned earlier regarding the specific nature of the previous one-leg training used by us, no general conclusions can be drawn regarding the limitations to aerobic performance in patients receiving therapy. It may seem reasonable to argue, in the light of our previous study (Davies & Sargeant, 1975c), that since the increase in two-leg $\dot{V}O_{2\,max}$ exactly parallels the improvement of each leg combined, the major limitation to maximal exercise in patients undergoing rehabilitation must be peripheral (within the muscle tissue) and not central (cardiovascular) in origin. The argument is supported by the relatively small change in f_{H} for two-leg work (Table 2) but it does ignore one important point: in the present investigation the patients were given specific exercises during their therapy programme to improve not only their injured limb function but also their general cardiovascular condition. Thus it is not surprising that we find the two-leg $\dot{V}O_{2\,max}$ value increases *pari passu* with the combined one-leg $\dot{V}O_{2\,max}$.

Finally, from a practical point of view the rehabilitation course as presented at the Joint Services Medical Rehabilitation Unit, achieves its stated object of returning servicemen to normal duty. At the end of rehabilitation the patients are able to achieve 95% of their aerobic power output with injured compared with uninjured leg and the two-leg $\dot{V}O_{2\,max}$ for a given LV (Fig. 4) is not significantly different from that found in a previous cross-sectional survey of normal (naval) servicemen (Davies, 1972). The spontaneous recovery occurring without benefit of a rehabilitation programme is, however, unknown and is an area needing further investigation if the efficacy of rehabilitation programmes such as the one studied is to be accurately assessed.

Acknowledgments

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References

Abbott, B.C., Bigland, B. & Ritchie, J.M. (1952) The physiological cost of negative work. *Journal of Physiology (London)*, **117**, 380–390.

Astrand, P-O. & Rodahl, K. (1970) *Text Book of Work Physiology*. McGraw-Hill, New York.

Cuddingham, J.H.P. (1973) Quadriceps femoris strength. *Rheumatology and Rehabilitation*, **12**, 77–83.

Davies, C.T.M. (1972) The oxygen transporting system in relation to age. *Clinical Science*, **42**, 1–13.

Davies, C.T.M. (1974) The relationship of leg volume muscle (plus bone) to maximum aerobic power on a bicycle ergometer: the effects of anaemia, malnutrition and physical activity. *Annals of Human Biology*, **1**, 47–55.

Davies, C.T.M. & Barnes, C.A. (1972) Negative (eccentric) work. I: Effects of repeated exercise. *Ergonomics*, **15**, 3–14.

Davies, C.T.M., Mbelwa, D., Crockford, G.W. & Weiner, J.S. (1973) Exercise tolerance and body composition of male and female Africans, aged 18–30 years. *Human Biology*, **45**, 31–40.

Davies, C.T.M. & Sargeant, A.J. (1974) Exercise performance with one- and two-legs breathing air and 45% oxygen. *Journal of Applied Physiology*, **36**, 142–148.

Davies, C.T.M. & Sargeant, A.J. (1975a) Physiological responses to exercise in patients following fracture of the lower limb. *Scandinavian Journal of Rehabilitation Medicine* (in press).

Davies, C.T.M. & Sargeant, A.J. (1975b) Use of anthropometry and radiography for the estimation of limb (and component tissue) volume of patients recovering from leg fractures. *Journal of Physiology (London)* (in press).

Davies, C.T.M. & Sargeant, A.J. (1975c) Effects of habituation and training on the physiological responses to 1- and 2-leg work. *Journal of Applied Physiology* (in press).

values are, with one exception, displaced to the left of the curve previously reported for normal subjects, the relationship is nevertheless of similar form (Fig. 2). It is therefore possible that there may be two essential processes governing the physiological improvement of performance in patients recovering from leg injury and that both are related to the initial level of aerobic power output of the lower limbs: first, an increase in $\dot{V}O_{2\,max}$ due to change in LV, which presumably will be self-limiting once the original LV has been achieved, and, secondly, a rise in $\dot{V}O_{2\,max}$ *per se* independently of LV. If therapy is prolonged or the initial level of muscle atrophy in the injured limb is small, both these processes will be observed, giving rise to a change in slope and intercept of the $\dot{V}O_{2\,max}$/LV relationship for a given individual. Clearly the two patients in Fig. 3 may fall into this category.

