THE ASTHMATIC ATHLETE: METABOLIC AND VENTILATORY RESPONSES DURING EXERCISE WITH AND WITHOUT PRE-EXERCISE MEDICATION

By

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ABSTRACT

To determine whether asthmatic athletes have normal physiological responses to exercise without pre-exercise medication, we studied 17 female and male asthmatic subjects, 9 highly trained (HT) (age = 26.1 ± 5.7 yrs; ht = 173.6 ± 10.5 cm; wt = 66.4 ± 10.8 kg; $\dot{V}O_2max$ = 57.0 ± 4.9 ml·kg^{-1}·min^{-1}), and 8 moderately trained (MT) (age = 24.1 ± 3.1 yrs; ht = 183.1 ± 11.8 cm; wt = 78.6 ± 15.3 kg; $\dot{V}O_2max$ = 51.3 ± 4.8 ml·kg^{-1}·min^{-1}) with exercise-induced asthma (EIA) under 2 randomly assigned experimental conditions: salbutamol (S)(2 puffs = 200 μg) or placebo (PL) was administered via metered-dose inhaler 15 minutes prior to exercise. The exercise task was 4 continuous 5 minute increments on an electronically braked cycle ergometer representing 25, 50, 75, and 90% of the subject's $\dot{V}O_2max$. $\dot{V}O_2$, minute ventilation ($\dot{V}_E$), respiratory exchange ratio (RER), % saturation (SaO_2), and HR were continuously measured during exercise. A venous catheter was inserted in the subject's antecubital vein to allow measurement of blood lactate (La) each minute throughout exercise and recovery. Post-medication, exercise, and recovery measurements of peak expiratory flow rates (PEFR) were made using a Mini-Wright flow meter.

The data failed to show significance ($p > 0.05$) between treatment conditions at any stage of exercise with respect to $\dot{V}O_2$, $\dot{V}_E$, RER, HR, and SaO_2. However, among the HT group the mean HR for the 4 exercise conditions was significantly higher under placebo (151.7 (PL) vs. 147.2 (S): $p = 0.01$). No difference was found in La during exercise or in recovery. Pre-exercise PEFR was significantly higher (582(S) vs. 545 L·sec^{-1}(PL): $p = 0.003$) when pretreatment was salbutamol, but prior to treatment there was no difference between the two pre-exercise PEFR's. Mean PEFR measures for the exercise and recovery conditions were significantly higher (600.1 (S) vs. 569.6 (PL): $p = 0.002$) with the salbutamol treatment. Scheffe's post-hoc comparisons indicated a

significant difference in mean PEFR measures with respect to the two treatments between low intensities (25 % and 50 %) and high intensities (75 % and 90 %) of exercise. There was no difference in the physiological response to exercise between groups based on training status. It was concluded that although salbutamol affects the PEFR, these asthmatic athletes do not have altered metabolic or ventilatory responses during exercise.

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List of Abbreviations &Symbols

α	alpha
(A-a)DO_2	alveolar-arterial difference
(A-a)PO_2	alveolar-arterial partial pressure of oxygen
ANOVA	analysis of variance
β	beta
Ca^{++}	calcium ion
cAMP	cyclic adenosine monophosphate
CNS	central nervous system
EIA	exercise-induced asthma
EIH	exercise-induced hypoxemia
EIh	exercise-induced hyperventilation
FEF_{25-75}	mid-maximal expiratory flow
FEV1	forced expiratory volume in one second
FVC	forced vital capacity
HR	heart rate
HT	highly trained
IOC	International Olympic Commission
La	blood lactate
MMEF	mid-maximal expiratory flow
MT	moderately trained
PEFR	Peak expiratory flow rate

PaO_2	arterial partial pressure of oxygen
$PaCO_2$	arterial partial pressure of carbon dioxide
PC_{20}	concentration of agent that will provoke a 20 % fall in FEV_1
pH_a	arterial pH
RER	respiratory exchange ratio
RMANOVA	repeated-measures analysis of variance
SaO_2	oxygen saturation of arterial hemoglobin
VA/Q	alveolar ventilation-perfusion ratio
$\dot{V}_E$	volume of air expired per minute
$\dot{V}O_2$	rate of oxygen uptake
$\dot{V}O_{2max}$	maximal rate of oxygen uptake

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INTRODUCTION

Exercise-Induced Asthma (EIA) is a reversible airway disease that occurs in almost all individuals with asthma when challenged under appropriate exercise conditions. Among competitive athletes the prevalence of asthma is higher than one would expect; sixty-seven of the 597 (11.2%) athletes competing in the 1984 Olympic games suffered from EIA (67).

The type of exercise performed plays a major role in the severity of bronchoconstriction. Running outdoors is the most asthmogenic followed by treadmill running indoors, cycling, swimming, and walking (2). Intermittent activities such as soccer or baseball are better tolerated than continuous activities such as rowing or cross -country skiing. 5-8 minutes of exercise at an intensity of 60-80 % of predicted maximal oxygen consumption increase the chances of an attack; exercising any longer than this, may diminish the response (59). Exercising in environmental conditions where the air is warmed and humidified can provide a protective effect on the airways (19, 37). Similarly, warm-up exercises and regular aerobic conditioning can attenuate and decrease the incidence of EIA (31, 48). Although many preventative measures can be taken to modify the severity of asthma, pharmacological intervention is oftened required . Inhaled salbutamol (Ventolin®), a β_2- agonist, is a commonly used medication in the prophylactic management of EIA (20, 28). Its powerful bronchodilating effect and β_2 selectivity can virtually abolish bronchospasm when taken 10-15 minutes prior to exercise. The effects of salbutamol on physiological parameters such as pH, arterial gas tensions for oxygen (PaO_2) and carbon dioxide ($PaCO_2$), maximal oxygen consumption

($\dot{V}O_2max$) and minute ventilation ($\dot{V}_E$ max) during exercise have been shown to be minimal in untrained asthmatics (33, 56).

Few studies have looked at the physiological responses of asthmatics to exercise without the use of pre-exercise medication. Physiological parameters such as maximal heart rate (HR), $\dot{V}_E$max, $\dot{V}O_2$max , $PaCO_2$, and PaO_2 have all been shown to be within normal range in asthmatics when free of an attack; any abnormalities seen in these variables have been concluded to be due to the untrained state of the asthmatic subjects tested. For example, higher blood lactates have been reported in asthmatics by several authors (1, 5, 10, 53), but these individuals were untrained and their higher levels could be more representative of their lower fitness level. Conversely, Anderson et al., (1) found asthmatics to have higher plasma lactate (LA) compared to non-asthmatics of similar fitness level exercising at the same oxygen consumption.

Oxyhemoglobin saturation (SaO_2) and arterial oxygen tension (PaO_2) in healthy individuals stay relatively consistant throughout exercise, but approximately 50 % of highly trained (HT) athletes who are free of asthma, exhibit arterial hypoxemia and desaturation of hemoglobin at maximal exercise. This phenomenon known as exercise-induced hypoxemia (EIH), defined as a reduction in SaO_2 of 4% below resting values, is thought to be attributed to two causes: a lower alveolar PO_2 (PAO_2) due to an inadequate ventilatory response to exercise, and secondly, excessive widening of the alveolar-arterial PO_2 difference ($(A\text{-}a)DO_2$)) caused by veno-arterial shunt, ventilation/perfusion (VA/Q) non-uniformity, and diffusion limitations (15, 55). HT athletes are capable of achieving extreme metabolic capacities ($\dot{V}O_2$max values greater than 5.0 $l \cdot min^{-1}$ and cardiac outputs as high as 30-35 $l \cdot min^{-1}$) through physiological adaptations of the cardiovascular

system and oxidative capacities of skeletal muscle. However, the pulmonary system is thought to be the least trainable organ system which may, in turn, limit exercise performance (16). In asthmatics, Anderson et al., (1) found in one subject a significant decrease in arterial oxygen tension during exercise. Therefore, the HT asthmatic athlete, who may experience gas exchange limitations, and experience other abnormalities due to their asthma, may be compromised at maximal exercise. All of the studies addressing the metabolic and ventilatory response of asthmatics to exercise have been conducted on untrained asthmatic subjects. To date, no study has looked at these variables in HT asthmatics. Therefore, the purpose of this study is to examine the metabolic and ventilatory responses to submaximal and maximal exercise in highly trained asthmatic athletes with and without pre-exercise medication.

METHODS

Subjects

Seventeen subjects, 9 highly trained athletes (5 females, 4 males; age = 26.1 ± 5.7 yrs; ht. = 173.6 ± 10.5 cm; wt. = 66.5 ± 10.6 kg; $\dot{V}O_2$ max = 57.2 ± 4.8 ml·kg $^{-1}$·min $^{-1}$), and 8 moderately trained athletes (1 female, 7 males; age = 24.1 ± 3.1 yrs; ht. = 183.1 ± 11.8 cm; wt. = 78.8 ± 15.5 kg; $\dot{V}O_2$ max = 51.2 ± 4.8 ml·kg $^{-1}$·min^{-1}), with EIA participated in this study. Subjects in this study demonstrated mild to moderate airway responsiveness and all but three of the subjects had a history of asthma. Baseline spirometry indicated 6 of the 17 subjects had a FEV_1% of < 80 %. The criteria for inclusion in the study was a positive methacholine challenge test which was defined as a decrease in Forced Expiratory Volume of 20% or greater in one second (FEV_1) at a methacholine concentration of 16.0 mg·ml^{-1} or less ($PC_{20} \leq 16$ mg·ml^{-1}). Subjects were placed into one of the two groups depending on their fitness level; the highly trained group consisted of subjects who had achieved a $\dot{V}O_2$ max ≥ 60 ml·kg $^{-1}$·min^{-1} for males and ≥ 50 ml·kg $^{-1}$ ·min $^{-1}$ for females; all other subjects were placed in the moderately trained group, but had to achieve a minimum $\dot{V}O_2$max ≥ 45 ml·kg^{-1}·min $^{-1}$ for males and ≥ 40 ml·kg $^{-1}$ ·min $^{-1}$ for females. Prior to entering the study, informed consent was obtained. This study was approved by the Clinical Screening Committee for Experimental Involvement of Human Subjects.

