THE TIME COURSE OF PULMONARY DIFFUSION CAPACITY CHANGES FOLLOWING MAXIMAL EXERCISE

by

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B.P.E., The University of New Brunswick, 1993

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF

THE REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE STUDIES

SCHOOL OF HUMAN KINETICS

We accept this thesis as conforming
to the required standard

THE UNIVERSITY OF BRITISH COLUMBIA

August 1995

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ABSTRACT

Pulmonary gas transport has not been typically recognized as a limiting factor to physical exercise. Dempsey et al. (1984; 1986) have suggested that the pulmonary system remains unchanged despite chronic aerobic training. Adaptations to other physiological systems may impose metabolic demands which the respiratory system can not meet. In essence, the lung's capacity for gas exchange becomes surpassed by other training adaptations. Supporting evidence is seen as decreases in arterial oxygenation at near maximal work rates in highly trained male endurance athletes (Dempsey et al., 1984; Powers et al., 1988; 1989; Hopkins and McKenzie 1989). Decreased arterial oxygenation has been termed exercise-induced arterial hypoxemia (EIH), and has direct consequences on $\dot{V}O_2max$ (Lawler et al., 1988; Powers et al., 1989; Martin and O'Kroy, 1993) and maximal performance capacity (Koskolou and McKenzie, 1994). It is estimated that approximately fifty percent of highly trained male endurance athletes exhibit EIH (Powers et al., 1988; 1993; Martin et al., 1992b). One mechanism that has been advanced to explain this phenomenon is a diffusion limitation. Diffusion capacity of the lung (DL) may be depressed during exercise and not allow for complete gas equilibrium to occur. If a structural alteration were present during exercise, it would continue to depress DL during recovery.

To investigate the time course of change in pulmonary diffusion capacity for carbon monoxide (DL_{CO}) ten (N=10) highly trained male cyclists (HT) and ten (N=10) moderately (MT) male subjects were selected for this study. Subjects cycled to exhaustion to determine maximal oxygen consumption ($\dot{V}O_2max$) on an electronically braked cycle ergometer (Mijnhardt KEM-3) (mean ± SD: HT $\dot{V}O_2max$ = 68.0 ± 4.9; MT $\dot{V}O_2max$ = 51.6 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$). Percent arterial oxygen saturation ($\%SaO_2$) was monitored by a pulse oximeter (Ohmeda Biox 3740) to determine if subjects demonstrated exercise-induced arterial hypoxemia (defined as $\%SaO_2 \leq 91\%$) ($\%SaO_2min$ HT = 91.4 ± 1.6; MT = 94.6 ± 1.1). At a second data collection period, pulmonary function testing was performed. All subjects demonstrated normal pulmonary function. Initial diffusion measurements were made to obtain resting DL_{CO}, diffusion capacity of the alveolar membrane (DM), and pulmonary capillary blood volume (Vc). Both spirometry and diffusion

measurements were made using the same apparatus (Collins PLUS DS II). DM and Vc were calculated by measuring DL_{CO} at two inspired O_2 concentrations using the technique of Roughton & Forster (1957). Subjects then cycled to fatigue at a workrate that corresponded to the highest workrate attained during the $\dot{V}O_2$max test. Expired gases and $\%SaO_2$ data were collected during the time to fatigue cycle test. Five additional measurements of pulmonary diffusion were made at 1, 2, 4, 6 and 24 hours following the cycle test.

One hour post-exercise, DL_{CO} was significantly decreased in both groups compared to baseline. The decrease reached a minimum value at 6 hrs and approached normal values 24 hrs after the exercise. Only HT subjects exhibited EIH yet both groups experienced similar changes in DL_{CO}. The correlation between %SaO2min and change in DL_{CO} was low (r=-0.3), implying that EIH can not be explained by post exercise decrease in DL_{CO}. The change in DL_{CO} can be explained primarily by a parallel decrease in Vc. Vc decreased below baseline values in both groups, perhaps indicating a compensatory shunting mechanism. A smaller degree of change was observed in DM, and played less of a role in the decreased DL_{CO}.

The results of this study are the first to compare diffusion capacity in two separate groups, based on training status, following maximal exercise. Both moderately trained and highly trained subjects exhibited similar decreases in pulmonary diffusing capacity. This supports the theory that the lung may not adapt to aerobic training and behaves in a similar manner regardless of training status.

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LIST OF ABBREVIATIONS AND SYMBOLS

$A\text{-}aDO_2$	Alveolar-arterial oxygen difference
BHT	Breath hold time
D_L	Diffusion capacity of the Lung
D_{LCO}	Diffusion capacity of the lung for carbon monoxide
D_M	Diffusion capacity of alveolar membrane
D/VA	Diffusion capacity per alveolar volume
EIH	Exercise-induced arterial hypoxemia
$FEF_{25\text{-}75\%}$	Forced expiratory flow at 25-75% of forced vital capacity
FVC	Forced vital capacity
FEV_1	Forced expired volume in first second
FEF_{max}	Maximal expiratory flow rate
HT	Highly trained endurance athletes
Hb	Hemoglobin
[Hb]	Concentration of hemoglobin
He insp	Fraction of helium inspired
He exp	Fraction of helium expired
MT	Moderately trained subjects
P_ACO_2	Alveolar partial pressure of carbon dioxide
$PaCO_2$	Arterial partial pressure of carbon dioxide
P_AO_2	Alveolar partial pressure of oxygen
PaO_2	Arterial partial pressure of oxygen
PB	Barometric pressure
$PcapO_2$	Capillary partial pressure of oxygen
$\dot{Q}$	Cardiac output
$\dot{Q}c$	Capillary Perfusion

RBC	Red blood cell
RER	Respiratory exchange ratio
$\%SaO_2$	Percentage of arterial oxyhemoglobin saturation
$\%SaO_2min$	Minimal percentage of arterial oxyhemoglobin saturation during exercise
θ	Reaction rate of hemoglobin and carbon monoxide
$\dot{V}A$	Alveolar ventilation
VA	Alveolar volume
$\dot{V}A/\dot{Q}c$	Ventilation-perfusion ratio
Vc	Pulmonary capillary blood volume
$\dot{V}E$	Expired ventilation per minute
$\dot{V}E/\dot{V}O_2$	Ventilatory equivalent for oxygen
VI	Inspired volume
$\dot{V}O_2$	Rate of oxygen uptake
$\dot{V}O_2max$	Maximal rate of oxygen uptake

ACKNOWLEDGMENT

This thesis is the result of support and encouragement from many individuals. I would like to thank all those who have lent a hand along the way, specifically:

Dr. Don McKenzie	My advisor, who provided inspiration through example. He has made a great impression on me that will last a lifetime.
My Committee	Dr. Ken Coutts, Dr. Pierce Wilcox, Dr. Pat Neary whose contributions made this thesis possible.
Diana Jesperson	Without Diana, NOTHING would ever get done in the lab. Many mistakes were avoided by listening to her, as she has made most of them.
Iris and Jim	My diffusion buddies.
My Parents	Who always let me fall, but were there to pick me up.
Jen Phillips	Who stood by me, from afar.

INTRODUCTION

Exercise physiologists have generally accepted the conventional view that oxygen (O_2) delivery to working muscle is the primary determinant of maximal oxygen uptake ($\dot{V}O_2max$) and exercise performance (McArdle et al., 1991). Pulmonary gas transport has not been typically recognized as a limiting factor to physical exercise. This belief is based on data which shows that arterial blood gases are maintained during exercise (Asmussen and Nielson, 1960; Saltin et al., 1968). It is well known that endurance training produces adaptations to both the cardiovascular and the musculoskeletal systems. However, Dempsey et al. (1984; 1986) have suggested that the pulmonary system remains unchanged despite chronic aerobic training. Adaptations to other physiological systems may impose metabolic demands which the respiratory system can not meet. In essence, the lung's capacity for gas exchange becomes surpassed by training adaptations to separate organ systems. Supporting evidence has been documented by several authors who have reported decreases in arterial oxygenation at near maximal work rates in highly trained ($\dot{V}O_2max \sim 5\ L \cdot min^{-1}$) male endurance athletes (Dempsey et al., 1984; Powers et al., 1988; 1989; Hopkins and McKenzie 1989). These studies demonstrate that the pulmonary system may not be capable of maintaining blood gas homeostasis during maximal exercise. Decreased arterial oxygenation has been termed exercise-induced arterial hypoxemia (EIH). This phenomenon has direct consequences for competitive athletes as a lower percentage of arterial oxyhemoglobin saturation ($\%SaO_2$) can lower $\dot{V}O_2max$ (Lawler et al., 1988; Powers et al., 1989; Martin and O'Kroy, 1993) and impair maximal performance capacity (Koskolou and McKenzie, 1994). It is estimated that approximately fifty percent of highly trained male endurance athletes exhibit EIH (Powers et al., 1988; 1993; Martin et al., 1992b).

Several mechanisms have been advanced to explain this phenomenon: relative hypoventilation, veno-arterial shunts, ventilation ($\dot{V}A$) to pulmonary capillary blood perfusion ($\dot{Q}c$) heterogeneity ($\dot{V}A/\dot{Q}c$), and diffusion limitations. Athletes with high aerobic capacities may have an inappropriate hyperventilatory response to maximal exercise (Dempsey et al., 1984; Wagner, 1992). This would result in a lower alveolar PO_2 (PAO_2) reducing the driving

force of O_2 transfer across the blood-gas barrier. Inadequate exercise hypernea in athletes may be the result of diminished response to humoral factors by peripheral and/or central chemoreceptors. $\dot{V}A/\dot{Q}c$ mismatch may also contribute to EIH, where the ratio becomes less uniform with increasing exercise intensity (Gale et al., 1985; Hammond et al., 1991; Hopkins et al., 1994). During maximal exercise, cardiac output ($\dot{Q}$) increases to ~ 33 $L \cdot min^{-1}$ (Hopkins et al., 1994) and may reach values as high as 40 $L \cdot min^{-1}$ (Ekblom et al., 1968). Pulmonary capillary blood volume expands with increases in $\dot{Q}$ and exercise intensity, but may reach its anatomic limit despite further increases in $\dot{Q}$. Capillary transit time may therefore be decreased such that diffusion equilibrium does not occur (Dempsey et al., 1984; Hopkins et al., 1994).

The formation of pulmonary edema is another possible diffusion limitation. The mechanism for the accumulation of extravascular water, or pulmonary edema, could be caused by increased capillary hydrostatic pressure, increased capillary permeability, increased capillary surface area or a lymphatic insufficiency (West, 1977). The process of gas diffusion through tissues is proportional to the tissue area and the difference in gas partial pressure between the two sides, and inversely proportional to the tissue thickness. Pulmonary edema would increase the distance across the gas exchange barrier, impairing diffusion. Pulmonary edema may occur during exercise as a result of stress failure of the pulmonary capillary membrane (Tsukimoto et al., 1991; West et al.,1993) related to the extreme pressures associated with high $\dot{Q}$ which are known to occur in highly trained athletes (Reeves et al., 1988). Given the thinness of the blood-gas barrier (~ 0.3 μm), it seems highly possible that the integrity of the membrane could be compromised when extremely high $\dot{Q}$ are achieved.

A number of authors have reported a decrease in the diffusing capacity of the lung (DL) following a period of maximal exercise (Miles et al., 1983; Rasmussen et al., 1988; Manier et al., 1993; Hanel et al., 1994). If sufficient pulmonary edema accumulates during exercise to widen the alveolar-arterial difference, there should be a necessary time period for fluid clearance. During recovery from maximal exercise, relative homeostasis is observed in a short time. If a structural alteration were present it would continue to depress DL, despite a return to normal of heart rate and other exercise-induced disturbances. However, data examining DL

have been conflicting. Diffusing capacity of the lung for carbon monoxide (DL_{CO}) was reduced 2% twenty-four hours following a marathon run (Miles et al., 1983); was depressed by 10.5% two and one-half days after a short duration maximal rowing effort (Rasmussen et al., 1988); and was at baseline values 0.5 hours following maximal cycle ergometry (Manier et al., 1993). Despite these divergent results, it appears that a change occurs to the diffusion capacity of the lung following maximal exercise.

By partitioning DL into its two components: 1) the diffusion capacity of the alveolar membrane (DM) and 2) the reaction rate of the gas with Hb within the red blood cell (θ) and pulmonary capillary blood volume (Vc), a more detailed view of DL can be obtained. To date, there have been few studies that have followed and separated DL for an extended period post-exhaustive exercise. Studies that have successfully divided DL have also produced variable results. Miles et al. (1983) found DL_{CO} and DM to be significantly lower than baseline values, while Vc had returned to normal 24 hours after a marathon run. In contrast, Hanel et al. (1994) have reported that six hours following maximal rowing subjects had significantly lower DL_{CO}, normal DM, and Vc had dropped significantly below resting values.

Highly trained endurance athletes that develop EIH may do so by the accumulation of interstitial fluid due to capillary stress failure, and DL decreases following maximal exercise for up to 24 hours. The time course of change in DL post-exercise is unclear. Therefore, this study investigated the changes in DL following a bout of maximal exercise and compared highly trained endurance athletes to moderately trained subjects. The relationship between the lowest $\%SaO_2$ ($\%SaO_2min$) during exercise and DL post-exercise was also investigated.

The hypothesis tested were:

(1) DL_{CO} will be depressed significantly in highly trained endurance cyclists following a time to fatigue maximal cycle ergometry test when compared to baseline values, and remain depressed for 2 hours post exercise.

(2) Moderately trained subjects will not show a significant decrease in DL_{CO} following a time to fatigue maximal cycle ergometry test when compared to baseline values.

(3) There will be a positive correlation between $\%SaO_2min$ during the time to fatigue cycle ergometer test and the greatest ΔDL_{CO} post-exercise.

METHODOLOGY

Subjects

Ten highly trained (HT) male endurance cyclists and ten moderately trained (MT) non-smoking male subjects were recruited to participate in this study. HT subjects were from local competitive cycling clubs and MT subjects were university students not involved with regular aerobic training. Prior to any testing, subjects received a verbal description of the experiment, and completed a written informed consent form. This study was approved by the Clinical Screening Committee for Research and Other Studies Involving Human Subjects of the University of British Columbia. Upon giving written consent, all subjects performed two separate sessions of data collection. Criteria for participation was a maximal oxygen consumption ($\dot{V}O_2max$) $\leq$ 55 mL·kg^{-1}·min^{-1} or $\leq$ 4 L·min^{-1} in the MT group, $\geq$ 60 mL·kg^{-1}·min^{-1} or $\geq$ 5 L·min^{-1} in the HT group. Additionally, all subjects were required to have normal pulmonary function with no history of respiratory disease. Subjects who satisfied these criteria were included in the study.