The increase in the aerobic power output of the patients' injured and uninjured legs is almost exactly paralleled by the observed rise in the combined (two-leg) $\dot{V}O_{2\,max}$ (Table 3). This again is in direct contrast to findings on normal subjects where training (and improving) the $\dot{V}O_{2\,max}$ of each limb individually had minimal effect on the $\dot{V}O_{2\,max}$ of the two limbs combined during work on the bicycle ergometer (Davies & Sargeant, 1975c). However, for reasons mentioned earlier regarding the specific nature of the previous one-leg training used by us, no general conclusions can be drawn regarding the limitations to aerobic performance in patients receiving therapy. It may seem reasonable to argue, in the light of our previous study (Davies & Sargeant, 1975c), that since the increase in two-leg $\dot{V}O_{2\,max}$ exactly parallels the improvement of each leg combined, the major limitation to maximal exercise in patients undergoing rehabilitation must be peripheral (within the muscle tissue) and not central (cardiovascular) in origin. The argument is supported by the relatively small change in $f_{H\,1.5}$ for two-leg work (Table 2) but it does ignore one important point: in the present investigation the patients were given specific exercises during their therapy programme to improve not only their injured limb function but also their general cardiovascular condition. Thus it is not surprising that we find the two-leg $\dot{V}O_{2\,max}$ value increases *pari passu* with the combined one-leg $\dot{V}O_{2\,max}$.

Finally, from a practical point of view the rehabilitation course as presented at the Joint Services Medical Rehabilitation Unit, achieves its stated object of returning servicemen to normal duty. At the end of rehabilitation the patients are able to achieve 95% of their aerobic power output with injured compared with uninjured leg and the two-leg $\dot{V}O_{2\,max}$ for a given LV (Fig. 4) is not significantly different from that found in a previous cross-sectional survey of normal (naval) servicemen (Davies, 1972). The spontaneous recovery occurring without benefit of a rehabilitation programme is, however, unknown and is an area needing further investigation if the efficacy of rehabilitation programmes such as the one studied is to be accurately assessed.

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References

Abbott, B.C., Bigland, B. & Ritchie, J.M. (1952) The physiological cost of negative work. *Journal of Physiology (London)*, **117**, 380–390.

Åstrand, P-O. & Rodahl, K. (1970) *Text Book of Work Physiology*. McGraw-Hill, New York.

Cuddingham, J.H.P. (1973) Quadriceps femoris strength. *Rheumatology and Rehabilitation*, **12**, 77–83.

Davies, C.T.M. (1972) The oxygen transporting system in relation to age. *Clinical Science*, **42**, 1–13.

Davies, C.T.M. (1974) The relationship of leg volume muscle (plus bone) to maximum aerobic power on a bicycle ergometer: the effects of anaemia, malnutrition and physical activity. *Annals of Human Biology*, **1**, 47–55.

Davies, C.T.M. & Barnes, C.A. (1972) Negative (eccentric) work. I: Effects of repeated exercise. *Ergonomics*, **15**, 3–14.

Davies, C.T.M., Mbelwa, D., Crockford, G.W. & Weiner, J.S. (1973) Exercise tolerance and body composition of male and female Africans, aged 18–30 years. *Human Biology*, **45**, 31–40.

Davies, C.T.M. & Sargeant, A.J. (1974) Exercise performance with one- and two-legs breathing air and 45% oxygen. *Journal of Applied Physiology*, **36**, 142–148.

Davies, C.T.M. & Sargeant, A.J. (1975a) Physiological responses to exercise in patients following fracture of the lower limb. *Scandinavian Journal of Rehabilitation Medicine* (in press).

Davies, C.T.M. & Sargeant, A.J. (1975b) Use of anthropometry and radiography for the estimation of limb (and component tissue) volume of patients recovering from leg fractures. *Journal of Physiology (London)* (in press).

Davies, C.T.M. & Sargeant, A.J. (1975c) Effects of habituation and training on the physiological responses to 1- and 2-leg work. *Journal of Applied Physiology* (in press).