Methacholine Challenge Test

This procedure was used to assess the bronchial reactivity of each subject. Before the inhalation test, a baseline FEV_1 was measured using a Medical Graphics Metabolic Cart with 1070 Pulmonary Function Software. Aerosols were administered using a Wright nebulizer attached to a face mask , calibrated to deliver the aerosols at a rate of 0.13 $ml \cdot min^{-1}$. Aerosols were inhaled for periods of 2 minutes followed by 30 and 90 second FEV_1 determinations. After a baseline FEV_1 was established with saline, methacholine was inhaled in doubling concentrations (.125, .25, .5, 1.0, 2.0, 4.0, 8.0, and 16.0 $mg \cdot ml^{-1}$) every 5 minutes (34). FEV_1 was measured every 30 and 90 seconds after each concentration until a fall in FEV_1 of 20 % (PC_{20}), compared to the saline control was achieved. The percentage fall in FEV_1 was calculated from the lowest FEV_1 after each methacholine inhalation and the PC_{20} was determined by using the following equation;

$$PC_{20} = \text{antilog} \left[\log C_1 + \frac{(\log C_2 - \log C_1)(20 - R_1)}{R_2 - R_1} \right]$$

where:

C_1 = second last concentration (< 20% FEV_1fall)
C_2 = last concentration (> 20 % FEV1 fall)
R_1 = % fall FEV1 after C_1
R_2 = % fall FEV1 after C_2

A $PC_{20} \leq 16$ $mg \cdot ml^{-1}$ was chosen as indicative of asthma for this study (41). Prescribed inhaled bronchodilators were withheld for 12 hours prior to the test, however, subjects on inhaled steroids were allowed to continue taking their medication in regular doses.

Maximal Oxygen Uptake test

Prior to this test subjects were permitted to take their pre-exercise asthmatic medication. The maximal oxygen uptake test was performed on an electronically braked Mijnhardt KEM 3 cycle ergometer ramped continuously at 30 watts·min $^{-1}$ until the subject reached volitional fatigue. Oxygen uptake ($\dot{V}O_2$), carbon dioxide ($\dot{V}CO_2$), and minute ventilation ($\dot{V}_E$) were continuously sampled with a Metabolic Measurement Cart (Beckman LB-2 CO_2 Analyzer, and Ametek Oxygen Analyzer S-3A/1), which calculated and reported 15 second averages. Heart rate (HR) was monitored continuously with a Polar Vantage XL™ heart rate monitor set to record HR's in 15 second intervals. A regression equation using workload and oxygen uptake was generated for each subject; from this data the workloads in watts were determined to elicit 25, 50, 75, and 90 % of the subject's $\dot{V}O_2$ max. Attainment of $\dot{V}O_2$max was determined when at least three of the following four criteria were met: (1) a plateau of oxygen consumption with increasing workloads, (2) a respiratory exchange ratio > 1.10, (3) 90 % of predicted maximal HR was achieved, or (4) volitional fatigue.

Experimental Procedures

Subjects performed two randomized exercise tests one week apart, one using pre-exercise salbutamol and the other a pre-exercise placebo. All bronchodilator drugs were withheld for 12 hours prior to each session, while subjects on corticosteroids were allowed to continue taking their medication. Fifteen minutes prior to testing subjects received two puffs from a coded metered-dose inhaler containing either salbutamol (200

μg) or the placebo given in a double blind fashion. Before the start of exercise a 20 gauge venous catheter (kept patent with normal saline and heparin, 1000 units/500ml) was inserted in the subject's antecubital vein and a pre-exercise blood sample (~ 0.5 ml) was withdrawn. Pre - and post-medication Peak Expiratory Flow Rates (PEFR) were measured using a Mini-Wright flow meter. The exercise protocol consisted of a 20 minute cycle on an electronically braked cycle ergometer divided into 4 continuous five minute increments. The workloads, predetermined from the $\dot{V}O_2$max test, were set to elicit 25, 50, 75, and 90 % of the subject's $\dot{V}O_2$max. Respiratory gas exchange variables, $\dot{V}O_2$,$\dot{V}CO_2$, $\dot{V}_E$, and RER, were continuously measured with a Metabolic Cart (Beckman LB-2 CO_2 Analyzer, and Ametek Oxygen Analyzer S-3A/1). The means of the four consecutive 15 second averages in the third minute of each increment were reported. SaO_2 was measured with a Hewlett Packard (47201A) oximeter attached to the subject's ear and secured by a head band. To improve perfusion of blood to the ear, the helix of the ear was rubbed with Finalgon (Boehringer Ingelheim), a vasodilator cream, The ear oximeter, interfaced to an IBM compatible computer, reported SaO_2 in 15 second averages. For the purpose of this study only 1 minute averages of $\dot{V}O_2$,$\dot{V}_E$, HR, RER, and SaO_2 were calculated 3 minutes into each stage of exercise. In the fourth minute of each exercise task the subjects momentarily removed the mouth piece (measuring respiratory gases) and forcibly expired into the peak flow meter , this was followed by a blood sample. PEFR measurements were made 3, 5, 10, and 15 minutes of recovery and blood samples were taken 1, 3, 5, and 10 minutes after the cessation of exercise.

Lactate Analysis

The initial 0.5 ml of blood drawn from the subject was added to 2 ml of chilled perchloric acid (10%). After vortexing, the samples were placed in an ice bath for at least 5 minutes. These samples were centrifuged at 2500 rpm for 10 minutes and the supernatant was collected and split into duplicates before being stored at -70 ° C. The lactate concentrations were measured using a modification of an enzymatic assay commercially available from Sigma Diagnostics®. The samples were allowed to thaw to room temperature before proceeding. The pH of the samples was neutralized by adding 500µL of the sample to 150µL of Tris-OH buffer (pH). After mixing, 20µL of the buffered sample was added to 1ml of the lactate reagent. Samples were incubated for 15 minutes which allowed for colour development. The absorbance of each sample was measured at 540 nm with a UV-160 Spectrophotometer, and the blank, consisting of the lactate reagent alone, and the samples were compared to 10µL of a Lactate Standard Solution (4.44 $m \cdot mol^{-1}$ lactic acid (40 $mg \cdot dL^{-1}$)).

Statistical Analysis

The independent variables were the treatment factor which had two levels; Salbutamol and Placebo, and the exercise condition which had 4 levels for the dependent variables; $\dot{V}O_2$, $\dot{V}_E$, HR, RER, SaO_2; 8 and 9 levels for PEFR and LA, respectively. The 4 levels of the exercise condition consisted of 25 % , 50 %, 75 %, and 90 % of the subject's $\dot{V}O_2max$ and the 9 levels included the resting condition, the 4 exercise conditions, and 1, 3, 5, and 10 minutes into recovery for the dependent variable LA. The

8 levels for the dependent variable PEFR included the four exercise conditions and 3, 5, 10, and 15 minutes into recovery .

All subject comparisons between the 2 treatments for the 7 dependent variables were made by a repeated measures analysis of variance (ANOVA). $\dot{V}O_2$, $\dot{V}_E$, HR, RER, and SaO_2 were statistically analysed with a 2 (Treatment factor) X 4 (Exercise condition) ANOVA with repeated measures on both factors. PEFR and blood lactates were analysed with a 2 X 8 and 2 X 9 repeated measures ANOVA, respectively.

Between and within-group comparisons were also performed by a repeated measures ANOVA to determine any differences between the male and female subjects, males in the HT group from males in the MT group, and the highly trained from the moderately trained group. A post-medication rise in PEFR was expected after the administration of salbutamol, so independent t-tests were conducted on pre- and post-medication measures with a level of significance (α) set at $p < 0.01$. Post hoc comparisons using Tukeys HSD and Scheffe's method were performed on significant main effects and significant interaction effects, respectively. The level of significance (α) was set at a $p < 0.05$ for all of the analyses of variance comparisons. All statistical analyses were performed using Systat software (5.0 version, Systat, Inc.)

RESULTS

Mean values for the physical characteristics of the highly trained and moderately trained subjects are presented in Table 1 .

Table 1. Physical Characteristics (mean ± SD , range)

Subjects		Highly trained	Moderately trained
SEX		5 females, 4 males	1 female, 7 males
AGE	(years)	26.1 ± 5.7 (19-35)	24 .1 ± 3.1 (21-31)
HEIGHT	(cm)	174.0 ± 10.5 (162-190)	183.1± 11.8 (161-200)
WEIGHT	(Kg)	66.4 ± 10.8 (51-85)	78.6 ± 15.3 (49-94)
$\dot{V}O_2max$	($ml \cdot Kg \cdot min^{-1}$)	57.0 ± 4.9 (50-63)	51.3 ± 4.8 (45-57)*
PC_{20}	($mg \cdot ml^{-1}$)	7.2 ±5.8 (0.7-15.8)	7.6 ± 5.0 (0.8-15.9)

* $P < 0.05$

All subjects passed the baseline criteria of a positive methacholine($PC_{20} \leq 16.0$ $mg \cdot ml^{-1}$) with a mean PC_{20} of 7.2 ± 5.8 $mg \cdot ml^{-1}$ for the highly trained group and 7.6 ± 5.0 $mg \cdot ml^{-1}$ for the moderately trained group. There was a statistically significant difference in mean $\dot{V}O_2max$ values between the highly trained and moderately trained groups (57.0 ± 4.9 vs. 51.3 ± 4.8; p = 0.002) and male and female subjects (55.5 ± 6.0 vs. 52.3 ± 4.4; p = 0.007). Although the duration of the experimental test varied for each subject, there was no statistical difference in duration of the exercise protocol between the placebo and salbutamol.

Analysis of variance performed on all subjects revealed no significant difference in the pretreatment with either salbutamol or placebo at any stage of exercise with respect to $\dot{V}O_2$, $\dot{V}_E$, HR, RER, SaO_2, and LA. The group means and standard deviations are shown in Tables 2 and 5.