Maximal Cycle Ergometer Test

Subjects reported to the laboratory after a 24-hour period of no intense exercise and performed a 5 minute self-selected cycling warm-up (50-100 watts) immediately prior to a maximal cycle ergometer test. All cycling was completed on an electronically braked cycle ergometer (Mijnhardt KEM-3) equipped with a racing saddle and pedals. During the maximal test subjects pedaled at a self-chosen cadence at an increasing workload which started at 0 watts and increased 30 watts·min^{-1} until volitional fatigue was achieved. While cycling, subjects breathed through a two-way non-rebreathing valve (Hans-Rudolph, #2700B). Analysis of expired respiratory gases and minute ventilation ($\dot{V}E$) was performed using an automated metabolic system (Rayfield System). Heart rate was recorded every 15 seconds using a heart rate monitor (Polar Vantage XL). Percent arterial oxygen saturation (%SaO_2) was measured by a validated (Martin et al., 1992a) pulse oximeter (Ohmeda Biox 3740) and averaged every 15 seconds. Prior to placement of the oximeter ear sensor, a topical vasodilator cream

(Finalgon®, Boehringer/Ingeheim) was applied to the lobe of the ear to increase local perfusion. Additional indicators for achieving $\dot{V}O_2max$, beyond volitional fatigue were a plateau in $\dot{V}O_2$ with increasing work rate, heart rate ≥ 90% of predicted maximum heart rate, and a respiratory exchange ratio (RER) ≥ 1.15. Other descriptive physical information was also obtained, including age, height, body mass, and peak power output during the cycle test.

Experimental Protocol

The maximal cycle ergometer test and the experimental protocol were separated by at least 72 hours in all subjects. Upon arrival at the laboratory subjects sat and rested for 30 minutes to stabilize the pulmonary system for measurement of the diffusing capacity of carbon monoxide (DL_{CO}) (Billiet, 1974). Initially subjects performed at least 3 flow:volume maneuvers to determine forced vital capacity (FVC), forced expired volume in 1 second (FEV_1), forced expiratory flow at 25-75% of FVC ($FEF_{25-75\%}$), and maximal forced expiratory flow rate (FEF_{max}). Following completion of spirometry, baseline values of DL_{CO} were obtained. Both spirometry and diffusion measurements were collected using the same commercial apparatus (Collins PLUS DS II). A time to fatigue cycling test was then performed. A total of six diffusion measurements were made, including baseline and 5 measurements at 1, 2, 4, 6, and 24 hours following the time to fatigue cycling test. Subjects did not participate in any physical activity following the time to fatigue cycling test beyond light walking. At all diffusion measurement periods hemoglobin concentration was measured using a direct reading hemoglobinometer (HemoCue, Helsingborg, Sweden) to correct DL_{CO} measures (Cotes et al., 1972).

Time to Fatigue Test

All subjects completed a 5-10 minute cycling warm-up at a workload equivalent to 25-50% of the subject's $\dot{V}O_2max$ obtained from the preliminary test. The test began when workrate was manually increased to correspond to the highest workrate achieved during the maximal cycle ergometer test. Changes in saturation are known to occur when high metabolic

rates are achieved by endurance-trained athletes (Dempsey et al., 1984; Powers et al., 1988; 1989). Subjects were instructed to cycle to complete exhaustion, and time was recorded. All subjects received the same degree of verbal encouragement but were not informed of elapsed time during the test. Expired gases, heart rate and $\%SaO_2$ were monitored as detailed above. Following the test, subjects recovered by cycling for 5 minutes at a self-selected workrate and cadence. Before the time to fatigue test, and at each DL_{CO} measurement, subjects were weighed. Throughout all testing subjects were encouraged to consume fluids to prevent dehydration and shifts in plasma volume.

Pulmonary Diffusion Data Collection

Pulmonary diffusing capacity was determined by the single-breath method of Roughton and Forster (1957) as modified by Ogilvie et al. (1957). The single-breath technique was chosen over a steady-state method because of its ability to represent the true characteristics of the membranes and pulmonary capillary bed of the ventilated parts of a subject's lungs. The steady-state technique requires analysis of arterial PCO_2, where slight errors can lead to large errors in calculating the diffusing capacity for carbon monoxide (Forster et al., 1986). Seated subjects made a maximal inspiration from residual volume of a gas mixture containing 20.9% O_2, 9.7% He, 0.3% CO balanced with N_2. The breath was held for approximately 10 seconds, and then expired. The first litre of expired gas was discarded, and the next 750 mL was considered to be an alveolar sample uncontaminated by dead space gas. Concentrations of CO were measured using an infrared analyzer. For all measurements of DL_{CO} subjects were encouraged to relax against a closed glottis and remain calm during the breath-hold in order to avoid performing a Valsalva or Muller maneuver which could decrease or increase DL_{CO} respectively. Each diffusion measurement was examined to ensure that the inspired volume was always at least 90% of FVC, the total time of inspiration was less than 2 seconds and breath-hold time was between 9 and 11 seconds as determined by the methods of Ogilvie et al. (1957). Measurements were made in duplicate separated by 5 minutes. Both tests were within

3 $mL \cdot min^{-1} \cdot mmHg^{-1}$ or a third test was performed. The average of the two closest values was recorded. The diffusion apparatus was calibrated daily for both volume and carbon monoxide.

Calculation of Diffusing Capacity

Diffusion measurements were calculated automatically by the Collins system using the following equations:

Alveolar Volume (single breath)

$$VA\ (sb) = \frac{He\ insp}{He\ exp} \times VI \times 1.05 \times BTPS$$

VA = alveolar volume

VI = volume inspired

He insp = Fraction of inspired Helium

1.05 = constant

He exp = Fraction of expired Helium

BTPS = body temperature and pressure saturated

Diffusion of the Lung/Alveolar Volume

$$DL/VA = (60/BHT) \times (1000/PB-47) \times Ln\ [He\ exp/CO\ exp] \times (STPD/BTPS)$$

BHT = breath-hold time

Ln = natural logarithm

PB = barometric pressure

CO exp = carbon monoxide expired

STPD = standard temperature and pressure dry

Diffusion of the Lung (single breath)

$$DL\ (sb) = VA\ (sb) \times DL/VA$$

Calculation DM of and Vc

In order to calculate diffusion of the membrane (DM) and pulmonary capillary blood volume (Vc), a second DL_{CO} (DL_{CO} 90% O_2) test was performed similar to the methods of Roughton and Forster (1957) and Ogilvie et al. (1957). Subjects breathed for 5 minutes through a low resistance valve (Hans Rudolph, #2700B) attached to a Douglas bag filled with a gas mixture of approximately 90% O_2, 10% N_2. The DL_{CO} 90% O_2 test was immediately

performed in the same manner as the 21% O_2. The 10 second breath hold was comprised of a gas mixture of 90% O_2, 10% He, and 0.3% CO.

The reciprocal of DL_{CO} ($1/DL_{CO}$), or resistance, is the sum of two resistances: (1) the resistance to diffusion of CO from the alveoli through the alveolar epithelium, basement membrane and capillary endothelium and then through a plasma layer to the surface of the red blood cell (1/DM) and (2) the resistance dependent on the rate of chemical reaction of CO with hemoglobin (θ), and the total volume of red blood cells in the pulmonary capillary bed (Vc). By adding the resistances, an overall relationship is observed:

$$\frac{1}{DL_{CO}} = \frac{1}{DM} + \frac{1}{\theta \cdot Vc}$$

By measuring DL_{CO} at two different inspired O_2 concentrations (DL_{CO} 21% O_2, and DL_{CO} 90% O_2) and plotting each value of $1/DL_{CO}$ against each $1/\theta$, a linear regression line can be formed. The slope of the line estimates 1/Vc, and the Y-intercept represents 1/DM. Each value of $1/\theta$ was calculated as described by Forster et al. (1986) where mean capillary oxygen ($PcapO_2$) tension can be estimated by using the alveolar gas equation assuming a respiratory exchange ratio (RER) of 0.8 and that arterial pressure of carbon dioxide ($PaCO_2$) is equal to an alveolar PCO_2 ($PACO_2$) of 40 mm Hg.

Alveolar Gas Equation

$$PAO_2 = [\, FIO_2 \times (PB - 47)\,] - PACO_2 \left[\, FIO_2 + \left(1 - \frac{FIO2}{RER}\right)\right]$$

FIO_2 = fraction of inspired oxygen

End $PcapO_2$ is typically the same as PAO_2, while mean $PcapO_2$ is approximately 15 mm Hg lower. Therefore, mean $PcapO_2$ is expressed as PAO_2 - 15. Theta, or θ, depends on the number of red cells present or hemoglobin concentration, [Hb] . It is then necessary to take [Hb] into account when calculating $1/\theta$. The calculated value becomes:

$$1/\theta = \frac{0.034 + [\,0.006 \times (P_{AO_2} - 15)\,]}{\frac{[Hb]}{15}}$$

This technique was observed to be highly reliable between test and re-test during preliminary data collection (Appendix D). Pearson product-moment correlations for DL_{CO} $21\%O_2$, DL_{CO} $90\%O_2$, DM and Vc were .98, .96, .84, and .92 respectively.

Statistical Analyses

Data was examined using a 2 (group) by 6 (time) factorial analysis of variance (ANOVA) with repeated measures across time periods. Time effects were analyzed using the Dunnet Test for multiple comparisons to a control group, where post-exercise means were compared to resting values. If a significant interaction occurred, Scheffe's *post-hoc* procedure was applied for further comparison. Student's *t*-tests were used to compare descriptive data. Pearson product-moment correlations were used to determine the relationship between $\%SaO_2min$ and changes in DL_{CO}. The level of significance was set at $P < 0.05$ for all statistical comparisons.

RESULTS

General Data

Subjects in both groups were similar in age and height (Table 1). MT subjects had a higher mean body mass than HT ($t=2.53$, $df=9$, $P=0.0322$). Individual anthropometric data can be found in Tables 13 and 14.

Table 1. Age, height and mass, group data.

GROUP	AGE (yrs)	HEIGHT (cm)	MASS (kg)
HT (N=10)	25.4 (4.8)	178.6 (4.3)	73.6* (4.6)
MT (N=10)	25.8 (2.6)	179.2 (4.7)	81.3 (6.9)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.

* significantly different compared with MT ($P < 0.05$).

Resting pulmonary function data was normal for all subjects (Table 2). Both MT and HT subjects had similar values for FVC, FEV_1, $FEF_{25-75\%}$, FEV_1/FVC, and FEF_{max}. Pulmonary function data for individual subjects can be found in Tables 15 and 16.

Table 2. Pulmonary function, group data.

GROUP	FVC (L)	FEV_1 (L)	$FEF_{25-75\%}$ ($L \cdot sec^{-1}$)	FEV_1/FVC (%)	FEF_{max} ($L \cdot sec^{-1}$)
HT (N=10)	5.81 (.56)	4.78 (.53)	4.75 (1.29)	82.40 6.57	10.60 (1.80)
MT (N=10)	5.63 (.51)	4.78 (.47)	5.00 (.98)	84.91 (4.86)	10.04 (1.77)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.

Maximal Cycle Ergometry

Results from the maximal cycle ergometer test (Table 3) show that absolute maximal $\dot{V}O_2$ was significantly higher in HT (t=4.40, df=9, P=0.0017) as was relative $\dot{V}O_2$max (t=8.89, df=9, P<0.0001). HT subjects achieved a significantly lower %SaO_2min (t=6.27, df=9, P<0.0001), and a higher peak power (t=6.51, df=9, P<0.0001). Maximal heart rate was similar between groups. Using the criteria %SaO_2min ≤ 91% (Powers et al., 1988), 3 of 10 HT subjects exhibited EIH. No MT subjects attained a %SaO_2min that would qualify them as demonstrating EIH. Individual data obtained from the maximal cycle ergometer test is found in Table 17 and 18.

Table 3. Maximal oxygen consumption ($\dot{V}O_2$max), peak power, minimal percentage of arterial oxyhemoglobin saturation (%SaO_2min) and maximal heart rate (HRmax) during maximal cycle ergometer test, group data.

GROUP	$\dot{V}O_2$max ($L \cdot min^{-1}$)	$\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$)	PEAK POWER (watts)	%SaO_2min (%)	HRmax (bpm)
HT (N=10)	4.99*	68.0*	446.5*	91.4*	186.1
	(.31)	(4.9)	(17.3)	(1.6)	(5.3)
MT (N=10)	4.24	51.6	359.6	94.6	189.6
	(.44)	(4.7)	(30.4)	(1.1)	(11.6)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.
* significantly different compared with MT (P < 0.01).

Time to Fatigue Cycle Ergometry

Table 4 shows a comparison between HT and MT subjects during the time to fatigue cycle test. Absolute (t=6.13, df=9, P=0.0002) and relative (t=10.05, df=9, P<0.0001) $\dot{V}O_2$ were higher in HT. $\%SaO_2min$ was significantly lower in HT (t=2.67, df=9, P=0.026). Time to fatigue and maximal heart rate were not different between groups. Individual subject information from the time to fatigue test can be found in Table 19 and 20. $\dot{V}O_2$ values were similar for both groups between maximal cycle ergometry (HT $\dot{V}O_2max$ = 68.0±4.9; MT = 51.6±4.7 $mL \cdot kg^{-1} \cdot min^{-1}$) and time to fatigue cycling (HT $\dot{V}O_2max$ = 68.0±3.9; MT = 50.3±4.4 $mL \cdot kg^{-1} \cdot min^{-1}$). Mean $\%SaO_2min$ was higher for HT during time to fatigue (92.9±1.9) than maximal cycling (91.4 ±1.6). MT $\%SaO_2min$ was similar between both exercise tests (94.6 ±1.1 and 94.8 ±1.1).

Table 4. Maximal oxygen consumption ($\dot{V}O_2max$), time to fatigue, minimal percentage of arterial oxyhemoglobin saturation ($\%SaO_2min$) and maximal heart rate (HRmax) during time to fatigue cycle ergometer test, group data.

GROUP	$\dot{V}O_2max$ ($L \cdot min^{-1}$)	$\dot{V}O_2max$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	PEAK POWER (watts)	TIME (s)	$\%SaO_2min$ (%)	HRmax (bpm)
HT (N=10)	4.89* (.39)	68.0* (3.9)	446.5* (17.3)	113.9 (29.8)	92.9* (1.9)	178.3 (8.9)
MT (N=10)	4.03 (.38)	50.3 (4.4)	359.6* (30.4)	127.6 (25.6)	94.8 (1.1)	183.9 (13.7)

Values are means ± (SD). HT, highly trained endurance athletes; MT, moderately trained.
* significantly different compared with MT ($P < 0.05$).

Pulmonary Diffusing Capacity for Carbon Monoxide

Pulmonary diffusing capacity for carbon monoxide was not significantly different between groups (F=1.507, df=1/18, P=0.2354) nor was there a significant group x time interaction (F=2.068, df=5/90, P=0.0766). A significant time effect was found, indicating that DL_{CO} measures were different between time periods (F=18.495, df=5/90, P<0.0001). DL_{CO} was decreased 1 hr after exercise and attained a minimum value at 6 hrs. The Dunnett test for multiple comparisons was applied to the means across time. DL_{CO} was statistically different from baseline values at 1, 2, 4, 6 (P<0.01) and 24 hours (P<0.05) (Table 5). Figure 1 shows overall values over time. Figure 2 displays group means over time. Individual measures of diffusion can be found in Tables 21 and 22.