Davies, C.T.M., Tuxworth, W. & Young, J.M. (1970) Physiological effects of repeated exercise. *Clinical Science*, **39**, 247–258.

Durnin, J.V.G.A. & Rahaman, M.M. (1967) The assessment of the amount of fat in the human body from measurements of skinfold thickness. *British Journal of Nutrition*, **21**, 681–689.

Jones, P.R.M. & Pearson, J. (1969) Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. *Journal of Physiology (London)*, **204**, 63P–66P.

Zohn, D.A., Leach, R.E. & Stryker, W.S. (1964) A comparison of isometric and isotonic exercise of the quadriceps after injuries to the knee. *Archives of Physical Medicine and Rehabilitation*, **45**, 571–574.

APPENDIX 4

Reprint of: Davies C.T.M. and Sargeant A.J. (1975d) Effects of training on the physiological responses to one- and two-leg work. Journal of Applied Physiology [illegible].

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Effects of training on the physiological responses to one- and two-leg work

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DAVIES, C. T. M., AND A. J. SARGEANT. *Effects of training on the physiological responses to one- and two-leg work.* J. Appl. Physiol. 38(3): 377–381. 1975.—The effects of training resulting from one-leg exercise on a stationary bicycle ergometer have been studied. Seven subjects were habituated to one- and two-leg progressive exercise tests on 11 successive days and were then trained for 60 min·day^{-1} (30 min each leg) 3 times per wk for 5–6 wk at ~80% of their one-leg $\dot{V}_{O_2\,max}$. $\dot{V}_{E\,max}$ increased ($P < 0.05$) by ~14 l·min^{-1} and $\dot{V}_{O_2\,max}$ by ~0.34 l·min^{-1} (+14%; $P < 0.05$) in one-leg exercise. This latter increase was not, however, reflected in the two-leg $\dot{V}_{O_2\,max}$ which only increased 145 ml·min^{-1} (4.7%). It was concluded that training is specific and in one-leg work the phenomenon is mainly peripheral in origin, but in two-leg work the limitation to maximal exercise is still provided by the capacity of the central cardiovascular system to transport oxygen to a given effective muscle mass.

exercise; $\dot{V}_{O_2\,max}$; single-limb work; leg muscle (plus bone) volume; repeated exercise

FROM THE RESULTS of previous work by Davies, Tuxworth, and Young (7) it was suggested that the initial changes in the physiological responses to repeated exercise may be due to readjustments in central circulatory control and the redistribution of cardiac output in favor of the working muscles. Our data suggested that the effects of repeated work could be divided into two stages; the first four occasions in which there was a marked change in the cardiovascular responses to exercise without a concomitant change in maximal aerobic power output ($\dot{V}_{O_2\,max}$) and the second where a gradual change in $\dot{V}_{O_2\,max}$ and a slow decline in cardiac frequency for given oxygen intake were observed. We felt that these two processes (though possibly interrelated) were sufficiently distinct to warrant the terms habituation and training.

In the present experiments we have attempted to examine more specifically the nature of the training stimulus together with the possible role of central and peripheral cardiovascular factors underlying the phenomenon. To investigate these questions we have used our experience with one-limb work (4, 5) and have studied the sequential effects of repeated exercise, first with the right leg, then with the left, and finally with both legs combined. To our knowledge only Glaser (11) has studied the effects of training in one-leg work prior to this investigation. He studied six sedentary subjects (mean $\dot{V}_{O_2\,max}$ = 46.6, range 37.9 – 51.5 ml·kg^{-1}·min^{-1}), twice weekly, training at 75% $\dot{V}_{O_2\,max}$ over a period of 4 wk. His results demonstrated large changes in aerobic power output but they are difficult to interpret on two points. *1*) The subjects performed the one-leg work in pairs and shared the work load by standing each side of the bicycle and pedaling with the inside leg and using the other leg for support. The observed physiological responses to exercise will obviously depend on the degree of cooperation between subjects though the author claims to overcome this difficulty through practice and familiarization with the involved procedure. Nevertheless, *2*) except for one subject (*EW*), his data suggest that the more sedentary subjects improved least and a plot of his $\Delta\dot{V}_{O_2\,max}$ against initial $\dot{V}_{O_2\,max}$ values reveals a curvilinear relationship which is completely the opposite to that found for normal two-leg work (see Saltin et al. (18)).