Table 2. $\dot{V}O_2$, $\dot{V}_E$, HR, RER, andSaO_2 of all subjects (n = 17), group data

	Salbutamol				Placebo			
Variables	25%	50%	75%	90%	25%	50%	75%	90%
VO_2 l/min	1.17± .23	1.98 ± .39	3.09 ± .63	3.70 ± .81	1.16 ± .26	2.03 ± .49	3.14 ± .65	3.74 ± .76
VE btps	31.3 ± 5.6	51.8 ± 9.0	92.9 ± 19.6	131.8 ± 30.2	31.6 ± 4.8	52.9 ± 10.8	93.8 ± 20.8	135.7 ± 32.2
HR bpm	104.5 ± 10.0	134.4 ± 11.8	169.0 ± 9.5	183.9 ± 7.3	103.7 ± 10.9	135.6 ± 12.9	171.6 ± 10.1	186.7 ± 6.5
RER	0.80 ± .06	0.88 ± .08	0.99 ± .08	1.05 ± .09	0.81 ± .06	0.87 ± .06	0.99 ± .06	1.05 ± .07
SaO2	96.9 ± 1.4	96.7 ± 1.0	95.8 ± 0.8	94.6 ± 1.5	96.9 ± 0.6	96.5 ± 0.7	95.5 ± 0.9	94.7 ± 1.5

Pre-exercise PEFR was significantly higher (582 vs. 545 $l \cdot sec^{-1}$: p = 0.003) when the pretreatment condition was salbutamol, but prior to treatment there was no difference between the two PEFR's. PEFR increased significantly over the course of exercise for all subjects, and averaged over the exercise and recovery conditions was significantly higher with the salbutamol treatment (600.1 vs. 569.6: p = 0.002) than the placebo. The significant drug by exercise condition interaction (p = 0.001) indicates, with respect to the 2 treatments, a different pattern of change in PEFR measures over exercise and the recovery conditions. Post hoc pairwise comparisons using Scheffe's test revealed a significant difference between PEFR measures at low intensities (25 % and 50 %) with high intensities (75% and 90 %) of exercise and differences in the first two recovery

conditions (3 and 5 min.) with the last two (10 and 15 min.). There was a larger difference in the two treatments at lower intensities and not at the higher intensities of exercise and a greater difference 10-15 minutes as opposed to 3-5 minutes of recovery (Figure 1).

Comparisons made between the HT and MT groups indicated no significant difference at any stage of the experimental protocol between the two groups with respect to $\dot{V}O_2$, $\dot{V}_E$, HR, RER, SaO_2, and LA (Tables 3-6).

Table 3. $\dot{V}O_2$, $\dot{V}_E$, HR, RER, and SaO_2 of highly trained (n= 9), group data

	Salbutamol				Placebo			
Variables	25%	50%	75%	90%	25%	50%	75%	90%
VO2 L/min	1.08 ± 0.21	1.91 ± 0.38	2.98 ± 0.61	3.48 ± 0.66	1.06 ± 0.26	2.00 ± 0.59	3.08 ± 0.71	3.57 ± 0.77
VE btps	30.2 ± 6.1	51.0 ± 8.7	95.3 ± 21.4	132.5 ± 30.1	29.8 ± 4.3	52.5 ± 11.9	98.5 ± 22.2	139.4 ± 35.2
HR bpm	104.1 ± 8.9	133.8 ± 11.1	168.4 ± 10.2	182.4 ± 8.2	104.3 ± 7.9	139.8 ± 11.0	175.8 ± 9.3	186.7 ± 7.6
RER	0.79 ± 0.05	0.87 ± 0.06	1.00 ± 0.06	1.05 ± 0.08	0.81 ± 0.06	0.86 ± 0.06	1.00 ± 0.06	1.05 ± 0.08
SaO_2	97.1 ± 1.7	96.6 ± 1.3	95.7 ± 1.0	93.9 ± 1.2	97.0 ± 0.7	96.4 ± 0.8	95.2 ± 0.8	94.2 ± 0.9

Table 4. $\dot{V}O_2$,$\dot{V}_E$, HR, RER, and SaO_2 of moderately trained (n = 8), group data

	Salbutamol				Placebo			
Variables	25%	50%	75%	90%	25%	50%	75%	90%
VO2 L/min	1.27 ± 0.21	2.06 ± 0.41	3.21 ± 0.67	3.96 ± 0.92	1.28 ± 0.21	2.08 ± 0.39	3.21 ± 0.61	3.91 ± 0.75
VE btps	32.6 ± 5.0	52.6 ± 9.8	90.2 ± 18.5	130.9 ± 32.3	33.6 ± 4.8	53.3 ± 10.1	88.5 ± 19.2	131.5 ± 30.1
HR bpm	104.9 ± 11.7	135.2 ± 13.2	169.7 ± 9.3	185.7 ± 6.2	103.0 ± 14.1	130.9 ± 14.0	166.9 ± 9.2	186.7 ± 5.6
RER	0.82 ± 0.07	0.89 ± 0.09	0.98 ± 0.10	1.04 ± 0.10	0.80 ± 0.06	0.88 ± 0.06	0.97 ± 0.06	1.05 ± 0.07
SaO_2	96.5 ± 1.0	96.6 ± 0.5	95.8 ± 0.7	94.7 ± 1.0	97.1 ± 0.8	96.8 ± 0.5	95.9 ± 0.9	95.1 ± 1.6

However, among the HT group the mean HR averaged over the 4 exercise conditions was significantly higher under the placebo condition (147.2 (S) vs. 151.7 (PL) bpm: $p = 0.01$). The significant drug by exercise condition interaction ($p = 0.002$) demonstrates a greater change in HR under the placebo treatment than the salbutamol for the same level of exercise (Figure 6). A Tukey's post hoc analysis indicated significance between the two treatments only at a workload of 75 % $\dot{V}O_2max$ (168.4 (S) vs. 176.8 (PL) bpm: $p < 0.05$) .

Table 5. Lactate ($mmol \cdot l^{-1}$) of all subjects, highly trained and moderately trained, group data

LACTATE ($mmol \cdot l^{-1}$)	n = 17		n = 9		n = 8	
CONDITION	Salbutamol	Placebo	HT-Salb.	HT-Placebo	MT- Salb.	MT- PL
REST	0.8 ± 0.5	0.9 ± 0.3	0.9 ± 0.6	1.0 ± 0.3	0.8 ± 0.5	0.8 ± 0.4
25 % VO_2max	1.1 ± 0.8	1.2 ± 0.6	1.0 ± 0.8	1.1 ± 0.4	1.3 ± 0.9	1.3 ± 0.7
50 % VO_2max	1.5 ± 0.6	1.6 ± 0.7	1.6 ± 0.7	1.5 ± 0.4	1.4 ± 0.5	1.7 ± 0.9
75 % VO_2max	5.7 ± 2.4	5.4 ± 2.2	6.0 ± 2.6	6.4 ± 1.9	5.3 ± 2.3	4.3 ± 2.0
90 % VO_2max	10.3 ± 3.9	11.1 ± 4.0	10.6 ± 4.4	12.5 ± 4.2	10.0 ± 3.4	9.6 ± 3.4
1 min Post Ex.	11.1 ± 4.0	11.2 ± 3.7	11.6 ± 4.9	12.5 ± 3.5	10.5 ± 2.9	9.7 ± 3.5
3 min Post Ex.	10.7 ± 3.7	10.7 ± 3.6	11.7 ± 4.7	11.4 ± 3.2	9.6 ± 2.3	9.8 ± 4.1
5 min Post Ex.	9.8 ±4.1	10.4 ± 3.6	10.6 ± 5.8	10.8 ± 3.8	9.2 ± 2.8	9.9 ± 3.6
10 min Post Ex.	8.2 ± 4.2	8.3 ± 3.6	8.8 ± 5.1	9.1 ± 3.3	7.7 ± 3.2	7.4 ± 3.9

Analysis of subjects within the HT group revealed significantly higher mean PEFR values (569.3 vs. 539.3: $p = 0.009$) with the pretreatment of salbutamol (Figure 2) However, among the MT group no difference was found in PEFR at any stage of exercise or recovery between the two experimental conditions (Figure 3). The means and standard

deviations for PEFR measures for all groups are presented in Table 6 and illustrated in graphical format in Figures 1- 4. Between-group analysis of variance revealed no significant difference in mean PEFR values between the two groups based on training status

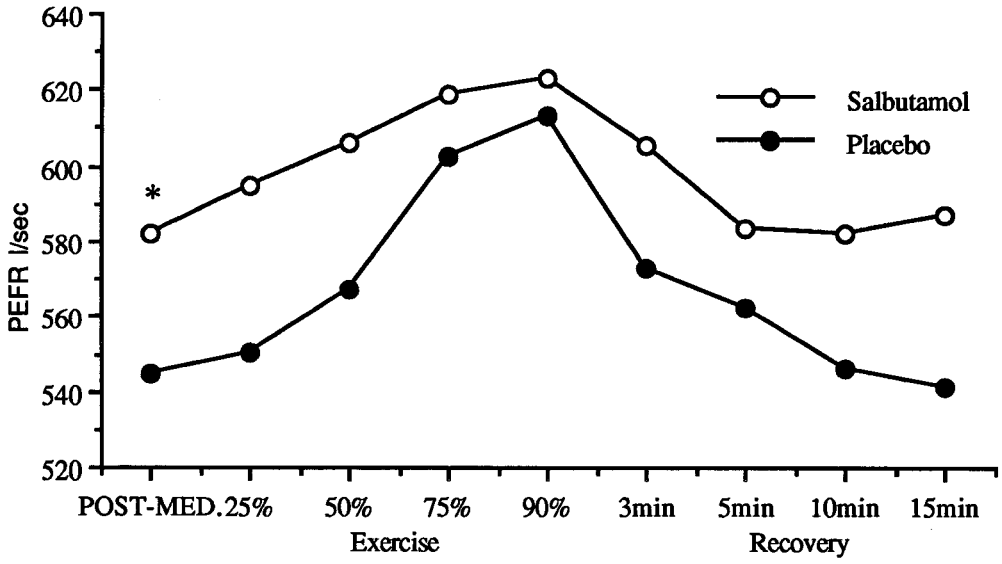
Table 6. PEFR ($l \cdot sec^{-1}$) of all subjects, highly trained and moderately trained, group data