Table 5. Pulmonary diffusing capacity for carbon monoxide ($mL \cdot min^{-1} \cdot mmHg^{-1}$) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	34.88 (5.03)	32.21 (4.37)	31.80 (3.80)	31.10 (4.13)	29.78 (4.22)	33.62 (3.65)
MT (N=10)	32.47 (5.50)	29.53 (4.51)	29.00 (4.56)	29.23 (4.41)	29.11 (4.48)	29.97 (5.12)
Mean (± SD)	33.67 (5.27)	30.87* (4.53)	30.40* (4.33)	30.17* (4.27)	29.44* (4.25)	31.79† (4.71)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.
* Significantly different from BASE (P < 0.01). † Significantly different from BASE (P < 0.05)

Figure 1. Overall pulmonary diffusing capacity for carbon monoxide during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.). * significantly different from BASE ($P < 0.01$). † significantly different from BASE ($P < 0.05$)

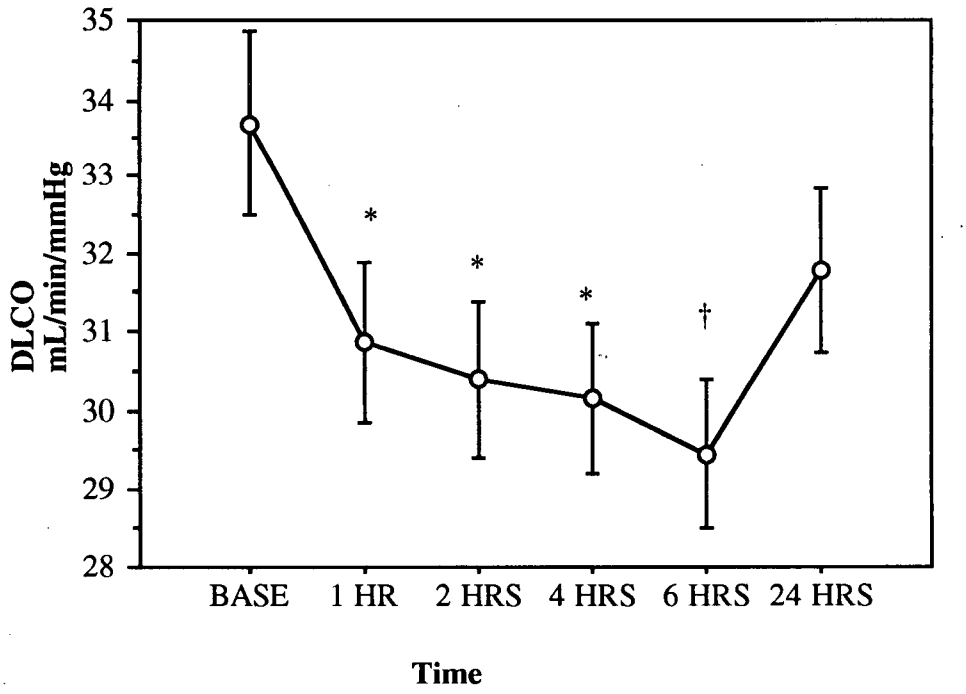
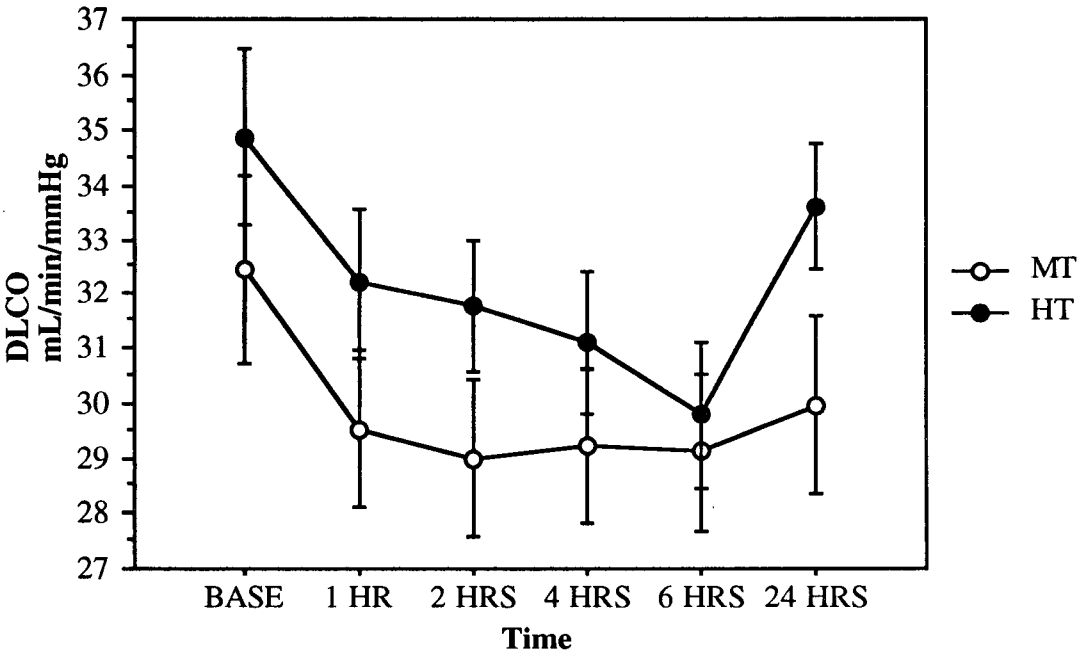


Figure 2. Group pulmonary diffusing capacity for carbon monoxide during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.).



Pulmonary Diffusion Capacity per Alveolar Volume

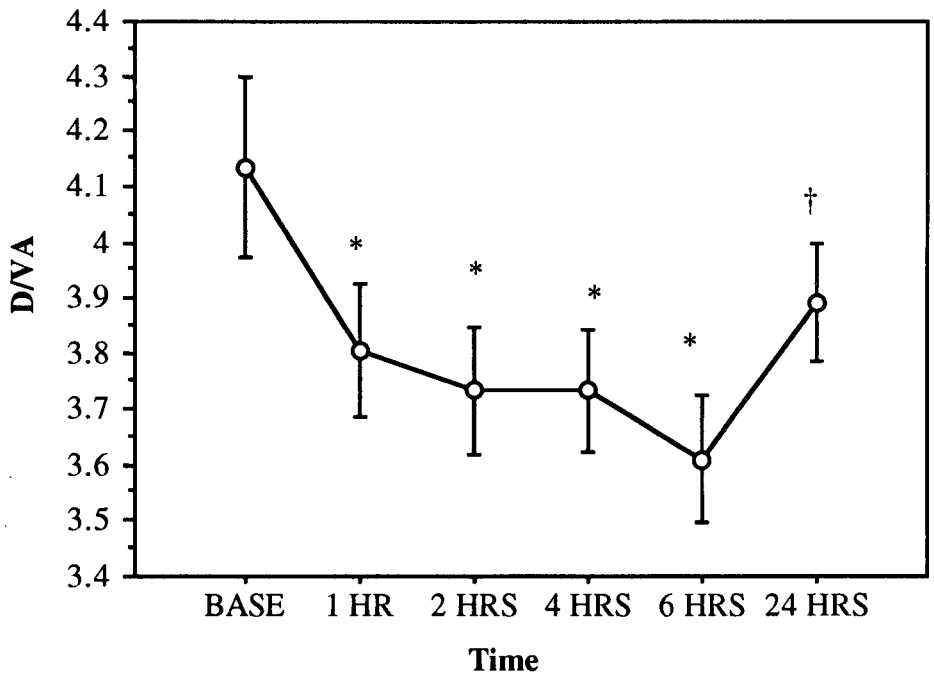
Pulmonary diffusion capacity per alveolar volume (D/VA) was similar to the results of D_{LCO}. D/VA was not different between groups (F=.123, df=1/18, P=.7299) and a group x time interaction was not observed (F=1.044, df=5/90, P=.3967). Means across time were significantly different (F=12.623, df=5/90, P<0.0001). A subsequent Dunnett test for multiple comparisons showed that D/VA was different from baseline at 1, 2, 4, 6 ($P < 0.01$) and 24 hours ($P < 0.05$) (Table 6). Means over time are shown in Figure 3.

Table 6. Pulmonary diffusion capacity per alveolar volume (D/VA) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	4.07 (.84)	3.79 (.63)	3.74 (.60)	3.64 (.51)	3.51 (.53)	3.91 (.44)
MT (N=10)	4.20 (.62)	3.82 (.48)	3.72 (.46)	3.83 (.49)	3.71 (.48)	3.88 (.53)
Mean (± SD)	4.14 (.72)	3.81* (.55)	3.73* (.52)	3.73* (.52)	3.61* (.50)	3.89† (.47)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained. * Significantly different from BASE ($P < 0.01$). † Significantly different from BASE ($P < 0.05$)

Figure 3. Pulmonary diffusion capacity per alveolar volume (D/VA) during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.). * significantly different from BASE ($P < 0.01$). † significantly different from BASE ($P < 0.05$)



Membrane Diffusing Capacity

HT and MT subjects did not differ significantly with regards to membrane diffusing capacity (F=1.778, df=1/18, P=0.1990). It was found that means for DM changed significantly over time (F=3.016, df=5/90, P=0.0146). Further analyses showed that DM was significantly lower at 6 hours post-exercise (43.0 ± 7.3) than while at rest (46.55 ± 7.7) ($P < 0.05$). Overall mean changes are summarized in Table 7. No interaction was detected for group x time (F=.406, df=5/90, P=0.8434). The trend is visually depicted in Figures 4 and 5.

Table 7. Membrane diffusing capacity ($mL \cdot min^{-1} \cdot mmHg^{-1}$) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	48.4 (6.9)	45.2 (6.5)	45.9 (5.3)	46.0 (6.9)	44.0 (7.8)	46.0 (6.9)
MT (N=10)	44.7 (8.4)	41.3 (5.9)	41.5 (7.3)	41.6 (7.4)	41.9 (6.9)	41.6 (8.4)
Mean (± SD)	46.5 (7.7)	43.3 (6.4)	43.8 (6.6)	43.8 (7.3)	43.0* (7.3)	43.9 (7.9)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.
* Significantly different from BASE ($P < 0.05$).

Figure 4. Membrane diffusing capacity (DM) during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.). * Significantly different from BASE ($P < 0.05$).

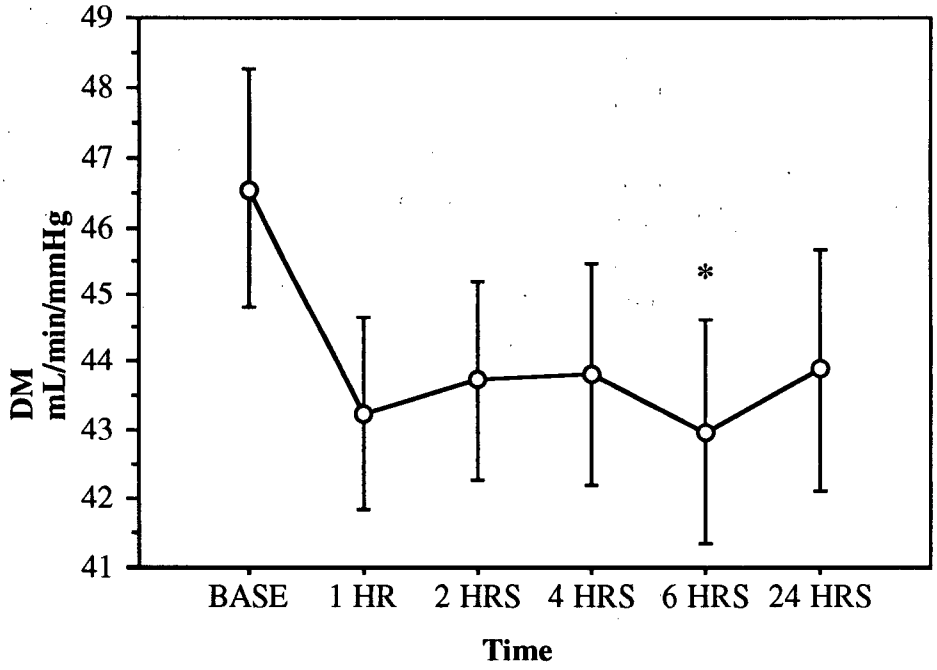
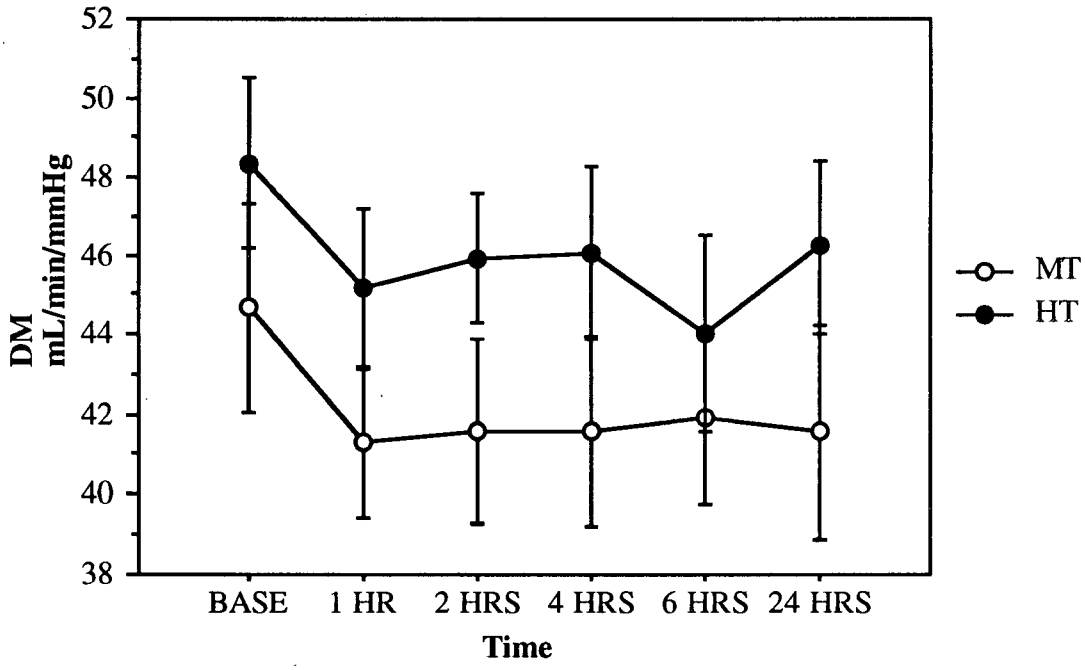


Figure 5. Group membrane diffusing capacity (DM) during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.).