METHODS

The subjects were first habituated to exercise. They performed submaximal exercise on the first four occasions with one-leg (left or right), the second four occasions with the other leg, and finally the last three occasions with both legs. Following the period of habituation definitive submaximal and maximal one- and two-leg exercise measurements were taken immediately prior to, and at the cessation of, the training period. During one-leg exercise the foot of the active limb was fitted with a plimsoll which was secured to the bicycle pedal by bolts and two metal plates. The standard Monark stationary bicycle ergometer had a fixed wheel and no attempt was made to return the "passive" pedal during cycling. In both one- and two-leg exercise care was taken to ensure that saddle height was correctly adjusted on the first occasion of measurement and maintained throughout the period of the study. At submaximal work loads oxygen intake ($\dot{V}_{O_2}$), minute ventilation ($\dot{V}_E$), carbon dioxide output ($\dot{V}_{CO_2}$), and respiratory (f_R) and cardiac frequencies (f_H) were measured during the last 2 min of a 5-min period by the standard open-circuit techniques (6) using a dry gas (Parkinson Cowan), paramagnetic (Servomex), and infrared (Hilger Watts) meters for ventilation volumes and O_2 and CO_2 concentrations, respectively. Maximum determinations were made and assessed using criteria previously developed (2, 4, 5) by the standard Douglas bag technique, a collection being taken over the last minute of a final 3-min work load during which the subjects were encouraged to pedal as hard as possible. If they were able to sustain this load the level was raised again and a second collection taken.

Mechanical efficiency (defined as the ratio of work performed to aerobic energy expenditure) was calculated from the $\dot{V}O_2$ work data using a base line of pedaling against zero load (13, 20).

The training of each subject was supervised in the laboratory. They trained for 60 min·day⁻¹ (30 min with each leg), 3 times per wk over a 5- to 6-wk period at ~80% of their (one-leg) $\dot{V}O_{2\,max}$. During each training period work output and cardiac frequency were monitored continuously.

During the study the subjects were measured for height and weight, and the sum of four skinfold thicknesses taken for the estimation of lean body mass after the method of Durnin and Rahaman (8). In addition leg volume (LV, muscle plus bone) was measured according to the method of Jones and Pearson (14). The physical characteristics are summarized in Table 1.

RESULTS

During the period of habituation to exercise, minute ventilation at a carbon dioxide output of 1.5 l·min⁻¹ ($\dot{V}E_{1.5}$), tidal volume at a minute ventilation of 30 l·min⁻¹ (V_{T30}) and oxygen intake at a work level of 450 kpm/min ($\dot{V}O_{2\,450}$) remained essentially constant. At the commencement of measurement these parameters averaged 50.38 ± 6.84 l·min⁻¹, 1.14 ± 0.05 l, and 1.43 ± 0.12 l·min⁻¹ with the first leg and 49.23 ± 2.20 l·min⁻¹, 1.09 ± 0.17 l, and 1.44 ± 0.11 l·min⁻¹ with the second leg, respectively. At the conclusion of the study these parameters had changed by −6.09 and −2.96 l·min⁻¹, −0.08 and +0.10 l, and −0.03 and −0.02 l·min⁻¹ for the first and second legs, respectively. On the other hand, $f_{H\,1.5}$ remained constant during the first two occasions with first leg and then showed small but significant ($P < 0.05$) (−5 beats·min⁻¹) fall on the third occasion and thereafter remained constant. The small change in $f_{H\,1.5}$ (−6 beats·min⁻¹) was observed in the second leg but following the first (and not second) occasion. However, the magnitude of the mean changes in f_H was partly masked by the fact that two of the subjects were athletic and the $\Delta f_{H\,1.5}$ observed were related to the initial level of $\dot{V}O_{2\,max}$ of the subject. The changes in $f_{H\,1.5}$ were more marked in the two sedentary subjects, the results from one of these is shown in Fig. 1. During two-leg work (occasions 9–11 inclusive), all the physiological responses to exercise measured remained constant. The responses to maximal one-leg work measured after 1st, 4th, and 8th occasions and two-leg work after 9th and 11th occasions, showed no significant changes: $\dot{V}E_{max}$, $\dot{V}O_{2\,max\,net}$ and $f_{H\,max}$ for one- and two-leg work remained essentially constant throughout the period of habituation.