PEFR $l \cdot sec^{-1}$	n = 17		n = 9		n = 8	
CONDITION	**Salbutamol**	**Placebo**	**HT-Salb.**	**HT-Placebo**	**MT- Salb.**	**MT- PL**
PRE-MED	563.8 ± 102.1	555.9 ± 96.1	528.9 ± 103.8	527.0 ± 92.4	603.0 ± 90.6	588.5 ± 95.1
POST-MED	581.8 ± 100.4	545 ± 94.8	551.6 ± 98.6	522.8 ± 88.9	615.8 ± 97.0	570.0 ± 100.8
25 % VO2max	595.0 ± 98.2	550.6 ± 101.7	565.0 ± 92.8	513.3 ± 88.9	628.8 ± 98.8	592.5 ± 103.9
50 % VO2max	605.9 ± 96.4	567.7 ± 103.5	575.6 ± 88.7	536.1 ± 97.9	640.0 ± 98.6	603.1 ± 103.9
75 % VO2max	618.5 ± 101.1	602.9 ± 103.0	589.4 ± 93.0	571.7 ± 105.8	651.3 ± 105.6	638.1 ± 93.7
90 % VO2max	622.9 ± 108.3	612.9 ± 101.9	591.1 ± 99.5	572.8 ± 87.5	658.8 ± 112.9	658.1 ± 102.9
3min Post Ex.	605.6 ± 103.2	572.9 ± 108.2	572.8 ± 100.4	550.6 ± 105.4	642.5 ± 99.4	598.1 ± 112.7
5min Post Ex.	583.5 ± 92.0	562.1 ± 103.1	561.7 ± 89.7	540.0 ± 95.6	608.1 ± 94.0	586.9 ± 111.8
10min Post Ex.	582.4 ± 91.0	546.5 ± 103.1	556.1 ± 86.3	521.1 ± 92.9	611.9 ± 92.3	575.0 ± 112.6
15min Post Ex.	587.1 ± 103.3	540.9 ± 97.5	560.6 ± 97.5	526.1 ± 97.5	616.9 ± 107.8	557.5 ± 101.2

Comparing male and female subjects, males had significantly higher mean $\dot{V}O_2$ (2.79 vs. 1.97 $l \cdot min^{-1}$: p = 0.000), $\dot{V}_E$ (84.2 vs 65.9 l : p = 0.008) values, but there were no differences in HR, RER, SaO_2, and blood lactate. Male subjects did have statistically higher PEFR values than female subjects. Comparisons made between males in the HT group with males in the MT group revealed no differences with respect to any of the variables measured.

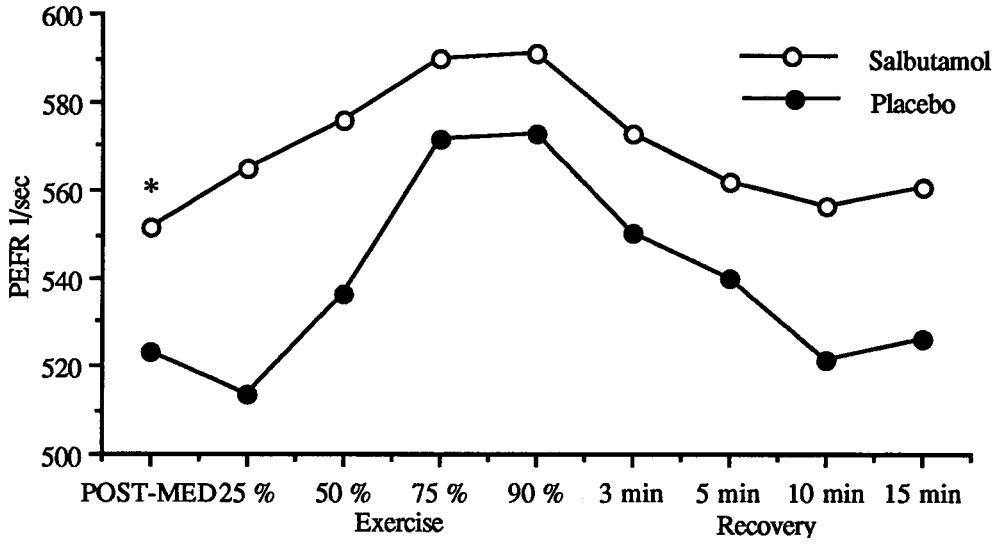
Statistical analysis performed on data of those subjects with a PC_{20} < 4.0 $mg \cdot ml^{-1}$ (n = 6) showed no significant main drug effect with respect to HR, $\dot{V}O_2$, $\dot{V}_E$, RER, SaO_2, or lactate. Although not significantly different (p = 0.058), $\dot{V}O_2$ was higher when pretreatment was the placebo. PEFR (559.3 vs. 506.5: p = 0.03) averaged over the exercise and recovery conditions for this group was significantly higher with salbutamol (Figure 4). Post hoc comparisons were performed on the significant drug by exercise condition interaction (p = 0.047). Figure 1. illustrates the larger differences in PEFR measures under the two treatments at the lower intensities as compared to little difference at higher intensities. For all subject groups tested, the greatest mean difference in PEFR measures between the two treatments was seen in the more severe asthmatic subjects 10-15 minutes post-exercise.

Figure 1. PEFR (l ·sec $^{-1}$) measures under salbutamol and placebo conditions at various exercise intensities (% $\dot{V}O_2$max) and 3 to 15 minutes into recovery, all subjects data (n = 17)



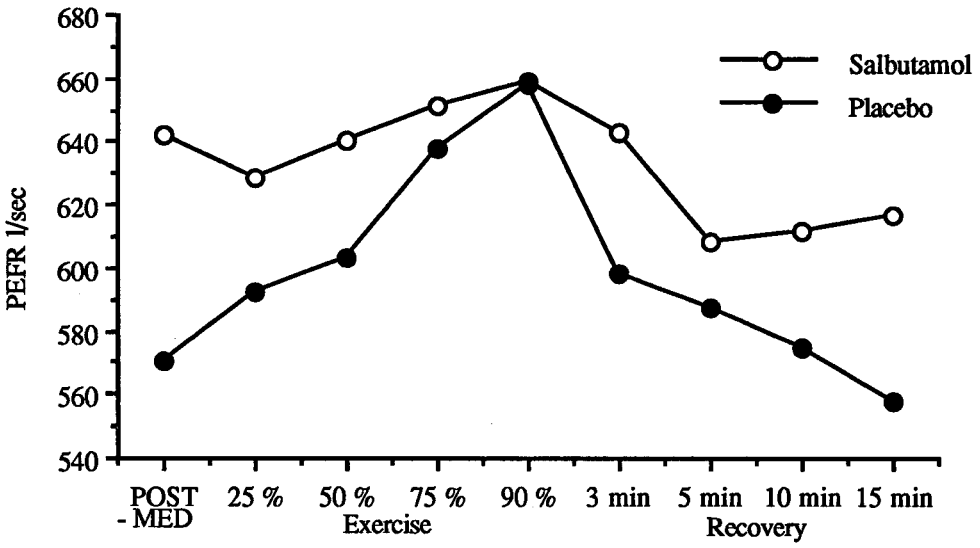
Mean values plotted; open circles, salbutamol; closed circles, placebo. The overall mean PEFR measures were statistically higher with salbutamol: $p = 0.002$. Post-medication PEFR values were statistically higher with salbutamol (* $p < 0.05$).

Figure 2. PEFR ($l \cdot sec^{-1}$) measures at various exercise intensities (% $\dot{V}O_2$ max) and 3 to 15 minutes into recovery, HT group data (n = 9)



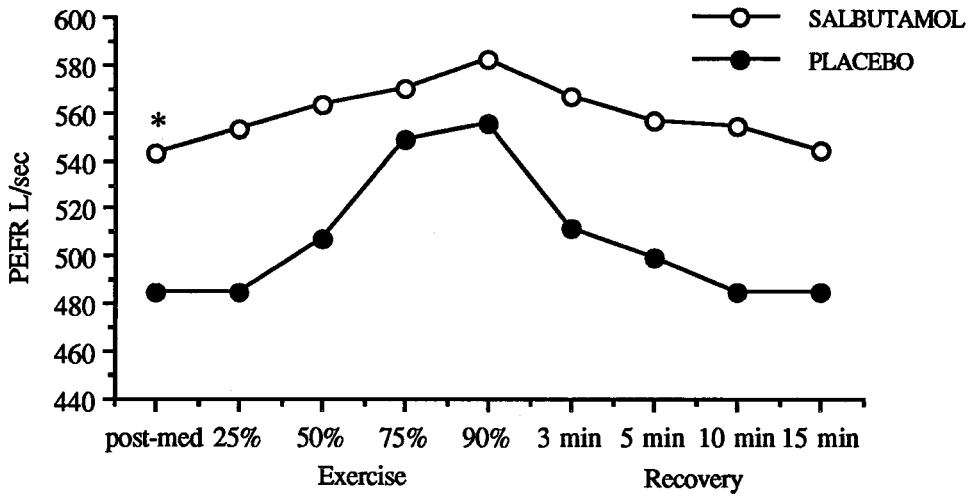
Values are means; open circles, salbutamol; closed circles, placebo. The overall mean PEFR measures were statistically higher with salbutamol: $p = 0.009$. Post-medication PEFR measures were statistically higher with salbutamol(* $p < 0.05$).