Pulmonary Capillary Blood Volume

A non-significant group effect was observed, indicating that mean Vc values did not differ significantly between HT and MT (F=.570, df=1/18, P=0.4601). Mean Vc averaged over time was different among groups (F=20.601, df=5/90, P<0.0001). At 1, 2, 4, and 6 hours post- time to fatigue cycling Vc was different from resting values (P < 0.01) (Table 8). Figure 6 demonstrates the overall change in Vc over time. Although Vc was lower 24 hrs post-exercise (66±12.0 mL) compared to rest (71.8±14.7 mL), the difference was not statistically significant. A significant group x time interaction (F=3.688, df=5/90, P=0.0044) was detected. The interaction indicates that the groups were heterogeneous over time (Figure 7). Scheffe's procedure was applied and revealed that Vc was significantly different between HT (72.0±10.0) and MT (60.0±11.1) 24 hrs post-exercise (P<0.05).

Table 8. Pulmonary capillary blood volume (Vc) (mL) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	74.6 (14.0)	66.2 (12.8)	61.2 (13.0)	57.4 (10.4)	53.3 (11.0)	72.0 (10.0)
MT (N=10)	69.1 (15.6)	60.8 (15.5)	58.0 (14.7)	56.6 (11.0)	56.9 (12.0)	60.0 (11.1)
Mean (± SD)	71.8 (14.7)	63.5* (14.1)	59.6* (13.6)	57.0* (10.5)	55.1* (11.4)	66.0 (12.0)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained.
* Significantly different from BASE (P < 0.01).

Figure 6. Pulmonary capillary blood volume (Vc) during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.). * Significantly different from BASE ($P < 0.01$).

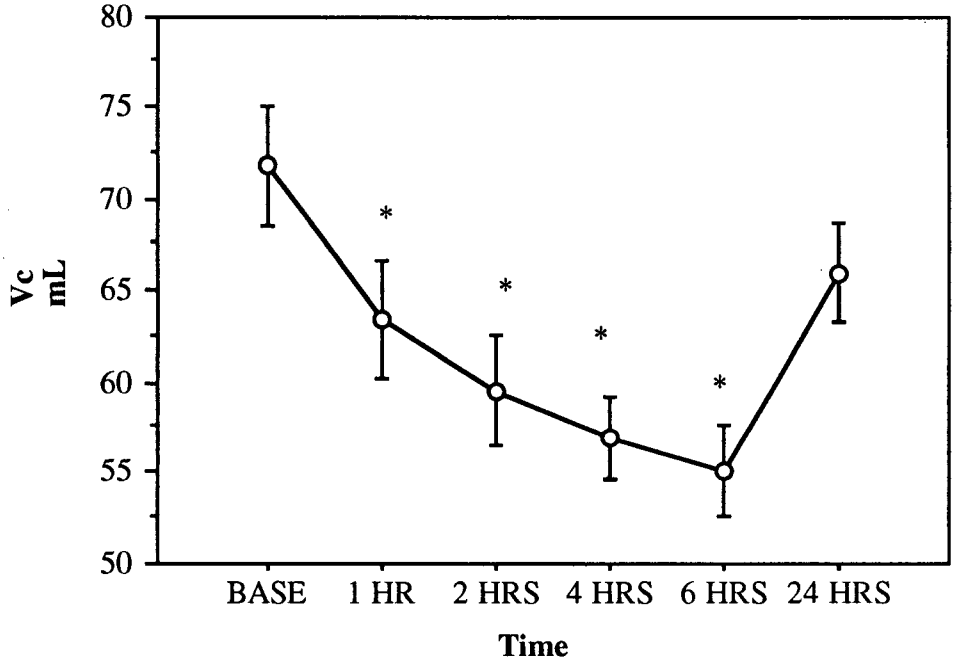
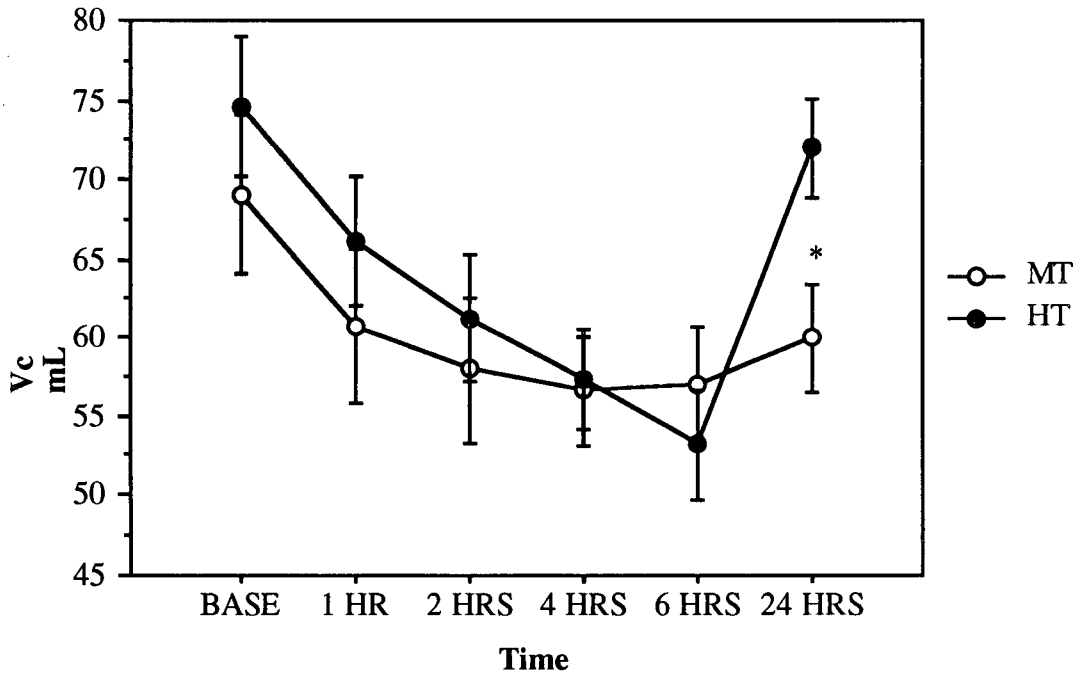


Figure 7. Group pulmonary capillary blood volume (Vc) during rest (BASE) and following time to fatigue cycle ergometry (Mean ± S.E.). * Significantly different between MT and HT ($P < 0.05$).



DL_{CO} 90% O_2

No group effect was observed for pulmonary diffusing capacity for the 90%0_2 mixture (F=.526, df=1/18, P=0.4778). Means were significantly different over time (F=27.967, df=5/90, P<0.0001) (Table 9). DL_{CO} 90% O_2 was significantly lower than baseline at 1, 2, 4 and 6 hours (P<0.01) (Figure 8). A significant time x group interaction was detected (F=2.929, df=5/90, P=0.0170). However, Scheffe's *post-hoc* test failed to detect a significant difference between group means at any of the individual time periods. Figure 9 shows an interaction plot.

Table 9. Pulmonary diffusing capacity for carbon monoxide and 90%O_2 ($mL \cdot min^{-1} \cdot mmHg^{-1}$) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	14.16 (2.24)	12.90 (1.86)	12.19 (1.77)	11.60 (1.74)	11.20 (1.74)	13.97 (1.08)
MT (N=10)	13.53 (2.61)	12.10 (2.70)	11.55 (2.34)	11.57 (1.73)	11.32 (1.92)	12.29 (1.94)
Mean (± SD)	13.84 (2.39)	12.50 (2.29)	11.87 (2.05)	11.58 (1.69)	11.26 (1.79)	13.13 (1.75)

Figure 8. Pulmonary diffusing capacity for carbon monoxide and 90%O_2 (mL·min^{-1}·mmHg^{-1}) during rest (BASE) and following time to fatigue cycle ergometry. * Significantly different from BASE ($P < 0.01$).

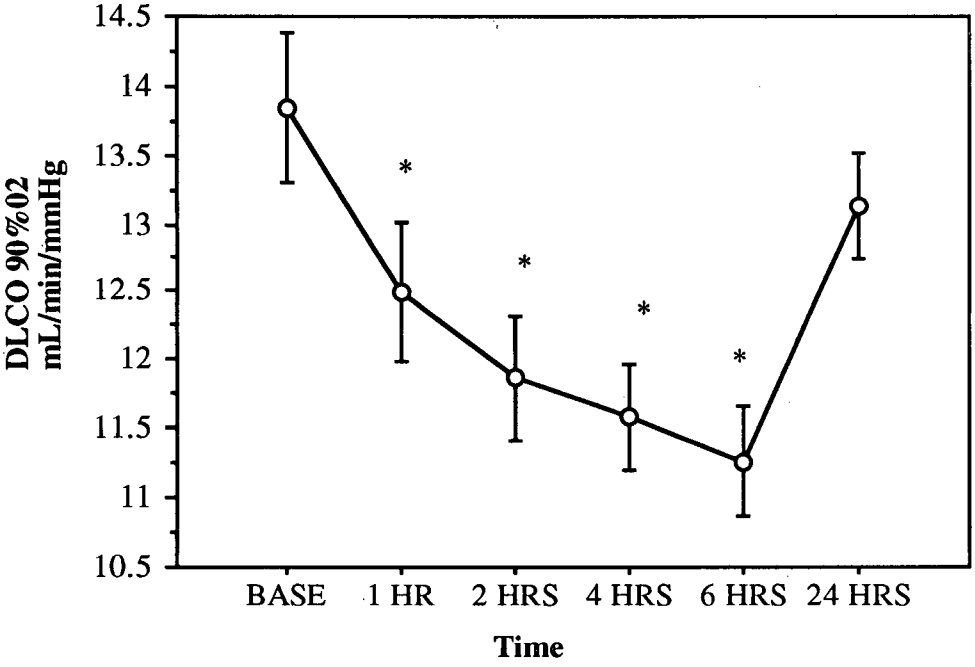
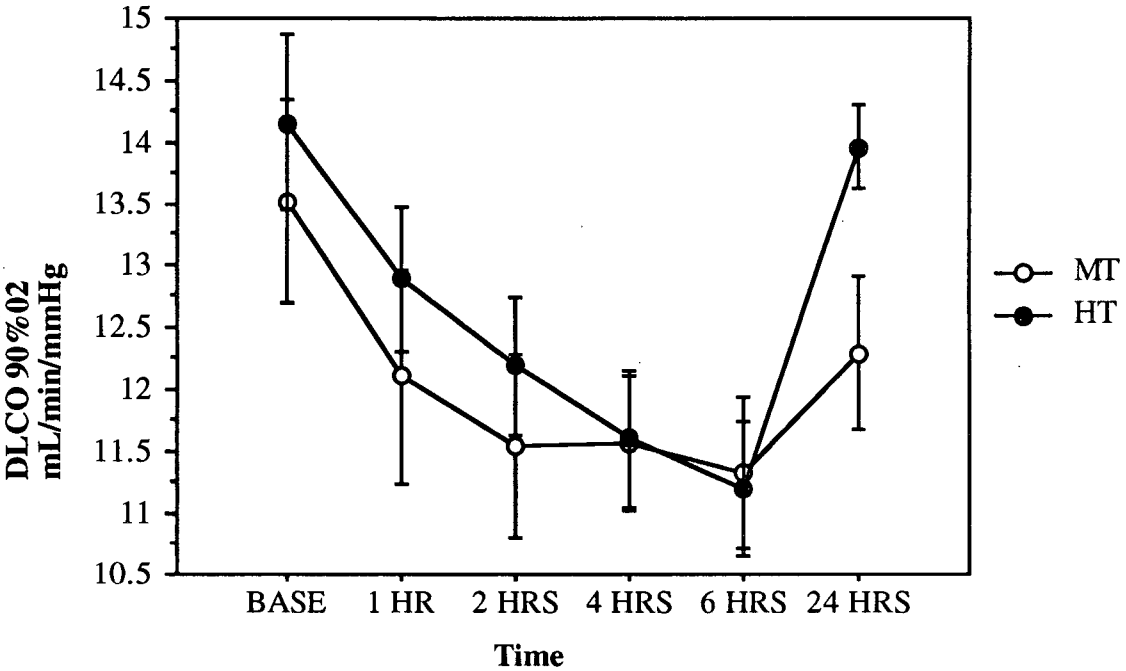


Figure 9. Group pulmonary diffusing capacity for carbon monoxide and 90%O_2 (mL·min^{-1}·mmHg^{-1}) during rest (BASE) and following time to fatigue cycle ergometry.



Alveolar volume, [Hb], and mass.

There were no time, group, or group x time interactions observed for alveolar volume and hemoglobin concentration (Appendix C). Body mass was significantly different between groups (F=6.288, df=1/18, P=0.0220) and over time (F=20.186, df=5/90, P<0.0001). Overall and group means are presented in Table 10. No group x time interaction was found indicating that change in weight over time was similar between groups.

Table 10. Body mass (kg) during rest (BASE) and following time to fatigue cycle ergometry, group data.

GROUP	BASE	1 hr	2 hrs	4 hrs	6 hrs	24 hrs
HT (N=10)	73.3 (4.3)	73.8 (4.0)	73.9 (4.2)	74.5 (4.1)	74.8 (4.3)	74.2 (4.3)
MT (N=10)	80.5 (7.6)	80.6 (7.6)	80.7 (7.5)	81.2 (7.4)	81.2 (7.4)	81.0 (7.2)
Mean (± SD)	76.9 (7.0)	77.2 (6.9)	77.3* (6.9)	77.8† (6.8)	77.8† (6.9)	77.6† (6.7)

Values are means (± SD). HT, highly trained endurance athletes; MT, moderately trained. * Significantly different from BASE ($P < 0.05$). † Significantly different from BASE ($P < 0.01$)

%SaO_2min and DL_{CO}

The greatest change in DL_{CO} (ΔDL_{CO}) observed for each subject was correlated with %SaO_2min achieved during the time to fatigue cycling test (Table 11). HT and MT groups were also analyzed seperately and correlated with ΔDL_{CO} and the lowest obtained (DL_{CO} LO)

Table 11. Correlation Matrix for $\%SaO_2min$ and DL_{CO}.

	ΔDL_{CO}	ΔDL_{CO} LO
Overall $\%SaO_2min$	- 0.335	0.028
MT $\%SaO_2min$	0.038	0.240
HT $\%SaO_2min$	- 0.504	0.094

DISCUSSION

Exercise-induced hypoxemia which occurs in approximately 50% of highly trained male endurance athletes (Powers et al., 1988) can negatively affect $\dot{V}O_2max$ (Lawler et al., 1988; Powers et al., 1989; Martin and O'Kroy, 1993) and exercise performance (Koskolou and McKenzie, 1994). Despite numerous investigations the cause of EIH remains unresolved. The possible mechanisms are: $\dot{V}A/\dot{Q}c$ mismatch, veno-arterial shunts, hypoventilation, shortened pulmonary transit time and pulmonary edema. A diffusion limitation, specifically due to pulmonary edema, may contribute to the hypoxemia observed in elite athletes at sea level (Younes and Burks, 1985; Caillaud et al., 1993; Schaffartzik et al., 1992) and should be reflected in measurements of pulmonary diffusion capacity.