The effects of 5- to 6-wk training program on the maximal responses of each leg is shown in Table 2. Before and after training there were no significant differences between the right and left leg of the subjects. The major effect of training was to effect an increase in $\dot{V}E_{max}$ (right leg) from 123.41 ± 10.60 to 140.73 ± 15.33 l·min⁻¹ and (left leg) from 125.32 ± 14.93 to 136.50 ± 10.74 l·min⁻¹ ($P < 0.05$), and the $\dot{V}O_{2\,max\,net}$ (right leg) from 2.43 ± 0.41 to 2.82 ± 0.43 l·min⁻¹ ($P < 0.05$) and (left leg) 2.43 ± 0.42 to 2.72 ± 0.39 l·min⁻¹ ($P < 0.05$); but $f_{H\,max}$ re-

TABLE 1. *Physical characteristics*

	Age, yr	Ht, cm	Wt, kg	Σsf, mm	LBM, kg	LV, l RL	LV, l LL
Before training (n = 7)	29.1 ±3.3	176.3 ±8.1	74.9 ±10.4	30.1 ±7.7	64.8 ±7.7	7.33 ±0.79	7.11 ±0.50
Δ After	0.1	0.1 ±0.7	0.11 ±1.34	−0.03 ±1.81	−0.22 ±1.46	+0.20 ±0.61	−0.06 ±0.29

Values are means ± SD. Σsf = sum of 4 skinfold thicknesses (biceps, triceps, subscapular, suprailiac); LBM = lean body mass; LV = leg muscle (plus bone) volume; RL and LL = right and left leg.

TABLE 2. *Effects of training on maximal one-leg minute ventilation rate, net aerobic power output, and cardiac frequency in seven subjects*

	Before $\dot{V}E_{max}$, l·min⁻¹	Before $\dot{V}O_{2\,max\,net}$, l·min⁻¹	Before $f_{H\,max}$, beats·min⁻¹	After $\dot{V}E_{max}$, l·min⁻¹	After $\dot{V}O_{2\,max\,net}$, l·min⁻¹	After $f_{H\,max}$, beats·min⁻¹
Right leg	123.41 ±10.60	2.43 ±0.44	[illegible]	[illegible]	[illegible]	[illegible]
Left leg	125.32 ±14.93	2.43 ±0.42	[illegible]	[illegible]	[illegible]	[illegible]
Two legs	132.59 ±17.32	3.06 ±0.52	[illegible]	[illegible]	[illegible]	[illegible]

Values are means ± SD. * [illegible] before–after [illegible] $P < 0.01$. † $P < 0.05$.

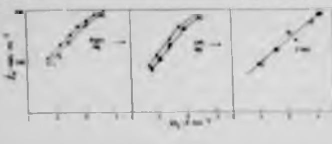

FIG. 1. [illegible]

mained unchanged at approximately 179 beats·min^{-1} throughout the period of the investigation.

The mean change of ~340 ml·min^{-1} in $\dot{V}O_{2\ max\ net}$ represents an improvement in aerobic performance of 14% for the group of subjects as a whole, but individually the % $\Delta\dot{V}O_{2\ max\ net}$ is clearly related to the initial level of $\dot{V}O_{2\ max\ net}$ expressed in ml·l(LV)$^{-1}$·min^{-1} (Fig. 2). The relationship is curvilinear ($P < 0.05$) and is adequately represented by the equation

$$\dot{V}O_{2\ max\ net}\ (\%) = 17.48 - 0.813\ (\text{initial } \dot{V}O_{2\ max\ net}\ \text{ml·l(LV)}^{-1}\text{·min}^{-1}) + 0.00097\ (\text{initial } \dot{V}O_{2\ max\ net}\ \text{ml·l(LV)}^{-1}\text{·min}^{-1})^2$$
$$SD = 5.3\%$$

The increase in $\dot{V}O_{2\ max\ net}$ with training is not accompanied by a concomitant increase in leg muscle (plus bone) volume. For a given rise in $\dot{V}O_{2\ max\ net}$, LV remains almost constant (Table 1), thus the linear regression line relating the two variables shows a parallel displacement to the left of the 'normal' relationship (Fig. 3).