Figure 3. PEFR ($l \cdot sec^{-1}$) measures at various exercise intensities ($\%\dot{V}O_2max$), and 3 to 15 minutes into recovery, MT group data (n = 8)



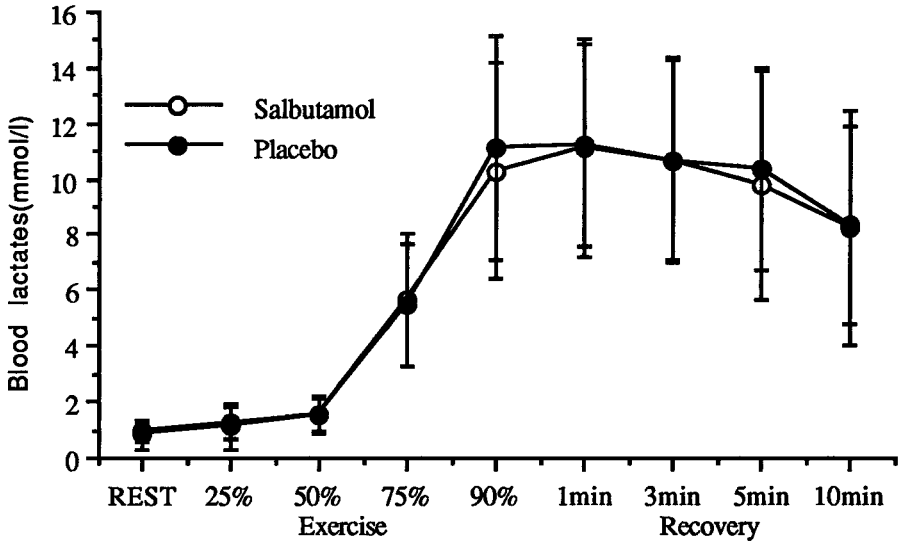
Values are means; open circles , salbutamol; closed circles, placebo : p = 0.078.

Figure 4. PEFR ($l \cdot sec^{-1}$) measures at various exercise intensities(% $\dot{V}O_2max$), and 3 to 15 minutes into recovery, $PC_{20} < 4.0$ $mg \cdot ml^{-1}$ (n = 6) group data.



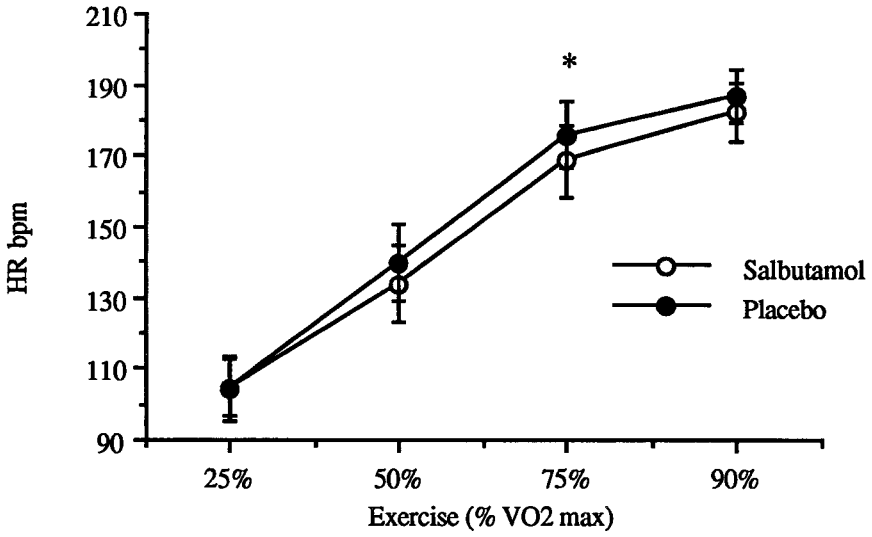
Values are means; open circles, salbutamol; closed circles, placebo. The overall PEFR measures were statistically higher with salbutamol: $p = 0.03$ Post - medication PEFR measures were statistically higher with salbutamol(* $p < 0.05$)

Figure 5. Blood lactate (mmol·l $^{-1}$) at various exercise intensities (% $\dot{V}O_2$max) and 1 to 10 minutes into recovery, all subject data (n = 17).



Values are means ± SD; open circles , salbutamol; closed circles, placebo : p = 0.688 .

Figure 6. HR (bpm) responses at various exercise intensities (% $\dot{V}O_2$max), HT group data (n = 9).



Values are means ± SD; open circles, salbutamol; closed circles, placebo. The overall mean HR measures were statistically higher with placebo: $p = 0.01$. Post hoc analysis on significant main effect revealed higher HR under the placebo condition only at 75 % VO_2max (* $p < 0.05$).

DISCUSSION

The findings of the present study have demonstrated that highly trained and moderately trained asthmatics have normal physiological responses during submaximal and maximal exercise. There was no difference between the pretreatment of salbutamol or placebo during all stages of exercise with respect to $\dot{V}O_2$, $\dot{V}_E$, HR, and SaO_2, thus suggesting no impairment in oxygen delivery to the exercising muscles in the asthmatic subjects that were tested. Packe et al., (53) found similar results in these variables when they compared untrained asthmatics and non-asthmatics exercising on a treadmill at 85 % $\dot{V}O_2$max. Ingeman-Hansen et al., (33) also found no difference between inhaled salbutamol and saline control for the variables $\dot{V}_E$, $\dot{V}O_2$, HR, $PaCO_2$ measured in 5 asthmatics during a 6 minute graded bicycle exercise test. Recently, PaO_2, $PaCO_2$, and pH were compared between asthmatics and non-asthmatics during steady state exercise and were found to have similar responses; however, $\dot{V}_E$ was significantly lower in the asthmatic than in the non-asthmatic. In this latter study the subjects were not highly trained and did not exercise to maximum (21).

Recent studies have shown that approximately 50 % of HT endurance athletes develop a significant reduction (< 91 %) in arterial hemoglobin saturation (SaO_2) during intense exercise ($\dot{V}O_2$ max $\geq$ 90 %) (15, 54). This has been shown to have an adverse effect on maximal oxygen consumption (~ 1% drop in $\dot{V}O_2$max for every % fall in SaO_2) (15, 55) and total work output when mild (90%) and more severe (87 %) saturation levels were induced (39). Therefore, the maximal performance capacity of the HT athlete's can be limited. Although, no study to date has looked at EIH in asthmatics, it is possible the HT asthmatic athlete, who may experience gas exchange limitations and experience other abnormalities due to asthma, may be even more limited at maximal exercise.

Deal and coworkers (14) demonstrated the impact that changes in $\dot{V}_E$ have on the rate of respiratory heat loss (RHL). They suggested that the degree of RHL was directly related to the severity of the post-exercise bronchoconstriction. McFadden found that the rate and magnitude of bronchial rewarming affected the severity of bronchospasm (25, 45). In other words, the greater the $\dot{V}_E$, the greater the RHL, which in turn increases the severity of exercise-induced bronchoconstriction. HT athletes have high minute ventilations at maximal exercise, this may cause a large RHL which, may in turn, increase airway resistance and the work of breathing. In HT asthmatics, the combination of a higher incidence of EIH and high minute ventilations may be limiting performance at exercise intensities $\geq$ 75 % $\dot{V}O_2max$. In this study there was no difference in SaO_2 at intensities of 75 or 90 % $\dot{V}O_2max$ between the placebo or salbutamol conditions and none of the subjects had any evidence of respiratory obstruction at the higher workloads as demonstrated by a significant rise in PEFR. Furthermore, none of the HT subjects desaturated (< 91%) at maximal exercise. Interestingly, however, the lowest drop in SaO_2 (91.5 %) in the HT group occurred in the most severe asthmatic tested (PC_{20} = 0.7 $mg \cdot ml^{-1}$). Difference in protocols and fitness level may explain the discrepancy seen in our results with respect to the incidence of EIH. Our subjects in the HT group were well trained, but their mean $\dot{V}O_2max$ is lower than other studies reporting higher incidences of EIH (15, 55). Also, the exercise protocols used in the studies reporting higher incidences were shorter in duration and ramped as compared with the stepwise progressive incremental exercise used in our study.

Previous studies have demonstrated a greater rise in blood lactate in asthmatics compared to non-asthmatics exercising at the same oxygen consumption (1, 5, 10). Although we did not compare our asthmatic subjects with normal subjects we found no significant difference between the two experimental conditions. The rise in blood lactate

over the course of exercise was similar to that reported in non-asthmatic trained individuals (62, 65). A moderate increase in lactate concentration from rest to intensities of 50 % $\dot{V}O_2$ max was followed by an exponential increase as the exercise continued to maximal levels (Figure 5). In this study, there was no statistical difference in LA concentrations at submaximal exercise (25 %, and 50 %) between the HT and MT groups. However, within the HT group higher LA values were measured under the placebo compared to the salbutamol condition at 90 % $\dot{V}O_2$max (12.5 (PL) vs. 10.6 (S)). Furthermore, at the higher exercise intensities, comparisons between the HT and MT groups demonstrated higher LA values for the HT group for both treatment conditions (HT=12.5 (PL) vs. MT=9.6(PL); HT=10.6(S) vs. MT= 9.9(S) mmol·l^{-1}), but this was not statistically significant.. The capacity of the lactic acid system can be greatly developed depending on the type of training ; for example, one competitive rower in the HT group, had LA levels as high as 19.0 mmol·l^{-1} at 90 % $\dot{V}O_2$max, but this would be expected for the type of training this sport demands. LA concentration of muscle and blood in individuals without asthma return to near resting levels within 30-60 minutes into recovery (30). In the present study subjects were not allowed to warm down, therefore reducing the rate of LA clearance; however, blood lactate samples taken up to 10 minutes post-exercise demonstrated a similar rate of clearance in the moderately and highly trained asthmatic subjects as reported in normal individuals (30).