The time course of DL following exercise has previously been described in an attempt to quantify the changes in diffusion (Miles et al., 1983; Rasumussen et al., 1988; Hanel et al., 1994). However, data from these studies have been conflicting, possibly due to varied exercise protocols and a wide range of subject training status. To date it has been unclear if the changes observed in DL are exclusive to elite athletic populations. This study represents the first attempt to examine changes in DL in two separate subject populations based on aerobic capacity.

Exercise Testing

Maximal Cycle Ergometry

Highly trained subjects in the present study attained $\dot{V}O_2max$ values that were comparable to other EIH investigations (Dempsey et al., 1984; Warren et al., 1991) as did moderately trained subjects (Powers et al., 1988). MT subjects had a somewhat high absolute $\dot{V}O_2max$ (4.24 ± 4.4 L·min^{-1}) compared to their relative value (51.6 ± 4.7 mL·kg^{-1}·min^{-1}). This discrepancy may be a reflection of their body composition.

The incidence of EIH in the HT group was 30%. This result is lower than previously reported for endurance athletes (Powers et al., 1988; Powers et al., 1993). The criteria for determining EIH was $\%SaO_2min \leq 91.0\%$ (Powers et al., 1988). This is derived from

findings that healthy, untrained individuals reduce their saturation to ~ 95% during maximal exercise (Astrand and Rodahl, 1986) and that 91% is approximately 1 SD below normal. Mean HT values ($\%SaO_2min = 91.4 \pm 1.6$) are comparable to other hypoxemia studies (Dempsey et al., 1984; Hopkins and McKenzie, 1989). An observed desaturation of 92-93% is severe enough to negatively affect $\dot{V}O_2max$ (Powers et al., 1989). In this study, 9 out of 10 HT subjects had a $\%SaO_2min < 93.0\%$. Six HT subjects ranged in $\%SaO_2min$ from 91.1-93.0%, with 4 of these being less than 92.0%. As with other EIH studies, the range of desaturation responses was varied but decrements below the normal range (95%) were consistently observed in HT subjects.

MT subjects maintained a normal arterial oxygenation ($94.6 \pm 1.1\%$) during the maximal test. None of the MT group demonstrated EIH, which is consistent with the theory that only highly trained athletes develop hypoxemia resulting from exercise (Dempsey et al., 1984; Powers et al., 1988). Peak power output was statistically different between subject groups, emphasizing the difference in training status (MT = 359.6 ± 30.4; HT = 446.5 ± 17.3 watts).

Time to Fatigue Cycle Ergometry

Oxygen consumption was similar between the maximal and the time to fatigue cycling for all subjects. This is in agreement with other reports where exercising at 100% of $\dot{V}O_2max$ workrate for 5 minutes elicits a similar $\dot{V}O_2max$ value as an incremental test to exhaustion (Hopkins and McKenzie, 1989). Subjects in this study cycled, on average, for approximately 2 minutes at the highest workrate (peak power output) achieved during the maximal test. The fatigue test workrate was higher than that at 100% $\dot{V}O_2max$, as oxygen consumption usually plateaus during an incremental test while workrate continues to increase. MT subjects cycled for a slightly longer time than HT subjects, however, the difference was not significant despite peak power output being significantly higher for HT.

Both cycling tests elicited the same $\%SaO_2min$ in the MT group. As expected, HT subjects had a significantly lower $\%SaO_2min$ than MT during the time to fatigue test. HT

subjects achieved a slightly higher %SaO_2min during the time to fatigue (92.9 ± 1.9%) than maximal testing (91.4 ± 1.6%). Ten of 10 HT subjects experienced decrements in %SaO_2, ranging from 89.9 to 95.5, and 20% experienced EIH. Interestingly, the HT group lowered their mean %SaO_2min to the range considered to impair $\dot{V}O_2$max. The discrepancy in %SaO_2min between the maximal and time to fatigue test is possibly related to the rapid onset of metabolic acidosis during the time to fatigue test when compared to the maximal test.

Pulmonary Diffusion Capacity for Carbon Monoxide

It is known that DL_{CO} is reduced following endurance activity (Miles et al., 1983; Manier et al., 1991) and short-term maximal exercise (Rasumussen et al., 1992; Hanel et al., 1994). This study confirms that DL_{CO} is decreased during recovery from short-term maximal exercise. DL_{CO} reached a minimum value at 6 hrs post-exercise and approached baseline at 24 hrs. These findings are in agreement with Rasmussen et al. (1992), where DL_{CO} normalized 20 hrs post exercise. The minimum DL_{CO} observed in the present study was 87% of pre-exercise, comparable to ~ 90% at 6 hrs observed by Hanel et al. (1994). The current study does not support the observation that DL_{CO} remains depressed 2.5 days following short-term exercise (Rasmussen et al., 1988). Other data has indicated that DL_{CO} returns to normal 30 minutes post-exercise (Manier et al., 1993), however subjects were not specifically endurance trained and 3 subjects were smokers making interpretation and comparison of these data difficult.

The most striking DL_{CO} finding is that both groups demonstrated a similar time course of change in DL_{CO}. Despite a lack of statistical significance (P=0.08) it is interesting to note that MT subjects reached their lowest value at 2 hrs, while HT subjects attained their lowest DL_{CO} at 6 hours. Figure 2 demonstrates the group changes over time. These data support the original hypothesis that highly trained endurance athletes experience a decrease in DL_{CO} following maximal exercise. The change in DL_{CO} seen in the MT group was not expected. Changes in DL_{CO} could be due to differences in body size and lung surface area available for diffusion. However, when D/VA was examined the changes were identical to those of DL_{CO}

(Figure 3), indicating that a discrepancy in lung size did not affect the pattern of change between groups.

Elevated blood concentration of carboxyhemoglobin (COHb) impedes the transfer of CO from alveolar gas to pulmonary capillary blood during a D_{LCO} measurement. COHb was not measured in this study. However, Hanel et al. (1994) measured D_{LCO} at similar time periods as this study and found that COHb levels were not at a level that would alter D_{LCO} (Brody and Coburn, 1970). In non-smokers, the effect of blood COHb concentrations are small, so that the effect of COHb on D_{LCO} in these individuals is inconsequential (Mohsenifar and Tashkin, 1979). The changes in D_{LCO} observed in this study were therefore not a result of carbon monoxide back pressure. The technique used in this study to obtain D_{LCO}, DM, and Vc has been found to be highly reliable in preliminary testing (Appendix D).

Pulmonary Capillary Blood Volume

Resting Vc was slightly lower than values previously reported (McNeil, 1958; Miles et al., 1983; Hanel et al., 1994). Mean Vc was decreased 1 hr after cycling in all subjects and reached a minimum value after 6 hrs. At 24 hrs Vc had returned to 92% of resting values, and was not significantly different from baseline. The decrease in Vc corresponded to the changes in D_{LCO}. These results (78% baseline) corroborate those of Hanel et al. (1994) where Vc was 74% of baseline at 6 hrs. Others have found contradicting results where Vc was normalized 1/2 hr post (Manier et al., 1993) 24 hrs post (Miles et al., 1983), and elevated 1/2 hr following exercise (Manier et al., 1991). Twenty-four hours after exercise HT subjects in this study had returned to 97% baseline, while MT were significantly lower at 87% baseline. The degree of change in Vc parallels the changes in D_{LCO} suggesting that the majority of decrease in D_{LCO} can be attributed to a lower capillary blood volume. With less blood flow and volume in the pulmonary capillaries, D_{LCO} would be reduced, as it is perfusion limited.

A reduction in central blood volume following exercise has been previously described using trans-thoracic electrical impedance (Rasumussen et al., 1992; Hanel et al.,1994) and by a decrease in Vc (Hanel et al., 1994). These data are contrary to the findings of Buono et al.

(1983), but are in agreement with the current results. A loss of fluid resulting from exercise could potentially alter the calculation of Vc. Subjects were weighed at each diffusion measurement and no significant reduction was observed. It is not known why a reduction of central blood volume would occur following maximal exercise, but a compensatory shunting mechanism may play a role.

Membrane Diffusion Capacity

Reductions in DM have been observed to persist for 2 hours following exercise (Manier et al., 1991; 1993; Miles et al., 1983). In this study the majority of change in DM occurred within the first hour and reached a statistically significant minimum at 6 hrs ($P < 0.05$). This is slightly different compared to the findings of Hanel et al. (1994) where DM reached it's lowest value 2 hrs after rowing and was restored by 4 hrs. Manier et al. (1991) found that DM decreased 29%. The present study found less of a decrease (8%) similar to a more recent study by Manier et al. (1993). MT and HT subjects did not differ in their DM response over time.

No obvious explanation is available to describe the pattern of change in DM. Stress failure due to high pressures in the pulmonary vasculature may have occurred and allowed the leakage of fluid into the interstitial space. Mean pulmonary arterial pressure and capillary wedge pressures can reach values greater than ~ 40 and 27 torr, respectively (Wagner et al., 1986; Reeves et al., 1988). When pressures develop in this range, the vascular endothelium may be injured allowing the movement of fluid from the vascular space to the interstitium of the lung. This effect has been observed in racehorses who achieve high pulmonary pressures (Jones et al., 1992; West et al., 1993) and in exercising pigs (Schaffartzik et al., 1993). Permeability of the pulmonary capillaries may have also been altered and allowed fluid accumulation, similar to high altitude pulmonary edema (Schoene et al., 1986). A final possibility is that the lymphatic system could not maintain the same fluid clearance rate during the later stages of recovery. It is possible that edema first presented itself as a result of a change to the peribronchial plexus and leaky bronchial venules. A change in DM would occur

later as fluid accumulated in the interstitial space. This hypothesis is consistent with the change in DM seen in the present study.

Normally the pathway for diffusion is short. Several factors exist to increase the distance, or DM: (i) thickening of the alveolar wall, (ii) thickening of the capillary endothelium, (iii) cell layers may be separated by interstitial edema, (iv) intra-alveolar edema, and (v) the intracapillary path may be increased if capillaries contain several red blood cells abreast (Forster et al., 1986). It is not known what degree of edema, or alteration to DM, impairs diffusion during exercise. A small amount of edema present during exercise may cause a decrease in $\%SaO_2min$, as an increase in the above factors, coupled with increased $\dot{Q}$ (i.e. shortened transit time), would present a diffusion limitation and impair diffusion equilibrium. A structural alteration such as pulmonary edema could contribute to a $\dot{V}A/\dot{Q}c$ inequality during exercise and during recovery. However, the time course of recovery of $\dot{V}A/\dot{Q}c$ following exercise is short (~ 20 min) compared to the results of this study (Schaffartzik et al., 1992). A mismatch of $\dot{V}A/\dot{Q}c$ may have played a role in the observed decrements in $\%SaO_2$, but was likely not responsible for the changes seen in diffusion measurments post-exercise.

Pulmonary edema has been implicated as a potential cause of EIH in HT athletes (Younes and Burks, 1985; Wagner et al., 1986; Caillaud et al., 1993). However, data from this study demonstrate a similar change in DM for HT and MT subjects, yet only HT experienced EIH, suggesting that the change in DM was not responsible for decreases in $\%SaO_2$ seen in the HT group. These results are in agreement with those of Hanel et al.(1993), where pulmonary diffusion capacity decreased following mild exercise (60% $\dot{V}O_2max$), making a change in DM, or edema, seem unlikely.

Adaptability of the Pulmonary System

The pulmonary system has traditionally been viewed as ideally designed to regulate ventilation and gas exchange at rest and at high metabolic rates. Dempsey et al. (1985; 1986) propose that the pulmonary system remains unchanged from it's original state despite regular aerobic training. Aerobic training produces increases in aerobic capacity through effects on the

heart, systemic vasculature, and the metabolic capacity of skeletal muscle. As the lung remains unchanged, it can no longer meet the demands of the other adapted systems. The authors further suggest that the pulmonary system may become a limiting factor to oxygen transport and utilization in the highly trained. If this theory is correct, and no training adaptations occur within the lung, then the time course of change in DL should be similar between different groups, regardless of training status. The parallel changes seen in HT and MT D_{LCO} support this theory. The correlation between $\%SaO_2min$ and ΔD_{LCO} was low (r=-0.3) suggesting that the two variables were mildly related and that the change in diffusion capacity was not responsible for the decline in HT $\%SaO_2$. When groups were analyzed seperately, the correlations between variables remained moderate. The current results confirm another low correlation (r=0.3) observed between ΔD_{LCO} and $\Delta \%SaO_2$ (Turner, 1992).

An untrained group ($\dot{V}O_2max < 45$ $mL \cdot kg^{-1} \cdot min^{-1}$) was not examined in this investigation, but may offer a valuable comparison to the two trained groups. Examination of exercise at different metabolic rates may also provide useful information to explain the pattern of change in pulmonary diffusion capacity.

Summary

The results of this study corroborate other findings that pulmonary diffusion capacity is reduced following short-term maximal exercise in highly trained male athletes. These are the first data to indicate that moderately trained and highly trained athletes experience the same changes in DL post-maximal exercise. Diffusion reaches a minimum value 6 hours post exercise and approaches resting values within 24 hrs. Decrements in arterial oxygenation during exercise could not be explained by decreases in DL following exercise. The change in DL appears to be primarily due to a decrease in Vc and partially caused by a decrease in DM. Although this has been observed by other authors, mechanisms responsible for the decrease in Vc post-exercise remain unknown. The change in DM occurred in both MT and HT subjects, indicating a diffusion limitation at the blood-gas barrier, possibly the accumulation of pulmonary edema.

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APPENDIX A
REVIEW OF LITERATURE
EXERCISE-INDUCED HYPOXEMIA

Limitations to Exercise

There are numerous factors which may restrict athletic performance. The traditional view is that oxygen (O_2) delivery to working muscle represents the primary limiting factor to exercise performance, and that the oxygen content of arterial blood is adequate to meet all exercise imposed metabolic demands. Most normal healthy individuals who engage in strenuous activity at sea-level maintain normal blood gas homeostasis for both O_2 and CO_2. Their pulmonary system is able to supply muscle with O_2 and eliminate excess CO_2. In contrast, several authors have challenged the pulmonary system's adequacy by showing decreases in arterial pressure of O_2 (PaO_2) in exercising elite aerobic athletes (Rowell et al., 1964; Dempsey et al., 1984; Powers et al., 1988, 1989; Hopkins & McKenzie, 1989). This phenomenon, exercise-induced arterial hypoxemia (EIH), has been found to occur in 50% of highly trained runners and cyclists and is defined as a 4% decrement in $\%SaO_2$ from resting values (Powers et al., 1988). It is not certain to what extent a decrease in $\%SaO_2$ can negatively affect endurance performance, however a $\%SaO_2$ of 92-93% may affect $\dot{V}O_2max$ (Lawler et al., 1988; Powers et al., 1989; Martin and O'Kroy, 1993) and $\%SaO_2 \leq 90\%$ may impair maximal performance capacity (Koskolou and McKenzie, 1994).