In contrast to the large changes in $\dot{V}O_{2\ max\ net}$ of one leg, the improvement in two-leg $\dot{V}O_{2\ max\ net}$ (following the training of each limb individually) was relatively small (Table 2). If the improvement of each $\dot{V}O_{2\ max\ net}$ limb was additive one would have expected a change in two-leg $\dot{V}O_{2\ max\ net}$ of the order of 671 ml·min^{-1} (22%), in fact, the measured change was only 145 ± 242 ml·min^{-1} (4.7%). This lack of improvement of two-leg $\dot{V}O_{2\ max\ net}$ following one-leg training has a profound effect on the relationship between the two variables. Before training, one-leg $\dot{V}O_{2\ max}$ was 79% of two-leg $\dot{V}O_{2\ max}$ and the linear regression relationship lay within the limits previously reported (4) for normal healthy subjects. Following training the $\dot{V}O_{2\ max\ net}$ of one leg rose to 87% of two-leg $\dot{V}O_{2\ max}$ and the line relating the two variables was displaced to the right. The respective equations relating one- and two-leg $\dot{V}O_{2\ max\ net}$ were before training

$$\text{two-leg } \dot{V}O_{2\ max\ net}\ (\text{l·min}^{-1}) = 0.05 + 1.229\ \text{one-leg } \dot{V}O_{2\ max\ net}\ (\text{l·min}^{-1})$$

after training

$$\text{two-leg } \dot{V}O_{2\ max\ net}\ (\text{l·min}^{-1}) = 0.32 + 1.042\ \text{one-leg } \dot{V}O_{2\ max\ net}\ (\text{l·min}^{-1})$$

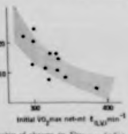

FIG. 2. Relationship of change in $\dot{V}O_{2\ max}$ (Δ%) to initial level of $\dot{V}O_{2\ max}$ for one-leg work. Initial $\dot{V}O_{2\ max}$ has been expressed in terms of ml·l(LV)$^{-1}$·min^{-1}.

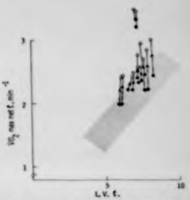

FIG. 3. Relationship of $\dot{V}O_{2\ max\ net}$ to estimates of limb muscle (plus bone) volume (LV) before (●) and after (○) training. Shaded area represents previous limits (mean ± SD) for normal subjects (4).

DISCUSSION

The present experiments were designed to evaluate the effects of training during work on a stationary bicycle ergometer.

Our data for habituation of one limb differ in some important respects from that previously reported (7) for two-limb work. In the present investigation, the $\dot{V}O_2$ for given $\dot{W}$, the $\dot{V}_T$ and $\dot{V}_E$ for given $\dot{V}CO_2$ (as before for two-limb work) remain constant, but there is a much smaller change in $f_{H\ 1.5}$ and the sequence of events differs from those previously recorded. In two-leg work (7) there was a marked fall in cardiac frequency of 21 beats·min^{-1} from occasion 1 to 4; half the change being observed following the first exposure of the subjects to exercise. By comparison in the present experiments the change in $f_{H\ 1.5}$ was not seen until the second occasion of measurement and was reduced in magnitude to an average of 5 beats·min^{-1} for the four subjects. This small mean change in $f_{H\ 1.5}$ was not transferred directly to the second limb, but the prior habituation of one limb appeared to facilitate that of the other: as the same order of change in $f_{H\ 1.5}$ appeared following the first occasion of measurement of the second leg (Fig. 1). During the period of habituation the one-leg $\dot{V}O_{2\ max}$ remained unchanged. When the subjects performed two-leg work having habituated each limb individually and sequentially, there was no evidence of change in the physiological responses to repeated submaximal work. $\dot{V}O_{2\ 40\%}$, $\dot{V}_{E1.5}$, $\dot{V}_{T24}$ and $f_{H\ 1.5}$ remained constant. These findings cannot necessarily be extrapolated to other forms of exercise and markedly different types of subjects. In this context it should be noted that the present group of subjects were physically active and accustomed to performing laboratory experiments although they had not previously pedalled a bicycle ergometer: this contrasts with and may explain some of the differences with the previous study (7) where the subjects were sedentary and totally naive.