The asthmatics in this study demonstrated the typical pattern of response to exercise indicated by changes in pulmonary function. During exercise, bronchodilation occurred as indicated by a rise in PEFR measures followed by a fall in PEFR after exercise, reaching the lowest levels at 10-15 minutes after the cessation of exercise. Bronchodilation is a normal physiological response to exercise due to a decrease in vagal

tone, catecholamine release, and the slow release of an inhibitory prostaglandin (60). Under both the salbutamol and placebo conditions, PEFR increased significantly over the course of exercise, but these were only different from each other in the first two stages of exercise. Salbutamol proved to be an effective bronchodilator as the pre-exercise PEFR measure after inhalation of salbutamol was significantly higher (3.1% for all 17 subjects and a 6.6 % rise in the more severe asthmatic group ($PC_{20} < 4.0$ mg·ml^{-1})) than the pre-exercise salbutamol or placebo condition, and provided protection throughout the exercise and recovery period (see Figure 4). Meeuwisse et al., (49) also showed a similar rise (4.5 %) after the administration of salbutamol, but in highly trained non-asthmatic subjects. A rise in circulating catecholamine levels during exercise has been demonstrated in normal and asthmatic subjects (9). In this study, at higher intensities of exercise (> 75 % $\dot{V}O_2max$), the rise in PEFR under the placebo condition was no different from measures under the salbutamol condition, thus suggesting that the asthmatic subjects had a sufficient concentration of circulating adrenaline, enough to prevent any bronchoconstriction from occurring during exercise. Some studies have suggested that asthmatics have a blunted sympathoadrenal system, which is responsible for the post-exercise bronchoconstriction (6, 64). Although catecholamine concentrations were not measured in this study, this does not appear to be the case in the asthmatics tested. Fifteen minutes after stopping exercise, the mean PEFR for all subjects fell 12 % under the placebo and 6 % with salbutamol. The duration, intensity, and type of exercise are determinants of the severity of the exercise-induced bronchospasm; this may explain why a greater fall in PEFR was not seen under the placebo condition as compared to other studies reporting larger falls in PEFR (1, 35, 56). The exercise protocol of 20 minutes in duration on a cycle ergometer would account for this, as running has been shown to be more asthmogenic than cycling and a duration of 6-8 minutes at 60-85 %

$\dot{V}O_2$max has been found to cause the greatest post exercise bronchoconstriction.(4, 59). Beyond this time the severity of the response is reduced and asthmatics have been observed to " run through " their asthma (19). Also, the first 10 minutes of the experimental test consisted of a slow increase in workloads of intensities of 25 and 50 % $\dot{V}O_2$max; this submaximal warm-up could provide protection against EIA by facilitating the release of catecholamines. A recent study demonstrated a continuous warm-up of 15 minutes at 60 % $\dot{V}O_2$max can significantly minimize EIA in moderately trained asthmatics (48). Thus, a more progressive, short duration exercise protocol may have produced a greater physiological response in the asthmatics tested.

A logical concern is whether the severity of one's asthma is a determinant of disturbances in performance-related variables such as $\dot{V}_E$, $\dot{V}O_2$, SaO_2, RER, and LA. In the present study we chose a PC_{20} of < 16 mg·ml^{-1} of methacholine as indicative of current asthma. Cockroft et al., (13) used a cut off point of 8 mg/ml and below to be a sensitive indicator of asthma and concluded concentrations between 8 and 16 mg·ml^{-1} to be a " gray area" or borderline hyper-responsiveness. Malo et al., (41) suggested PC_{20} < 16 mg·ml^{-1} as an acceptable concentration based on his findings that 8 % of a population would show a reaction in the asthmatic or abnormal range. The mean values for both the HT and MT groups were below 8 mg·ml^{-1} in the present study. Also, data analysis performed on the more severe asthmatic subjects (PC_{20} < 4.0 mg·ml^{-1}) revealed no significant difference in $\dot{V}_E$, $\dot{V}O_2$, RER, SaO_2, and LA between the two experimental conditions. However, mean PEFR measures averaged over the exercise and recovery conditions were significantly higher with the pretreatment of salbutamol. Therefore, the severity of asthma does not appear to have a greater disturbance on physiological parameters during exercise.

Of the 17 asthmatic subjects tested, 12 of the subjects felt the experimental test with the placebo to be more difficult than with the salbutamol, while 5 subjects found no difficulty in breathing in either of the exercise tests. Only one of the subjects found the exercise to be more difficult under the treatment of salbutamol. Other symptoms experienced by subjects were chest tightness, wheezing, and congestion, but these symptoms were only experienced under the placebo. Thus, although there were no measurable physiological changes associated with pre-exercise administration of salbutamol, there appear to be subjective differences.

Based on the results of this study, there was no difference in the physiological response to exercise between groups based on training status. It was concluded that although salbutamol does decrease airway resistance, as demonstrated by increases in PEFR measures, these asthmatic athletes do not have altered metabolic or ventilatory responses during exercise.

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APPENDIX A - Review of Literature

EXERCISE INDUCED ASTHMA

i) Introduction
ii) Clinical Presentation
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REVIEW OF LITERATURE

EXERCISE-INDUCED ASTHMA

i) Introduction

Exercise-Induced Asthma (EIA) is defined as a reversible airway narrowing precipitated by physical activity. Exercise can be a potent stimulus for producing bronchoconstriction within minutes after exercise in most individuals with asthma. However, with the proper medication and management, asthmatics are encouraged to participate in sports. In fact, the prevalence of asthma among competitive athletes is higher than one would expect; 11.2% of athletes competing in the 1984 Olympic games suffered from EIA (67). The attack of bronchoconstriction, classically displayed by signs of chest tightness, shortness of breath, wheezing, and coughing, is most apparent 5-15 minutes after exercise (2). Clinically, this airflow obstruction is represented by a decrease in flow rate which can be measured by simple spirometry, Forced Expiratory Volume in 1 second (FEV_1) or Peak Expiratory Flow Rate (PEFR).

While the precise mechanism of EIA is still unclear, it is generally accepted that cooling and drying of the airways associated with high ventilation represent the initiating stimuli for the post-exercise bronchoconstriction (3, 14, 63). This popular theory has been criticised and a new hypothesis suggesting EIA to be a vascular phenomenon has

been proposed (45). It has also been suggested that because exercise can cause airway narrowing in the absence of irritants or antigens, perhaps metabolic changes associated with exercise could trigger bronchoconstriction (5).

ii) Clinical Presentation:

The classical signs of an acute asthmatic attack are chest tightness, shortness of breath, coughing, and/or wheezing. However, some individuals with EIA may only complain of one of these symptoms, eg., breathlessness or coughing may be apparent during or shortly after moderate to strenuous exercise. Approximately 90 % individuals with asthma and 35-40% of those with allergic rhinitis/hay fever experience EIA(42). Exercising at a intensity of 65-85 % for 6-8 minutes produces maximal bronchoconstriction; above this intensity or duration diminishes the EIA response (59). The common physiological response of an individual with EIA to exercise is mild bronchodilation, usually persisting throughout exercise, followed by bronchoconstriction in recovery. This increase in airway resistance peaks 8-15 minutes after exercise has ceased and normal pulmonary function returns in 30 - 60 minutes.

iii) Diagnosis:

In diagnosing individuals with EIA, bronchial provocation tests with methacholine or histamine, or an exercise challenge can be used to measure the degree of bronchial hyperactivity in subjects. Bronchial provocation challenges with

pharmacological agents such as methacholine or histamine are performed by measuring changes in lung function followed by inhalation of the agent, increasing in doubling concentrations (60). The most popular method of administering pharmacological provocation tests is the continuous tidal volume breathing method from a nebulizer. The most commonly used index of bronchial reactivity is the PC_{20}, the concentration of methacholine/histamine which provokes a fall in FEV_1 to 20% below the control level. Histamine is thought to trigger airway constriction through stimulation of sensory receptors and direct action on bronchial smooth muscle (29). On the other hand, methacholine acts on cholinergic muscarinic receptors on airway smooth muscle, and in asthmatic airways, smaller doses of methacholine are needed to cause a bronchial response (40).

A standardized exercise challenge test described by Silverman & Anderson (59) consists of a 6-8 minutes of steady state exercise on the treadmill or cycle ergometer at 90% of the subjects predicted maximal HR. A 15 -20 % decrease in FEV_1 is considered to be a positive exercise challenge test (34, 40). Several authors have compared these tests and found the pharmacological challenge with methacholine to be better than the histamine or the exercise challenge in distinguishing the asthmatics from the controls (11, 40).

iv) Pulmonary Function Tests:

In asthmatics, the typical pattern of change in pulmonary function during exercise is a slight decrease in airway resistance which is measured by an increase in PEFR and FEV_1, compared to normal subjects (26,47). This appears to be due to the release of catecholamines (24). However, within minutes after exercise, airway resistance increases markedly with peak bronchospasm between 5-15 minutes (10) and recovers to baseline levels within 30 to 40 minutes (2, 36). The response to exercise can be determined by several indexes of pulmonary function: FEV_1, PEFR, and FEF 25-75% (MMEF). A change in large and small airway resistance is quantified by the ratio FEV_1/FVC. A fall in FEV_1 of 20-30% is considered to be mild to moderate obstruction while a fall greater than 30% is considered severe (36).

Forced expiratory flow between 25 and 75% (FEF 25-75% or maximal mid expiratory flow rate (MMEF)) of volume expired during Forced Vital Capacity (FVC) is a sensitive measure of airflow obstruction in the smaller airways (36,47). Peak expiratory flow rate (PEFR) measured by a Wright Flow Meter is the most commonly used method of determining airway resistance in the small and large airways because of its portability and convenience, but more variable results have been shown using this method compared to FEV_1 (66). Both FEV_1 and PEFR are effort dependent measures and are therefore not the most sensitive measure compared to the effort independent measure MMEF.