Elite athletes undergo training adaptations in skeletal muscle and the cardiovascular system which may eventually surpass the capabilities of their pulmonary system (Dempsey and Fregosi, 1985). Therefore, the athlete's pulmonary system may become the 'weak link' to maximal exercise capacity. Dempsey et al. (1986) have speculated that this occurs because of the pulmonary system's inability to adapt to training despite many years of aerobic exercise training. If this supposition holds true, then the respiratory system becomes a constraint to maximal exercise performance because of its inability to match the athlete's metabolic requirements brought about by adaptations to other systems.

Mechanisms of Exercise Induced Hypoxemia (EIH)

Despite considerable research efforts the mechanism responsible for EIH remains controversial. Four primary explanations have been discussed in the literature: hypoventilation, veno-arterial shunts, ventilation-perfusion inequalities, and diffusion limitations.

Hypoventilation

Hypoventilation is an alveolar ventilation below the rate metabolically required to maintain arterial blood gases at normal values. Dempsey et al. (1984, 1986) have suggested that a deficient hyperventilatory response during exercise may contribute to EIH in elite athletes by decreasing P_AO_2, thereby reducing the driving force of O_2 transfer across the blood-gas barrier. Minimal compensatory hyperventilation was observed during near maximal exercise in a group whose PaO_2 decreased to approximately 70 torr (Dempsey et al, 1984). Conversely, Hopkins and McKenzie (1989) observed a similar decrease in PaO_2 (~78 torr) with a high alveolar PO_2. Dempsey et al.(1984, 1986) have also proposed that hypoventilation can occur despite the presence of stimuli to increase ventilation, such as increases in arterial carbon dioxide tension ($PaCO_2$), body temperature, blood catecholamines, metabolic acidosis or a decrease in PaO_2. This was supported recently whereby athletes who exhibited EIH had reduced peripheral chemoresponsiveness to hypercapnia (Cooper, 1993). Perrault et al. (1991) examined endurance athletes who desaturated ($\%SaO_2min < 91\%$), and demonstrated that hypoventilation was significantly correlated with those subjects who desaturated. It is necessary to note that an elevated $PaCO_2$ is regarded as the cardinal marker of hypoventilation, while in this study hypoventilation was determined by the ventilatory equivalent for oxygen ($\dot{V}E/\dot{V}O_2$). Caillaud et al. (1993) found reduced P_AO_2 and elevated levels of $PaCO_2$ in highly trained subjects as compared to untrained subjects during maximal exercise. It was concluded that a lack of compensatory hypernea during exercise in the highly trained group was a major factor in the observed decrease in PaO_2. In contrast, Powers et al., (1992) detected a decrease

in $PaCO_2$ during maximal exercise in subjects who developed EIH making hypoventilation seem unlikely. Further study is required to completely examine the role of hypoventilation and the complex ventilatory control mechanisms involved, however the current consensus in the literature is that hypoventilation does not play a significant role in the development of EIH (Powers et al., 1993).

Veno-arterial Shunt

A veno-arterial shunt is an anatomical phenomenon that allows the mixture of venous blood with arterial blood causing a decrease in PaO_2. Early work suggests that fifty percent of the alveolar-arterial difference ($A\text{-}aDO_2$) in resting humans may be explained by veno-arterial shunts (Whipp & Wasserman, 1969; Gledhill et al., 1977) and could possibly account for as much as 49% of the $A\text{-}aDO_2$ during moderate exercise (Asmussen & Nielson, 1960). The role of shunts in the formation of EIH was later investigated by Dempsey et al. (1984) and Powers et al. (1992), who showed that breathing hyperoxic gas (24-26% O_2) at maximal exercise intensities, caused PaO_2 to return to normal levels. If veno-arterial shunts were the cause of EIH, breathing such a gas mixture would have little effect on PaO_2 because of the venous and arterial blood mixture. Based upon these findings, veno-arterial shunts have been ruled out as a major contributor to the formation of EIH.

Ventilation-Perfusion Mismatch

In normal healthy lungs, the ventilation-perfusion ratio ($\dot{V}A/\dot{Q}c$) is reasonably well matched and allows for adequate pulmonary gas exchange at rest and exercise, while an inequality in $\dot{V}A/\dot{Q}c$ hinders pulmonary gas exchange. Dispersion of $\dot{V}A/\dot{Q}c$ can occur when ventilation to an area of the lung is compromised and blood passing by this area does not participate in gas exchange. Blood flow increases at the base of the lung due to gravity while ventilation increases at a slower rate. Consequently, the alveoli at the apex of the lung have little blood flow but are well ventilated, while the base of the lung is well perfused but less well

ventilated. This concept has been related to the development of EIH, where a worsening of this ratio could occur during maximal exercise (Gale et al., 1985; Torre-Bueno et al., 1985; Wagner et al., 1986; Hammond et al., 1986). Data from Hammond et al. (1986), showed that a $\dot{V}A/\dot{Q}c$ mismatch increased with exercise intensity, to an oxygen consumption of approximately 3.5 $L \cdot min^{-1}$. When $\dot{V}O_2$ increased beyond this level no further dispersion of $\dot{V}A/\dot{Q}c$ occurred, yet the A-aDO_2 continued to widen. Most recently, Hopkins et al. (1994) found that $\dot{V}A/\dot{Q}c$ heterogeneity is the most important contributor (>60%) to the A-aDO_2 during high intensity cycle ergometry.

Why an increase in the $\dot{V}A/\dot{Q}c$ ratio occurs during exercise is unclear, but may be caused by non-uniform pulmonary vasoconstriction, reduced gas mixing in the large airways and the development of interstitial pulmonary edema (Schaffartzik et al., 1993). To determine the role of $\dot{V}A/\dot{Q}c$ inequality, Schaffartzik et al. (1992) exercised subjects at near maximal intensities while breathing a hypoxic gas mixture (inspiratory PO_2 = 91 torr). Approximately 50% (N = 7) of subjects developed a significant $\dot{V}A/\dot{Q}c$ mismatch during exercise which persisted for 20 minutes post-exercise. This time frame is beyond the period necessary for the recovery of ventilation and cardiac output, and is indicative of another mechanism. It appears that $\dot{V}A/\dot{Q}c$ inequality accounts for part of EIH but is not solely responsible.

Diffusion Limitations

Veno-arterial shunts and hypoventilation have been excluded as large contributors to EIH, and a $\dot{V}A/\dot{Q}c$ mismatch does not completely explain decreases in PAO_2 seen in high aerobic capacity athletes. By elimination this implies that a diffusion limitation is at least partly responsible for EIH (Powers et al., 1993). By using an exercising horse model, Wagner et al. (1989) suggest that approximately two-thirds of EIH can be related to diffusion limitations. Two possible diffusion limitations have been pursued: increased pulmonary capillary transit time and the accumulation of interstitial pulmonary edema.

Pulmonary Capillary Transit Time

During exercise there are several mechanisms which exist to help maintain adequate pulmonary gas exchange. Pulmonary capillary blood volume (Vc) increases through a 3 fold recruitment of capillaries above resting values. The rise in Vc accommodates exercise related increases in cardiac output and allows for adequate transit time of RBC in the pulmonary capillaries. In normal exercising individuals this is sufficient for diffusion equilibrium to occur. It has been theorized that when elite athletes exercise at high intensities cardiac output may continue to increase, while Vc plateaus because it has reached its anatomical limit (Dempsey et al., 1984; Dempsey and Fregosi, 1985). When pulmonary capillary blood flow continues to increase with exercise intensity, transit time will be compromised and complete diffusion equilibrium may not occur. Under normal conditions the RBC remains in the pulmonary capillary for ~ 0.75 s (Johnson et al., 1960), while during intense exercise transit time has been estimated to be reduced to ~ 0.25 s (West, 1979). When examining highly trained cyclists and runners, Warren et al. (1991) observed that Vc did not plateau, nor did mean transit time fall below 0.46 s despite further increases in exercise intensity. Hopkins (1993) observed that a decrease in PaO_2 during high intensity cycling could be partially explained by shortened pulmonary transit time, but that other factors may contribute more significantly. Although the results of these studies are not definitive, they do suggest that EIH originates elsewhere.

Pulmonary Edema

One of the primary factors which limits the rate of O_2 transfer through the alveolar membrane is the distance between the membrane and the RBC. An increase in this distance would decrease the diffusion capability of the respiratory system. It has been postulated that elite athletes could possibly enlarge the diffusion distance through the formation of interstitial pulmonary edema.

The mechanism for the accumulation of extravascular water remains to be determined, but is likely related to increases in capillary hydrostatic pressure, capillary permeability, capillary surface area or a lymphatic insufficiency (West, 1977). Mean pulmonary arterial pressure and capillary wedge pressures can reach values greater than ~ 40 and 27 torr, respectively (Wagner et al., 1986; Reeves et al., 1988). Stress failure of the pulmonary capillaries at these elevated pressures may cause leakage of fluid and temporary pulmonary edema. When pressures develop in this range, the vascular endothelium may be injured allowing the movement of fluid from the vascular space to the interstitium of the lung. Accumulation of interstitial fluid is usually removed by lymph flow, but highly trained athletes may accumulate more fluid than the lymphatic system can clear. Pulmonary lymph flow has been shown to increase approximately 3 fold in exercising sheep (Coates et al., 1984). A final possibility relates to the distention of the lung capillaries during exercise, where an increased blood volume could increase permeability and promote fluid shifts (Rasmussen et al., 1988). These results, in combination with increased vascular pressures, add to the circumstantial evidence for the accumulation of pulmonary edema.

Transthoracic electrical impedance (TEI) has been used in an attempt to quantify the accumulation of extravascular water. Buono et al. (1983) found that TEI was decreased for 30 minutes following exercise and postulated that this finding was related to the accumulation of lung water. However, data on the training status of the subjects was not reported nor was a measure of arterial oxygenation during exercise making interpretation of their results difficult. The physiological importance of these findings remains unclear because the measurement of TEI is non-specific and can not explain the exact source of hindered impedance. It is important to note that the decrease in TEI may have been due to an increase in thoracic intravascular volume and not interstitial edema. More recent results (Rasmussen et al., 1992) showed that TEI was increased following maximal exercise. These conflicting studies, and the non-specific nature of TEI, demonstrate the limitation of using TEI as a tool to evaluate interstitial pulmonary edema.

Circulating vascular proteins may also act to alter capillary permeability. Histamine has been implicated as a humoral contributor to increased lung water permeability. A significant positive correlation (r=.80) was observed between the increase in percentage of histamine released and the drop in PaO_2 (Anselme et al., 1994). However, it is unknown if increased histamine levels are a response to injury or the cause of decreased arterial oxygenation. The most direct evidence for edema was observed during high-intensity short-term exercise in pigs (Schaffartzik et al., 1993). A higher percentage of pulmonary arteries with perivascular edema was found in exercised than in non-exercised animals. The etiology of pulmonary extravascular fluid accumulation remains unclear, yet indirect evidence shows that some degree of pulmonary edema likely occurs in elite athletic populations following strenuous exercise.

Diffusion Capacity of the Lung

Measurement of the diffusing capacity of the lung (DL) with carbon monoxide (CO) is based on the early work of Krogh (1914), and was later modified by Roughten and Forster (1957) and Ogilvie et al., (1957). The process of diffusion through tissues is governed by Fick's law, where the rate of transfer of gas through a sheet of tissue is proportional to the tissue area and the difference in gas partial pressure between the two sides, and inversely proportional to the tissue thickness. The diffusion capacity from the alveoli to the pulmonary capillary blood is partitioned into two separate components. The membrane diffusing capacity (DM) is the transfer of gas from the alveoli to the RBC, including plasma. Once added to the blood, the combination of gas (O_2 or CO) with Hb is represented by θ, and the amount of blood in the vascular bed (Vc). The total resistance of the lung is represented as:

$$1/DL = 1/DM + 1/\theta \cdot Vc$$

During strenuous exercise, DL increases 2-3 fold due to recruitment of pulmonary capillaries and an increase in cardiac output (Ayers et al., 1975). Paradoxically, several studies have shown that DL_{CO} is significantly reduced following strenuous short-term exercise

(Manier et al., 1993; Rasmussen et al., 1991, 1992) and long-term exhaustive exercise (Miles et al., 1983). These findings are in agreement with Dempsey et al.'s (1984) hypothesis that a diffusion limitation could partially account for a decrease in arterial oxygenation.

If sufficient pulmonary edema accumulates during exercise to cause a decrease in PaO_2, there should be a necessary time period for fluid clearance. During recovery from maximal exercise, relative homeostasis is observed; heart rate and Vc return to normal resting values in a short time (Manier et al., 1993). If a structural alteration were present it would continue to depress DL, despite a return to normal of heart rate and Vc. Early work by Maron et al., (1979) failed to show a change in DL_{CO} following a marathon run. However, these results should be interpreted cautiously, as a significant correlation was observed between the change in DL_{CO} and heart rate at the time of the post-race measurement. An elevated cardiac output, as reflected by a high heart rate, likely caused an overestimation of DL_{CO}. Conversely, others have shown statistically significant decreases in DL_{CO} post-exercise. Miles et al., (1983) using two DL_{CO} measures at different gas mixtures found that DL_{CO} and DM decreased following a marathon race. This occurred despite the return of Vc and heart rate to normal 1-2 hrs post-race. These results were supported by Manier et al., (1991) who measured both DL_{CO} and DL_{NO} (nitric oxide) pre- and post-marathon. Both post-race measures were depressed when compared to pre-race values. Mean DM decreased 29% while Vc had returned to near control values suggesting that the endurance exercise had altered DL. It was concluded that the decreases in DL_{CO} and DL_{NO} were due to a modification in the membrane component of the DL equation.

Table 12 summarizes the results of studies that have measured DL_{CO} pre- and post-exercise. It is interesting to observe the range of data in those investigations which have determined DM and Vc post-exercise, particularly those results of Hanel et al. (1994) which show a decrease in Vc (26%) 6 hours post-exercise compared to baseline values. Reductions in central blood volume, as measured by TEI, were described as the cause of reduced DL_{CO} and Vc. This study also investigated the effects of multiple bouts of exercise on DL_{CO}. A second session of exercise did not influence DL_{CO} or DM beyond values observed following

the first bout, indicating that changes to diffusion capacity had plateaued. To date, only one study has examined changes to diffusion and decreases in arterial oxygenation. Turner (1992) measured DL_{CO} 1 hr post exhaustive exercise in a placebo trial group. A non-significant positive correlation (r = .30) was observed between the change in DL_{CO} and $\%SaO_2min$. The relationship between $\%SaO_2$ and DL following maximal exercise remains to be determined.