The large mean (≃14%) improvement of $\dot{V}O_{2\,max}$ of 1 leg following an intensive 5-wk period of training is in agreement with that found by Gleser (11), but our results differ decisively from his in that our changes are closely associated with the initial aerobic power output of the limb (Fig. 2). The $\dot{V}O_{2\,max}$/initial $\dot{V}O_{2\,max}$ relationship parallels that found previously for two-leg work in young (aged 20–30 yr) male (18) and older (+40 yr) subjects (9, 19). The training effect appears to be specific to the leg being exercised and is not transferred to the contralateral limb (cf. Klausen et al. (16), for arm and leg work). However, the combined improvement (22%) of each limb is not reflected by a concomitant increase in $\dot{V}O_{2\,max}$ of both legs when they are used together to pedal the ergometer. Following the training of each leg the change in two-leg $\dot{V}O_{2\,max}$ is minimal (~5%). This supports our view (4) and those of others (see Bevegård and Shepherd (1) for review) that the limiting factor to exercise where relatively large muscle groups are employed, such as in two-leg cycling, is the ability of the cardiovascular system to transport the required volume and not the capacity of the muscles to utilize oxygen.

The present results (Table 2) cannot be reconciled with those (e.g., 15) who argue that the increase in $\dot{V}O_{2\,max}$ during rhythmic two-leg exercise is solely limited by peripheral (tissue) events within the working muscle and unrelated to cardiovascular transport and the capacity of the heart to increase its output. Certainly we agree with Gleser (11) that in exercise where the effective muscle mass is reduced (as in one-leg work) and presumably $\dot{Q}$ is not limiting the case for peripheral improvement of $\dot{V}O_{2\,max}$ as found in the present experiments is overwhelming, but on the basis of one-leg–two-leg improvement we fundamentally disagree with him, that this can be used as argument for the unique peripheral nature of the training stimulus, in fact, quite the reverse.

Clearly in any integrated system such as the (cardiovascular) transport and (muscle) utilization of oxygen, it is unwise to argue purely in terms of peripheral and central events and this is not our case. Our view is solely that the improvement in $\dot{V}O_{2\,max}$ will depend ultimately on the balance between tissue and cardiovascular events. Where the effective muscle mass is limiting the balance will swing towards the periphery, but in work demanding larger muscle groups, it will move toward the delivery of oxygen from the central circulatory system and the limits imposed by $\dot{Q}$. It would seem axiomatic that transport and utilisation are the two fundamental links in the chain of improvement of maximal aerobic power, but the degree to which they are integrated will depend on the type of exercise and the state of training of the subject.

The displacement of the $\dot{V}O_{2\,max\,ml}$(one-leg):LV relationship following training again illustrates very clearly the point we have made several times (see Davies (3) for review) regarding the essential independence of leg muscle (plus) bone volume and aerobic power output. The $\dot{V}O_{2\,max\,ml}$ of the limb improves whilst the LV remains almost constant (Table 1 and Fig. 3). The large change in $\dot{V}O_{2\,max\,ml}$ following training demonstrates the great capacity of leg muscle to improve its oxidative capacity. In Fig. 3 we have also included the data on one extremely fit athlete (a marathon runner) and it will be seen that even his initial value $\dot{V}O_{2\,max\,ml}$ before training lies well outside the normal limits for trained (but not athletic) men. Following training the improvement in $\dot{V}O_{2\,max}$ was small (<4%) which is to be expected (Fig. 2), but it is intriguing to speculate how an athlete can reach a $\dot{V}O_{2\,max}$ of over 3 l·min^{-1} with one limb, which has a LV of just over 7 l. Theoretical consideration, for example, of limb blood flow would seem to suggest a rate in excess of previously observed maximal two-leg work values. Clearly if our results from one subject can be confirmed a study of the haemodynamic responses of high (aerobic) performance athletes during single leg exercise would well repay further study.