Flow-volume curves illustrate in greater detail the specific airway conductance or flow at different lung volumes. Obstruction in the upper expiratory phase is apparent when the curve appears "scooped" or "curved" rather than a smooth continuous line as

seen in normal loops. However, the flow-volume loop can be abnormal even when the FEV_1/FVC ratio is normal, thus implying the greater sensitivity of this test (66).

v) Pathogenesis:

For some time, asthma and EIA were thought to be two separate conditions. It is now known that exercise is just another stimulus in provoking an asthmatic attack. Although the exact etiology of EIA is still unclear, several theories have been proposed. Earlier studies have speculated hyperventilation, hypocapnia, and acidosis to be causally related to EIA (6, 10, 32, 43). The more widely accepted theory today is that water and heat loss from the respiratory mucosa represents the initiating stimulus for the post-exercise bronchoconstriction (3, 14, 63). This is based on earlier investigations which have consistently demonstrated that asthmatics exercising in warm, humid environments are less likely to experience an attack than while exercising in cool, dry environments (2). Recently, a new hypothesis by Mcfadden (45) suggests that EIA is a vascular phenomenon. This theory is built on the fact that asthmatics have a hyperplastic capillary bed in their airways that is highly sensitive to thermal stimuli.

a) HYPERPNEA, HYPOCAPNEA, AND LACTIC ACIDOSIS

Hyperventilation associated with exercise and consequent hypocapnia have been suggested as possible causes of EIA based on earlier studies demonstrating that voluntary hyperventilation at rest can increase airway resistance in asthmatics (10, 32). Fisher et

al., (18) demonstrated by breathing an 8% CO_2 gas mixture during vigorous physical activity, significantly reduced post-exercise bronchoconstriction. On the other hand, Chan-Yeung et al., (10) noted that the combination of hyper-ventilation and breathing CO_2 actually increased airway resistance, measured by a greater decline in FEV_1 compared to breathing room air. This author concluded that "EIA" is probably exercise-induced hyperventilation "(EIh)". Although the mechanism of EIh is probably different from EIA, people who suffer from EIA generally develop a bronchial response to voluntary hyperventilation. Some differences have been found between EIA and EIh; voluntary hyperventilation does not release catecholamines, so the bronchodilation normally seen in asthmatics during exercise does not occur during the period of hypernea and therefore a faster onset of bronchoconstriction occurs (29, 60). Also, with exercise a diminished responsiveness to exercise performed within 2 hours after the initial exertion has been seen in some asthmatics; this refractory period may not occur with voluntary hypernea (29, 60).

Higher blood lactate levels have been reported in asthmatics working at the same oxygen consumption as non-asthmatics with similar fitness levels (1). This lactic acidosis has been suggested to play a role in EIA based on the theory that high hydrogen ion concentrations may cause the release of mediators from mast cells (43). However, the administration of bicarbonate, which buffers the excess H^+ ions, did not appear to reduce post-exercise bronchospasm (43). Therefore, no substantial evidence in the literature confirms these earlier hypotheses that hypocapnea, hyperventilation, or acidosis are causally related to EIA.

b) HEAT AND WATER LOSS THEORY

Chen and Horton (12) demonstrated the importance of water loss and/or heat loss by demonstrating that asthmatics who breathe fully saturated air at 37 degrees Celsius during exercise prevent EIA. More recent studies by McFadden and co-workers (43, 63), who have looked at the effects of environmental conditions on exercise-induced bronchoconstriction, have helped to clarify some of the earlier controversies regarding etiology. Strauss and McFadden (63) demonstrated a greater bronchospastic response while breathing cold air during exercise, and a blunted response when breathing inspired air at 37 degrees celsius and fully saturated (BTPS). These findings suggest that this rapid rewarming of the airways significantly reduces EIA (63). Deal and co-workers (14) developed the heat-flux hypothesis using the following equation to determine heat loss:

$$RHL = VE\ (HC[\ Ti - Te] + Hv[\ Wi - We]\ )$$

where HC = heat capacity of air (3.04×10^{-4} Kcal·L^{-1} · ° C^{-1}), Ti and Te are temperature of inspired and expired air, respectively in ° C, Hv = latent heat of evaporization for water (5.8 Kcal·g^{-1}), and Wi and We = water content of the inspired and expired air at the mouth, respectively (mg H_2O·L in air $^{-1}$). This equation demonstrates that high minute ventilations will have a greater heat loss and a consequently greater airway obstruction (14). These authors also showed that voluntary hyperventilation while breathing cold air produced an increase in airway resistance, suggesting that the stimulus of EIA was heat loss from the respiratory mucosa and not exercise. A weak link in the respiratory heat loss (RHL) theory comes from the fact that inspiring air as warm as 80

degrees causes no less of a bronchoconstriction than while breathing air at body temperature.

Anderson and coworkers have emphasized the effects of drying of the airways to be a more important stimulus of EIA than cooling (3, 63). They suggested that the increase in osmolarity of the respiratory mucosa due to water loss was a possible stimulus of EIA (4). This is based on Schoeffel's findings which demonstrated that the inhalation of hyper- and hypo-tonic solutions could elicit bronchoconstriction in resting asthmatics (57). This increase in osmolarity was speculated to stimulate the release of mediators from lung mast cells, thus causing airway narrowing. This is thought to either act on smooth muscle or on cells in the respiratory mucosa by stimulating epithelial irritant receptors and/or disrupting epithelial junctions (4). Despite the evidence for the cooling/drying hypothesis, some subjects can still develop EIA while breathing warm humid air; thus implying that H_2O and RHL cannot be the sole trigger factors by themselves (8).

Gilbert and McFadden (24) have challenged the osmolarity theory, and have presented a new hypothesis suggesting that exercise-induced asthma is a vascular phenomenon. These investigators demonstrated little change in surface osmolarity when the intrathoracic thermal fluxes were measured during hypernea. This indicates that the respiratory tract has a protective mechanism that prevents drying of the airways (24). McFadden (45) proposed a new hypothesis that suggests cooling of the airways after exercise is followed by rapid warming and the development of mucosal hyperemia and edema, thus causing the airway narrowing. Recently Gilbert and McFadden tested this theory and found both airway cooling and rapid rewarming after isocapnic

hyperventilation played a key role in the production of bronchial narrowing (25) Although they were not able to determine how rapid bronchial rewarming causes the obstruction, they suggested the development of mucosal hyperemia and edema to be a possible explanation. If this theory is correct, the degree of hyperemia would depend on the rate of bronchial rewarming. Slow rewarming (ie. the subject warms down) has been found to abolish the effects of hyperventilation or hyperpnea during exercise, whereas rapid rewarming increases obstruction (45). It has also been shown that airways of asthmatics rewarm twice as fast in the first minute of recovery than normal individuals (24). Because hyperemia increases local heat in the bronchial circulation, the main heat source in the central airways, supports the hypothesis that EIA could be due to the heat-sensitive airway microcirculation responding to the fall that accompanies hyperpnea. However, rewarming may not be the trigger because asthmatics who are able to "run through" their asthma fail to develop bronchoconstriction after prolonged exercise, but still rewarm their airways (29).

vi) Prevention:

EIA can be prevented in many asthmatic athletes who choose not to use medication. Different types of activities are less asthmogenic; for example, exercise performed in warm humid environments, such as swimming, are less likely to provoke an attack than outdoor cold weather activities such as running, cycling, rowing, cross-country skiing, and hockey. The duration of exercise is another determinant of the severity of EIA; for example, sports involving intermittent running such as basketball, football, rugby, and baseball are better tolerated by the asthmatic athlete than continuous

running activities (2, 36). The intensity of exercise can also affect the severity of exercise-induced bronchospasm; the greatest degree of exercise-induced airway obstruction tends to occur most frequently in asthmatics exercising between 60 and 85 % of maximal oxygen consumption for 6-8 minutes (59). However, at greater exercise intensities the degree of post-exercise bronchoconstriction appears unaltered and exercising longer than this generally diminishes the response (1, 19, 47). Performing a continuous warm-up 15 minutes in duration at an intensity of 60 % of maximal oxygen consumption prior to exercise significantly protects the airways of asthmatics from bronchoconstriction (48). The improvement in fitness level through aerobic training has been shown to reduce the severity, frequency, and duration of attacks (22, 31). Other techniques useful in minimizing EIA occurance are making a conscious effort to prevent exaggerated hyperventilation by breathing slower and deeper and using nasal breathing, which warms and cleans the air (37).

vii) Treatment

Although preventative measures can be taken for EIA, some asthmatic athletes require pharmacological intervention to overcome their asthma while exercising. The most effective drugs for preventing EIA are the β_2 adrenergic agonists: salbutamol, terbutaline, fenoterol, or salmetorol. Salbutamol is the drug of choice by asthmatic athletes because of its powerful bronchodilator effects, β_2 selectivity, and its use is permitted by the International Olympic Committee (IOC) (67). Other classes of medication used are sodium cromoglycate, methyl xanthines, corticosteroids, and bella donna alkaloids.

a) β - Adrenergic receptor physiology

The β-receptors, stimulated by the sympathetic limb of the autonomic nervous system, can be divided into two groups, β_1 and β_2. β_1 receptors are more potently stimulated by norepinephrine and are responsible for the chronotropic and inotropic effects of the heart, decrease in intestinal motility, and lipolysis, while β_2 receptors mediate bronchodilation of airway smooth muscle, cause uterus, bladder, intestinal relaxation, and dilation of arteries supplying smooth muscle. β_2-receptors can be found in many different cell types within the lung; including smooth muscle of all airways from the trachea down to the terminal bronchioles. Activation of these receptors by β agonists causes relaxation of central and peripheral airways. In addition to relaxation of smooth muscle, β agonists also reduce the release of mediators from mast cells, and may reduce mucosal edema. Those drugs activating β_1 receptors cause a number of outcomes that are unacceptable for use in international sport competitiions. Therefore, drugs which have a greater selectivity for β_2-receptors with minimal effects on β_1-receptors are preferred because of fewer cardiovascular side effects and their use has been sanctioned by the International Olympic Commission (IOC) (52).

The cascade of events is initiated by the stimulation of β_2 receptors by a β_2 adrenoreceptor agonist (ie. catecholamines); this activates the enzyme adenylate cyclase, causing the formation of a second messenger, cyclic AMP (cAMP). Intracellular cAMP activates protein kinase A, which in the case of bronchial smooth muscle, causes a reduction of Ca^{++} dependent coupling of actin and myosin, resulting in smooth muscle relaxation. It has been suggested that the increase in bronchial reactivity seen in asthmatics is most likely caused by a decrease in the β-adrenergic response (50).

b) β_2 Adrenergic agonist (Salbutamol)

Salbutamol is one of the first generations of β_2 - adrenergic agonists developed for treating asthma. Inhaled Salbutamol given 15 minutes prior to exercise is very effective in preventing the post-exercise fall in PEFR (27, 58). Subjects given a placebo will show a 40% drop in peak flow and only a 10% drop with salbutamol, which is within normal limits. This drug has full bronchodilator effects for up to 3 hours with partial activity up until 6 hours (58). Inhalation of β_2 agonists is the more preferred method of delivery over oral, sublingual, or parental (intravenous or intramuscular) routes because of its rapid onset of action, direct route to the respiratory tract, and fewer side effects. However, some subjects have experienced tremors, which are caused by direct stimulation of β_2 adrenoreceptors in skeletal muscle (50). There is a growing concern of the overuse of sympathomimetic drugs based on a number of studies demonstrating the regular use of β_2 agonists can lead to an increase in bronchial hyperresponsiveness (54).