Table 12 Change in pulmonary diffusion capacity following exercise.

STUDY	SUBJECTS	Δ DL_{CO}	Δ DM	Δ Vc
Rasmusen et al. (1986)	canoeists	- 6.7% (2.1 hrs)	-	-
Rasmusen et al. (1988)	rowers	- 10.5% (2.5 days)	-	-
Rasmusen et al. (1992)	rowers	- 15% (2-3 hrs)	- -	- -
Hanel et al. (1993)	rowers	- 8% (2 hrs)	-	-
Turner (1992)	cyclists	- 6.8% (1 hr)	-	-
Miles et al. (1983)	marathon runners	- 2% (24 hrs)	- 9% (24 hrs)	baseline (24 hrs)
Manier et al. (1991)	marathon runners	- 10% (.5 hrs)	- 29% (.5 hrs)	+ 10% (.5 hrs)
Manier et al. (1993)	handball players	- 12.9% (.5 hrs)	- 13.3% (.5 hrs)	baseline (.5 hrs)
Hanel et al. (1994)	rowers	- 19% (6 hrs)	baseline (6 hrs)	- 26% (6 hrs)

Δ = percent change compared to baseline values, DL_{CO} = diffusion capacity of the lung for carbon monoxide, DM = membrane diffusing capacity, Vc = capillary blood volume. Time of measurement post exercise shown below reported values.

APPENDIX B
RAW DATA

Table 13 Age, height and mass, individual subject data for moderately trained subjects.

SUBJECT	AGE (yrs)	HEIGHT (cm)	MASS (kg)
MT-01	26	181.0	69.9
MT-02	27	181.2	82.9
MT-03	24	175.0	76.0
MT-04	28	176.6	84.8
MT-05	24	177.4	76.4
MT-06	24	173.4	87.5
MT-07	21	180.1	73.8
MT-08	30	190.4	87.6
MT-09	28	179.0	91.2
MT-10	26	178.3	82.5

Table14 Age, height and mass, individual subject data for highly trained subjects.

SUBJECT	AGE (yrs)	HEIGHT (cm)	MASS (kg)
HT-01	28	174.5	74.0
HT-02	33	177.4	68.8
HT-03	23	180.0	74.1
HT-04	26	174.1	68.4
HT-05	32	180.2	78.3
HT-06	20	182.8	76.1
HT-07	23	182.6	79.4
HT-08	20	170.8	65.3
HT-09	28	180.0	75.3
HT-10	21	184.1	76.2

Table 15 Pulmonary function, individual subject data for moderately trained subjects.

SUBJECT	FVC (L)	FEV_1 (L)	$FEF_{25-75\%}$ ($L \cdot sec^{-1}$)	FEV_1/FVC (%)	FEF_{max} ($L \cdot sec^{-1}$)
MT-01	6.31	4.78	3.61	75.68	12.17
MT-02	5.06	3.96	3.29	78.26	8.13
MT-03	4.99	4.43	5.40	88.87	9.24
MT-04	6.31	5.30	5.40	84.00	10.49
MT-05	5.86	5.29	5.84	90.12	10.42
MT-06	4.97	4.19	4.55	84.32	7.99
MT-07	6.05	5.25	5.23	86.87	9.03
MT-08	5.73	4.80	4.59	83.79	11.41
MT-09	5.51	4.76	5.64	86.69	8.41
MT-10	5.54	5.01	6.41	90.49	13.09

Table 16 Pulmonary function, individual subject data for highly trained subjects.

SUBJECT	FVC (L)	FEV_1 (L)	$FEF_{25-75\%}$ ($L \cdot sec^{-1}$)	FEV_1/FVC (%)	FEF_{max} ($L \cdot sec^{-1}$)
HT-01	6.15	4.88	4.15	79.41	9.97
HT-02	5.53	4.66	4.70	84.25	11.99
HT-03	5.97	5.28	6.38	88.45	14.16
HT-04	5.57	4.22	3.43	75.79	9.66
HT-05	4.67	3.66	2.99	78.41	10.98
HT-06	6.10	4.95	4.47	81.21	10.16
HT-07	5.84	4.65	4.38	79.65	7.49
HT-08	5.39	5.00	6.51	92.82	11.13
HT-09	6.78	4.95	3.95	73.00	11.42
HT-10	6.11	5.56	6.55	91.02	9.04

Table 17 Maximal heart rate (HRmax), maximal oxygen consumption ($\dot{V}O_2max$), peak power and minimal percentage of arterial oxyhemoglobin saturation (%SaO_2min) during maximal cycle ergometer test, individual subject data for moderately trained subjects .

SUBJECT	HRmax (bpm)	$\dot{V}O_2max$ ($L \cdot min^{-1}$)	$\dot{V}O_2max$ ($mL \cdot kg \cdot min^{-1}$)	PEAK POWER (watts)	%SaO_2min (%)
MT-01	190	3.96	56.6	348	94.8
MT-02	197	4.58	55.2	390	92.1
MT-03	174	3.66	48.3	324	93.5
MT-04	215	4.07	48.0	381	94.7
MT-05	183	3.84	50.3	339	95.5
MT-06	190	4.44	43.7	323	94.0
MT-07	186	4.05	54.9	361	94.1
MT-08	184	4.35	49.7	376	93.1
MT-09	198	5.09	55.8	414	94.7
MT-10	179	4.08	49.5	337	95.9

Table 18 Maximal heart rate (HRmax), maximal oxygen consumption ($\dot{V}O_2max$), peak power and minimal percentage of arterial oxyhemoglobin saturation (%SaO_2min) during maximal cycle ergometer test, individual subject data for highly trained subjects .

SUBJECT	HRmax (bpm)	$\dot{V}O_2max$ ($L \cdot min^{-1}$)	$\dot{V}O_2max$ ($mL \cdot kg \cdot min^{-1}$)	PEAK POWER (watts)	%SaO_2min (%)
HT-01	181	5.22	70.5	451	92.9
HT-02	187	4.94	71.8	445	89.4
HT-03	188	4.93	66.5	443	91.9
HT-04	177	4.80	70.2	431	91.6
HT-05	180	4.65	60.1	451	91.8
HT-06	188	4.46	60.3	418	93.5
HT-07	186	5.45	68.6	454	91.0
HT-08	194	4.81	73.7	430	91.4
HT-09	189	5.51	73.2	476	92.7
HT-10	191	4.98	65.4	466	88.3

Table 19 Maximal heart rate (HRmax), maximal oxygen consumption ($\dot{V}O_2max$), time to fatigue and minimal percentage of arterial oxyhemoglobin saturation (%SaO_2min) during time to fatigue cycle ergometer test, individual subject data for moderately trained subjects .

SUBJECT	HRmax (bpm)	$\dot{V}O_2max$ ($L \cdot min^{-1}$)	$\dot{V}O_2max$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	TIME (s)	%SaO_2min (%)
MT-01	189	3.74	55.5	117	95.8
MT-02	189	4.46	55.6	169	92.9
MT-03	177	3.96	53.6	149	95.1
MT-04	208	3.90	46.2	117	93.1
MT-05	185	3.75	49.8	136	95.6
MT-06	188	4.13	46.93	151	94.3
MT-07	178	3.76	51.0	105	95.6
MT-08	159	3.86	43.5	79	94.2
MT-09	196	4.92	54.6	126	94.9
MT-10	170	3.85	46.5	127	96.1

Table 20 Maximal heart rate (HRmax), maximal oxygen consumption ($\dot{V}O_2max$), time to fatigue and minimal percentage of arterial oxyhemoglobin saturation (%SaO_2min) during time to fatigue cycle ergometer test, individual subject data for highly trained subjects .

SUBJECT	HRmax (bpm)	$\dot{V}O_2max$ ($L \cdot min^{-1}$)	$\dot{V}O_2max$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	TIME (s)	%SaO_2min (%)
HT-01	163	4.54	61.9	59	95.5
HT-02	188	5.10	74.7	136	90.2
HT-03	173	4.95	67.6	107	94.8
HT-04	168	4.48	63.7	96	93.6
HT-05	174	5.16	66.5	173	89.8
HT-06	181	4.23	69.4	111	94.7
HT-07	179	5.32	67.8	119	91.8
HT-08	181	4.69	71.6	95	92.9
HT-09	192	5.40	71.4	130	94.4
HT-10	184	4.99	65.3	113	92.0

Table 21 Pulmonary diffusion capacity data pre and post time to fatigue cycle ergometer test, individual subject data for moderately trained subjects.

SUBJECT	TEST	DL_{CO} 21%	DL_{CO} 90%	DM	Vc
MT-01	baseline	39.1	16.02	53.8	85.1
	1 hour	37.67	15.6	51.5	71.4
	2 hours	36.75	14.78	51.2	81.0
	4 hours	35.5	14.03	50.0	77.6
	6 hours	35.86	14.02	50.8	73.1
	24 hours	38.45	14.52	55.8	67.0
MT-02	baseline	28.46	11.15	40.5	52.4
	1 hour	25.57	8.89	39.9	40.0
	2 hours	25.15	10.16	35.0	50.4
	4 hours	28.23	10.58	41.5	46.9
	6 hours	27.18	10.1	40.2	50.1
	24 hours	26.77	11.18	36.5	49.3
MT-03	baseline	31.45	14.49	40.4	81.9
	1 hour	26.54	11.77	34.8	63.6
	2 hours	23.37	11.15	29.5	64.1
	4 hours	22.1	10.22	28.3	53.7
	6 hours	22.43	11.1	27.8	60.8
	24 hours	22.96	10.89	29.0	56.9
MT-04	baseline	36.2	12.4	56.9	54.0
	1 hour	30.72	11.99	43.7	57.0
	2 hours	31.39	10.72	49.5	46.7
	4 hours	32.62	11.33	50.7	49.4
	6 hours	31.86	10.99	49.8	48.1
	24 hours	32.68	11.52	50.2	50.1
MT-05	baseline	36.48	15.95	48.2	80.9
	1 hour	32.2	15.07	41.0	80.8
	2 hours	31.16	13.25	41.9	65.8
	4 hours	31.04	13.64	40.9	69.0
	6 hours	31.31	11.71	45.8	53.3
	24 hours	32.56	14.31	42.9	71.9

MT-06	baseline	23.16	10.91	29.5	57.2
	1 hour	24.11	10.01	33.0	52.4
	2 hours	24.33	10.44	32.6	49.2
	4 hours	23.22	10.32	30.5	54.2
	6 hours	24.79	9.73	35.2	44.7
	24 hours	24.71	10.46	33.4	51.7
MT-07	baseline	24.05	8.82	35.7	45.9
	1 hour	23.56	7.67	38.8	37.5
	2 hours	23.92	6.92	44.7	32.1
	4 hours	25.54	8.42	41.5	39.6
	6 hours	23.88	7.75	39.4	38.1
	24 hours	24.15	8.9	35.8	44.6
MT-08	baseline	34.94	16.88	43.8	90.0
	1 hour	29.84	15.07	36.7	84.9
	2 hours	31.94	14.67	41.1	76.7
	4 hours	30.5	12.61	41.7	57.8
	6 hours	34.11	14.22	46.4	72.0
	24 hours	34.95	13.36	50.3	63.5
MT-09	baseline	35.26	14.5	48.4	73.7
	1 hour	32.51	11.81	48.7	59.5
	2 hours	29.32	11.1	42.6	61.3
	4 hours	30.19	11.86	42.7	63.6
	6 hours	28.82	11.5	40.3	68.7
	24 hours	31.19	13.93	40.7	78.2
MT-10	baseline	35.58	14.16	49.9	69.7
	1 hour	32.61	13.14	45.3	60.8
	2 hours	32.7	12.3	47.7	52.9
	4 hours	33.32	12.67	48.2	54.2
	6 hours	30.84	12.11	43.6	60.4
	24 hours	31.25	13.85	41.0	66.6

DL_{CO} 21% = pulmonary diffusion for 0.3% carbon monoxide, 21%O_2, 10% He, balance N_2 ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DL_{CO} 90% = pulmonary diffusion for 0.3% carbon monoxide, 90%O_2, 10% He ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DM = membrane diffusing capacity ($mL \cdot min^{-1} \cdot mmHg^{-1}$); Vc = pulmonary capillary blood volume (mL).

Table 22 Pulmonary diffusion capacity data pre and post time to fatigue cycle ergometer test, individual subject data for highly trained subjects.

SUBJECT	TEST	DL_{CO} 21%	DL_{CO} 90%	DM	Vc
HT-01	baseline	34.73	13.54	49.4	73.7
	1 hour	31.53	11.94	45.8	54.4
	2 hours	30.94	10.54	48.9	50.1
	4 hours	32.52	10.8	52.6	47.6
	6 hours	30.59	9.14	55.2	38.9
	24 hours	33.69	12.85	48.7	59.2
HT-02	baseline	31.18	12.98	42.3	71.0
	1 hour	27.31	12.47	35.2	74.0
	2 hours	31.15	12.00	44.5	63.5
	4 hours	26.86	11.57	35.7	57.6
	6 hours	26.17	10.83	35.7	50.4
	24 hours	28.92	13.73	36.6	76.8
HT-03	baseline	32.51	12.60	46.5	58.1
	1 hour	31.56	11.92	46.0	55.1
	2 hours	28.40	10.92	40.9	48.3
	4 hours	29.03	10.84	42.7	56.3
	6 hours	28.30	11.93	38.3	60.9
	24 hours	30.42	14.08	39.0	73.9
HT-04	baseline	26.37	9.81	38.9	50.8
	1 hour	23.67	9.51	33.1	48.8
	2 hours	26.22	9.62	39.1	43.9
	4 hours	23.31	7.91	37.1	39.4
	6 hours	20.76	7.96	29.9	35.6
	24 hours	29.23	14.28	36.5	75.5
HT-05	baseline	44.86	18.43	61.6	87.6
	1 hour	38.48	16.68	51.1	83.0
	2 hours	39.52	15.88	55.0	76.6
	4 hours	36.05	14.03	51.3	66.3
	6 hours	33.12	12.6	47.9	60.0
	24 hours	36.93	15.23	50.6	75.1

HT-06	baseline	37.77	14.97	53.0	99.4
	1 hour	35.69	13.98	50.5	84.5
	2 hours	35.75	13.13	53.0	82.5
	4 hours	35.54	13.59	51.2	71.4
	6 hours	35.66	13.27	52.4	68.6
	24 hours	39.33	15.29	55.9	93.3
HT-07	baseline	34.92	14.17	48.4	75.9
	1 hour	32.20	12.26	46.6	60.4
	2 hours	29.87	11.35	43.3	56.2
	4 hours	30.57	11.00	46.2	51.6
	6 hours	30.23	11.10	45.0	52.7
	24 hours	31.74	12.53	44.8	63.1
HT-08	baseline	34.62	14.99	46.0	85.4
	1 hour	35.08	13.92	49.2	78.0
	2 hours	32.68	13.46	44.7	74.5
	4 hours	31.4	12.9	43.0	71.7
	6 hours	33.18	13.49	45.8	66.9
	24 hours	35.96	15.09	48.7	76.0
HT-09	baseline	39.48	15.69	55.5	72.3
	1 hour	35.68	13.64	51.6	58.8
	2 hours	33.56	12.82	48.5	54.9
	4 hours	35.86	12.21	56.9	51.8
	6 hours	31.57	10.92	49.4	48.2
	24 hours	37.41	14.12	54.5	63.1
HT-10	baseline	32.35	14.39	42.4	71.7
	1 hour	30.93	12.65	42.7	64.9
	2 hours	29.91	12.15	41.4	61.6
	4 hours	29.94	11.14	44.1	59.9
	6 hours	28.23	10.73	40.9	50.4
	24 hours	32.52	12.42	47.0	47.0

DL_{CO} 21% = pulmonary diffusion for 0.3% carbon monoxide, 21%O_2, 10% He, balance N_2 ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DL_{CO} 90% = pulmonary diffusion for 0.3% carbon monoxide, 90%O_2, 10% He ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DM = membrane diffusing capacity ($mL \cdot min^{-1} \cdot mmHg^{-1}$); Vc = pulmonary capillary blood volume (mL).