Thus, in summary our results show that one limb can be trained independently of the other and of the volume of muscle (plus bone) present but the improvement in aerobic performance is not reflected in the two limbs when they are combined. This gives rise to the labile nature of the one- to two-leg $\dot{V}O_{2\,max}$ relationship already noted (p. 8 and Davies and Sargeant (4)), and further underlies the specificity of the training process. Further research is required to elucidate the initial effects of repeated exercise but taking our combined findings for two-leg (7) and one-leg work (present investigation) together it may well be that habituation is merely the earliest manifestation of a more general training phenomenon. Unfortunately this would suggest that the first time (and on each successive occasion) you subject a hitherto sedentary subject to exercise in the laboratory you change his physiological state. This may well confound the very variables you are trying to measure.

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REFERENCES

1. Bevegård, B. S., and J. T. Shepherd. Regulation of circulation during exercise in man. *Physiol. Rev.* 47: 178–213, 1967.
2. Davies, C. T. M. Limitations to the prediction of maximum oxygen intake from cardiac frequency measurements. *J. Appl. Physiol.* 24: 700–706, 1968.
3. Davies, C. T. M. Relationship of leg muscle (plus bone) volume to maximum aerobic power on a bicycle ergometer: the effects of anaemia, malnutrition and physical activity. *Ann. Human Biol.* 1: 47–55, 1974.
4. Davies, C. T. M., and A. J. Sargeant. Exercise performance with one and two legs breathing air and 45% oxygen. *J. Appl. Physiol.* 36: 142–148, 1974.
5. Davies, C. T. M., and A. J. Sargeant. Physiological responses to standardised arm work. *Ergonomics* 17: 41–49, 1974.
6. Davies, C. T. M., and D. S. Stirling. The rapid sampling, storage and analysis of expired air. *Ergonomics* 10: 187–190, 1967.
7. Davies, C. T. M., W. Tuxworth, and J. M. Young. Physiological effects of repeated exercise. *Clin. Sci.* 39: 247–258, 1970.
8. Durnin, J. V. G. A., and M. M. Rahaman. The assessment of

the amount of fat in the human body from measurements of skinfold thickness. *Brit. J. Nutr.* 21: 681–689, 1967.

9. Ekblom, B. Effect of physical training on oxygen transport system in man. *Acta Physiol. Scand. Suppl.* 328, 1969.
10. Freyschuss, U., and T. Strandell. Circulatory adaptation to one- and two-leg exercise in supine position. *J. Appl. Physiol.* 25: 511–515, 1968.
11. Gleser, M. A. Effects of hypoxia and physical training on haemodynamic adjustments to one-legged exercise. *J. Appl. Physiol.* 34: 655–659, 1973.
12. Grimby, G., E. Haggendal, and B. Saltin. Local xenon 133 clearance from the quadriceps muscle during exercise in man. *J. Appl. Physiol.* 22: 305–310, 1967.
13. Hill, A. V. *Trails and Trials in Physiology.* London: Arnold, 1965.
14. Jones, P. R. M., and J. Pearson. Anthropometric determination of leg fat and muscle plus bone volumes in young male and female adults. *J. Physiol., London* 204: 63–66, 1969.
15. Kaijser, L. Limiting factors for aerobic muscle performance. *Acta Physiol. Scand. Suppl.* 346, 1970.
16. Klausen, K., J. A. Clausen, B. Rasmussen, and J. Trap-Jensen. Effect of strenuous arm and leg training on pulmonary ventilation, metabolism and blood pH during submaximal exercise. *Acta Physiol. Scand.* 82, 8A, 1971.
17. Pirnay, F., R. Marechal, R. Radermecker, and J. M. Petit. Muscle blood flow during submaximum and maximum exercise on a bicycle ergometer. *J. Appl. Physiol.* 32: 210–212, 1972.
18. Saltin, B., G. Blomqvist, J. H. Mitchell, R. L. Johnson, Jr., K. Wildenthal, and C. B. Chapman. Response to exercise after bed rest and after training. *Am. Heart Assoc. Monograph* 23, 1968.
19. Saltin, B., and G. Grimby. Physiological analysis of middle aged and old former athletes: comparison with still active athletes of the same ages. *Circulation* 38: 1104, 1968.
20. Whipp, B. J., and K. Wasserman. The efficiency of muscular work. *J. Appl. Physiol.* 26: 644–648, 1969.