Table 23 Hemoglobin (Hb), mass, alveolar volume (VA), and diffusion/alveolar volume (D/VA) pre- and post- time to fatigue cycle ergometer test, individual subject data for highly trained subjects.

SUBJECT	TEST	Hb ($g \cdot dL^{-1}$)	Weight (kg)	VA (L)	D/VA
HT-01	baseline	13.4	73.3	9.89	3.51
	1 hour	15.7	74.1	9.18	3.44
	2 hours	14.2	74	9.4	3.24
	4 hours	15.1	74.8	9.74	3.34
	6 hours	14.9	74.6	9.69	3.16
	24 hours	15.6	73.3	9.74	3.46
HT-02	baseline	13.6	68.3	8.35	3.73
	1 hour	13.5	70	8.25	3.31
	2 hours	13.4	70	8.39	3.71
	4 hours	15.4	70.5	8.35	3.22
	6 hours	16.0	70	8.32	3.15
	24 hours	15.0	69.9	8.59	3.37
HT-03	baseline	15.8	73.2	8.14	3.99
	1 hour	15.5	73.3	7.9	3.99
	2 hours	16.4	73.4	7.93	3.58
	4 hours	13.7	74.2	7.98	3.64
	6 hours	15.1	74.2	7.86	3.60
	24 hours	15.8	73.9	7.88	3.86
HT-04	baseline	13.8	69.7	7.54	3.5
	1 hour	14.6	69.9	7.55	3.14
	2 hours	15.5	70.1	7.48	3.51
	4 hours	13.6	70.8	7.55	3.09
	6 hours	16.2	70.8	7.31	2.84
	24 hours	16.4	71	6.92	4.23
HT-05	baseline	15.8	77.6	7.13	6.29
	1 hour	15.7	77.9	7.39	5.21
	2 hours	15.3	79	7.54	5.25
	4 hours	15.3	79	7.58	4.76
	6 hours	15.0	79.3	7.59	4.36
	24 hours	15.3	79.4	7.77	4.76

HT-06	baseline	11.0	75.3	9.95	3.80
	1 hour	12.0	75.7	9.67	3.69
	2 hours	11.1	75.5	9.75	3.67
	4 hours	13.6	76.2	9.92	3.58
	6 hours	13.6	76.5	9.71	3.67
	24 hours	11.8	76.8	9.88	3.98
HT-07	baseline	14.0	75.3	9.95	3.80
	1 hour	14.6	75.7	9.67	3.69
	2 hours	14.5	75.5	9.75	3.67
	4 hours	14.8	76.2	9.92	3.58
	6 hours	14.8	76.5	9.71	3.67
	24 hours	14.6	76.8	9.88	3.98
HT-08	baseline	13.6	65.5	7.96	4.35
	1 hour	13.0	65.9	8.12	4.31
	2 hours	13.5	65.9	7.96	4.11
	4 hours	13.4	66.3	7.81	4.02
	6 hours	14.9	66.1	8.07	4.11
	24 hours	15.1	65.9	8.44	4.26
HT-09	baseline	16.1	75.6	11.12	3.55
	1 hour	16.8	76.1	10.89	3.28
	2 hours	16.9	76.7	10.76	3.12
	4 hours	16.0	77.3	10.86	3.30
	6 hours	15.5	77.2	10.66	2.96
	24 hours	16.0	76.1	11.11	3.37
HT-10	baseline	16.1	76.4	8.96	3.61
	1 hour	14.7	76.8	8.88	3.48
	2 hours	14.8	76.7	8.83	3.39
	4 hours	13.2	76.8	8.75	3.42
	6 hours	15.3	76.9	8.78	3.22
	24 hours	14.0	77.3	8.61	3.78

Table 24 Hemoglobin (Hb), mass, alveolar volume (VA), and diffusion/alveolar volume (D/VA) pre- and post- time to fatigue cycle ergometer test, individual subject data for moderately trained subjects.

SUBJECT	TEST	Hb ($g \cdot dL^{-1}$)	Weight (kg)	VA (L)	D/VA
MT-01	baseline	14.1	67.4	9.23	4.23
	1 hour	16.5	67.5	9.24	4.08
	2 hours	13.5	67.6	9.34	3.93
	4 hours	13.2	68	9.11	3.9
	6 hours	13.9	68.1	9.22	3.89
	24 hours	15.3	68.8	9.57	4.02
MT-02	baseline	15.7	80.2	6.73	4.23
	1 hour	15.3	81.1	6.66	3.84
	2 hours	15.2	80.9	6.68	3.76
	4 hours	16.2	81.7	6.71	4.21
	6 hours	14.4	81.1	6.62	4.11
	24 hours	17.5	80.4	6.66	4.02
MT-03	baseline	14.5	73.9	6.64	4.73
	1 hour	14.7	74.1	6.41	4.15
	2 hours	14.7	74.1	6.55	3.57
	4 hours	15.6	74.3	6.29	3.51
	6 hours	15.9	74	6.71	3.35
	24 hours	16.0	74.5	6.63	3.47
MT-04	baseline	15.5	84.5	9.16	3.95
	1 hour	15.3	84.7	8.9	3.45
	2 hours	15.5	84.7	8.76	3.58
	4 hours	15.6	84.8	8.37	3.90
	6 hours	15.5	85	8.58	3.54
	24 hours	15.8	84.9	8.62	3.92
MT-05	baseline	15.5	75.3	8.67	4.21
	1 hour	15.5	75.4	8.53	3.78
	2 hours	15.5	75.4	8.65	3.60
	4 hours	15.6	76	8.54	3.64
	6 hours	15.5	76	8.7	3.60
	24 hours	15.7	75.6	8.58	3.79

MT-06	baseline	16.1	88.0	5.39	4.29
	1 hour	14.6	87.8	5.89	4.09
	2 hours	16.6	87.8	5.84	4.16
	4 hours	15.3	88.1	5.30	4.38
	6 hours	16.0	88.1	5.98	4.15
	24 hours	15.7	87.9	5.57	4.43
MT-07	baseline	13.4	73.8	9.01	2.61
	1 hour	13.4	73.8	9.05	2.71
	2 hours	13.4	74.8	9.16	2.61
	4 hours	14.0	75.8	9.3	2.75
	6 hours	13.3	75.3	9.22	2.59
	24 hours	14.0	75.3	9.18	2.63
MT-08	baseline	16.1	88.8	8.04	4.34
	1 hour	15.9	88.5	8.41	3.55
	2 hours	15.7	88.5	8.5	3.76
	4 hours	16.5	89.4	8.51	3.58
	6 hours	15.0	90.2	8.82	3.87
	24 hours	15.0	88.3	9.04	3.87
MT-09	baseline	14.8	90.1	7.27	4.85
	1 hour	13.8	90.5	7.58	4.29
	2 hours	12.9	90.5	7.4	3.96
	4 hours	13.6	90.6	7.53	4.01
	6 hours	12.3	90.6	7.54	3.82
	24 hours	14.2	90.8	7.5	4.16
MT-10	baseline	14.9	82.8	7.74	4.60
	1 hour	16.0	82.9	7.68	4.25
	2 hours	16.5	82.9	7.67	4.26
	4 hours	16.7	83.2	7.57	4.40
	6 hours	14.6	83.5	7.39	4.17
	24 hours	16.6	83	7.01	4.46

APPENDIX C
STATISTICAL ANALYSES

ANOVA table for DL_{CO} 21% O_2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
TRAINING STATUS	1	165.464	165.464	1.507	.2354
Subject(Group)	18	1975.821	109.768		
TIME	5	224.812	44.962	18.495	<.0001
TIME * TRAINING ST...	5	25.143	5.029	2.068	.0766
TIME * Subject(Group)	90	218.795	2.431		

ANOVA table for DL_{CO} 90% O_2

	DF	Sum of Squares	Mean Square	F-Value	P-Value
TRAINING STATUS	1	11.023	11.023	.526	.4778
Subject(Group)	18	377.559	20.975		
TIME	5	97.210	19.442	27.967	<.0001
TIME * TRAINING ST...	5	10.179	2.036	2.929	.0170
TIME * Subject(Group)	90	62.566	.695		

ANOVA table for D/V_A

	DF	Sum of Squares	Mean Square	F-Value	P-Value
TRAINING STATUS	1	.200	.200	.123	.7299
Subject(Group)	18	29.283	1.627		
Time	5	3.295	.659	12.623	<.0001
Time * TRAINING STA...	5	.273	.055	1.044	.3967
Time * Subject(Group)	90	4.699	.052		

ANOVA table for DM

	DF	Sum of Squares	Mean Square	F-Value	P-Value
TRAINING STATUS	1	445.060	445.060	1.778	.1990
Subject(Group)	18	4504.919	250.273		
TIME	5	161.559	32.312	3.016	.0146
TIME * TRAINING ST...	5	21.761	4.352	.406	.8434
TIME * Subject(Group)	90	964.298	10.714		

ANOVA table for Hb

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Training Status	1	5.504	5.504	.942	.3447
Subject(Group)	18	105.209	5.845		
TIME	5	4.161	.832	1.279	.2801
TIME * Training Status	5	5.679	1.136	1.745	.1324
TIME * Subject(Group)	90	58.584	.651		

ANOVA table for VA

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Training Status	1	18.873	18.873	2.198	.1555
Subject(Group)	18	154.565	8.587		
TIME	5	.095	.019	.478	.7919
TIME * Training Status	5	.245	.049	1.238	.2982
TIME * Subject(Group)	90	3.561	.040		

ANOVA table for Vc

	DF	Sum of Squares	Mean Square	F-Value	P-Value
TRAINING STATUS	1	448.417	448.417	.570	.4601
Subject(Group)	18	14168.266	787.126		
TIME	5	3868.056	773.611	20.601	<.0001
TIME * TRAINING ST...	5	692.392	138.478	3.688	.0044
TIME * Subject(Group)	90	3379.634	37.551		

ANOVA table for Weight

	DF	Sum of Squares	Mean Square	F-Value	P-Value
Training Status	1	1391.964	1391.964	6.288	.0220
Subject(Group)	18	3984.742	221.375		
TIME	5	13.599	2.720	20.186	<.0001
TIME * Training Status	5	.705	.141	1.047	.3952
TIME * Subject(Group)	90	12.127	.135		

APPENDIX D
RELIABILITY DATA

Nine (5 female, 4 male) healthy, non-smoking subjects participated in data collection and repeated the experimental protocol at the same time on separate days. All subjects performed spirometry and diffusion measurements as described in the methods section. A pearson-product moment correlation coefficient was used to obtain the degree of correlation between pulmonary diffusion variables. Values obtained during the diffusion trials are presented in Table 25.

Pearson product-moment correlations between test and re-test measures of pulmonary diffusion data.

Measurement	Correlation
DL_{CO} 21% O_2	r = .98
DL_{CO} 90% O_2	r = .96
DM	r = .84
Vc	r = .92

DL_{CO} 21% O_2 = pulmonary diffusion for 0.3% carbon monoxide, 21%O_2, 10% He, balance N_2; DL_{CO} 90% O_2 = pulmonary diffusion for 0.3% carbon monoxide, 90%O_2, 10% He; DM = membrane diffusing capacity; Vc = pulmonary capillary blood volume.

These correlation values can be considered high, where a high correlation between two trials of a test is an indication of good test reliability. The results suggest that the measurement of DL_{CO} and the calculation of DM and Vc are reliable among non-smoking males and females aged 23-37. Pulmonary capillary blood volume values appear to be low in the present study when compared to other reported values of approximately 90 mL (Warren et al., 1991; Manier et al., 1993; Hanel et al., 1994). However, these studies used an exclusively male, athletic population. The discrepancy seen in Vc values may be a reflection of differences in gender, size and training status. Subjects in this investigation included both males and females, as well as highly trained and moderately trained individuals. The variety of subjects and the high

correlation coefficients emphasizes the reliability of the experimental measurements. In summary, the Collins diffusion system was found to be highly reliable when measuring pulmonary diffusion capacity and calculating DM and Vc.

Table 25 Subject characteristics and pulmonary diffusion capacity measurements.

SUBJECT	AGE (yr)	GENDER	DL_{CO} 21% O_2	DL_{CO} 90% O_2	DM	Vc
1	37	male	28.38	14.38	52.6	82.2
			29.80	15.07	55.3	86.6
2	25	male	32.68	14.95	74.3	77.7
			32.56	13.53	97.9	64.5
3	26	male	38.44	15.93	115.4	76.9
			38.29	16.90	96.2	83.6
4	24	male	39.22	17.47	97.3	85.3
			37.23	16.19	98.2	78.3
5	36	female	19.76	8.98	45.6	46.5
			18.72	8.10	49.7	39.5
6	23	female	25.25	10.67	71.2	52.2
			22.74	9.98	58.0	49.3
7	34	female	22.02	9.33	61.6	45.6
			18.52	8.02	49.6	38.4
8	27	female	24.88	11.92	51.5	63.4
			21.5	9.23	59.3	43.8
9	25	female	23.17	8.68	116.0	37.6
			21.03	8.02	93.4	35.4

Values are from test 1, with test 2 values directly below. DL_{CO} 21% O_2 = pulmonary diffusion for 0.3% carbon monoxide, 21%O_2, 10% He, balance N_2 ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DL_{CO} 90% O_2 = pulmonary diffusion for 0.3% carbon monoxide, 90%O_2, 10% He ($mL \cdot min^{-1} \cdot mmHg^{-1}$); DM = membrane diffusing capacity ($mL \cdot min^{-1} \cdot mmHg^{-1}$); Vc = pulmonary capillary blood volume (mL).