The use of salbutamol has been permitted by I.O.C. based on the assumption that this β-agonist has no ergogenic effect in the asthmatic athlete. Studies that have looked at this drug in asthmatics and non-asthmatics as a possible performance enhancer, have reported conflicting results (7, 46, 49, 56). Bedi et al., (7) found salbutamol to increase sprint time in normal subjects, while others have reported no ergogenic benefit in non-asthmatics (46,49). Schmidt et al., (56) also found this drug to have no effect on exercise performance in asthmatics, thus encouraging its use by the asthmatic athlete to minimize EIA in competitive events. More recently Meeuwisse et al., (49) conducted a similar study to Bedi et al., (7) on elite non-asthmatic cyclists and found salbutamol to have no performance enhancing effect when given in therapeutic doses.

c) Other Pharmacological Agents

Sodium Cromoglycate is a safe and effective drug for the prophylactic management of asthma. In the treatment of EIA sodium cromoglycate can be used in combination with other drug classes and has been shown to be effective in preventing EIA when given before the start of exercise, but has little effect once EIA has been induced. Its mode of action was once thought to be a mast cell stabiliser but appears to have effects on other systems. There are no cardiovascular effects or performance enhancing qualities, therefore, sodium cromoglycate is allowed in international sporting competition (20, 52).

Methyl Xanthenes; one of the most extensively ingested drug of this group is caffeine. It has been shown to cause relaxation of bronchial smooth muscle and can significantly prevent EIA in high doses (7 mg/Kg) (38). Caffeine is banned in competition if serum concentrations exceeds 12 $mg \cdot L^{-1}$ (61). Theophylline, a methylated xanthene, is not as effective of a bronchodilation in the management of asthma as β_2 agonists, but are used effectively by individuals who do not tolerate β_2 stimulants. Theophylline is comparable to sodium cromoglycate in inhibiting EIA. However, there are a number of side effects including tacchycardia, mild CNS stimulation, diarrhea, headache, and nausea which are not compatible for use by an athlete during competition (51).

Oral and intravenous glucocorticosteroids play a valuable role in the management of severe chronic and acute asthma. The use of systemic corticosteroids have been banned from international sport competitions due to their potential to enhance performance. Inhaled glucocorticosteroids , on the other hand, have been found to have

no ergogenic effects, but like oral glucocorticosteroids , stabilize asthma, and have little effect on EIA if administered just prior to exercise. Taken on a regular basis, inhaled glucocorticosteroids reduce inflammatory cell filtrate, bronchial hyperreactivity, and improve the effectiveness of pre-exercise β_2 agonist in reducing the severity of EIA (52).

Belladonna Alkaloids are anticholinergic agents that play a role in the management of asthma. Ipratropium bromide is an example of this class and is administered via aerosol or by a nebulised solution. As a bronchodilator ipratropium bromide is used by individuals who do not respond well to β agonists or given in combination with β agonists and/ or sodium cromoglycate to give better protection than using either drug alone. Side effects are rare with this drug, however some asthmatics complain of dryness of the throat. It is doubtful whether anticholinergic agents play a role in preventing EIA or whether these drugs will enhance performance (20).

vii) Circulatory, Ventilatory, and Metabolic Responses to Exercise

Few studies have examined the physiological responses of asthmatics during exercise. In the data available, asthmatics have generally responded similarly to normal subjects when free from an attack (44). Any differences in these variables have been concluded to be due to the sedentary state of the asthmatics tested; for example, higher blood lactate levels in asthmatics have been reported by several authors (1,5,10,53). These individuals were inactive, so these higher levels could be more representative of their lower fitness level. On the other hand, Anderson et al., (1) found unusually high levels of lactate in asthmatics working at the same oxygen consumption as similarly trained non-asthmatics. It is not clear whether this response is due to the presence of asthma. If so, this greater degree of metabolic acidosis may affect the optimal performance of these athletes with EIA.

During the initial phase of exercise, many asthmatics develop mild bronchodilation, which is thought to be due to the release of catecholamines (26, 29). This bronchodilation usually persists throughout the duration of exercise, but may gradually decrease as indicated by a fall in PEFR. However, within minutes of completing exercise, there is a profound drop in PEFR (or FEV_1) due to bronchoconstriction. The failure of normal catecholamine release during exercise may be responsible for this post-exercise airway narrowing seen in individuals with EIA. Much debate exists in the literature as to whether asthmatics actually have an altered catecholamine response to exercise. Some investigators have found significantly lower plasma adrenaline and noradrenaline levels in asthmatics when compared to matched

control subjects (6, 64), while other studies have not (9). This inconsistency may lie in the different protocols used. The former studies measured catecholamine levels at the end of exercise, whereas in the latter study blood samples were obtained throughout the exercise period.

The alveolar to arterial PO_2 [A-a DO_2] is a good indicator of the adequacy of pulmonary gas exchange. In normal subjects (A-a)DO_2 decreases during moderate exercise, due to an improvement of perfusion (Q) at the lung apices, but increases during higher intensities of exercise. Katz et al., (35) found the distribution of ventilation-perfusion (V_A/Q) over the lung became more uneven during a progressive exercise performance in asthmatic children. Changes that develop in gas tension in asthmatics during exercise have been shown to be variable. Some authors have found no change in arterial oxygen tension (21), while others have reported a significant rise in PaO_2 from resting levels in asthmatics performing progressive exercise (1, 35). After exercise, a fall in PaO_2 has been observed to develop concomitantly with bronchoconstriction. This hypoxemia may be a result of inequalities in the VA/Q relationship due to airway narrowing(1). Arterial PCO_2 was found to be variable in asthmatics during exercise (1, 21), while unchanged in others (35). Following exercise, hypercapnia may develop in asthmatics due to marked bronchoconstriction, but this does not occur in normal individuals.

Arterial oxygen (PaO_2) and arterial PCO_2 of normal subjects stay relatively consistant throughout exercise, although some HT athletes ($\dot{V}O_2max > 68$ ml·kg·min^{-1} who are free of asthma, exhibit arterial hypoxemia at maximal exercise. This phenomenon in HT athletes is called exercise-induced hypoxemia (EIH), and may suggest that the lungs are the "limiting" factor for exercise performance in these athletes

(16). Although the exact etiology is still unknown, one of the causes is due to the excessive widening of (A-a) DO_2 . It would be interesting to determine whether HT asthmatic athletes, who show arterial desaturation, are limited at maximal exercise.

Several investigators have found physiological parameters such as HR, $\dot{V}O_2$, $\dot{V}_E$, FEV_1, and work capacity in asthmatics during submaximal and/or maximal exercise to be within normal range (1, 33, 53, 56). Anderson et al., (1) compared metabolic and ventilatory responses in 5 asthmatic subjects during a 6-8 minute test on both a cycle ergometer and a treadmill. The treadmill running did produce the greatest bronchoconstriction, indicated by a fall in PEFR measures, and the higher lactates were observed during the cycle. The levels of lactate observed in these asthmatics during the cycle were found to be higher when compared to non-asthmatics exercising at similar oxygen consumptions. Packe et al., (53) tested 10 untrained asthmatics with 10 matched non-asthmatics during progressive exercise test on a treadmill to 85 % maximal $\dot{V}O_2$. No difference was found between the two groups with respect to $\dot{V}O_2$, $\dot{V}_E$, SaO_2, and RER during exercise, but RER values were higher in the asthmatics thus, indicating a normal fat metabolism in these subjects. Also, the similar levels of $\dot{V}O_2$, $\dot{V}_E$, and SaO_2 in comparison to the non-asthmatics, indicated no impairment of oxygen delivery to exercising muscle in asthmatics (53). Ingemann-Hansen et al., (33) measured metabolic and ventilatory variables (maximal $\dot{V}O_2$, $\dot{V}_E$, and HR) in asthmatics during a graded bicycle exercise and found no difference between inhaled salbutamol and saline control. All of the studies to date, investigating the metabolic and ventilatory responses of asthmatics to exercise, have tested unfit subjects; therefore,the lower maximal oxygen consumption ($\dot{V}O_2max$), work capacity, and higher levels lactate reported in asthmatics have been due to the lower fitness level of these individuals .

In the literature, no study has looked at metabolic and ventilatory variables in highly trained athletes ($\dot{V}O_2max$ > 60 ml/kg/min). If higher lactate levels and alterations in gas exchange develop in asthmatics due to the presence of their disease, it is possible these abnormalities could limit these individuals in athletic performance.

APPENDIX B

Tables

TABLE 7. Age, height, weight, $\dot{V}O_2max$, and PC_{20}, individual data of subjects in the Highly trained group

SUBJECT	SEX	AGE years	HEIGHT cm	WEIGHT kg	$\dot{V}O_2max$ $ml \cdot kg \cdot min^{-1}$	PC_{20} $mg \cdot ml^{-1}$
HT group						
CL	F	22	175	63.3	57.8	3.9
JH	M	23	180	72.9	63.4	6.3
PMS	F	24	158	50.8	53.9	6.1
PH	M	24	180	72.8	63.3	15.8
PM	F	33	162	55.3	54.4	0.7
PR	M	32	190	85.0	58.8	11.5
RH	M	19	182	74.1	60.3	3.1
SH	F	35	170	64.0	50.3	15.6
SS	F	23	165	59.1	50.9	1.6
MEAN±SD		26 ± 6	174 ± 11	66.4 ± 10.8	57.0 ± 4.9	7.2 ± 5.8

Table 8. Age, height, weight, $\dot{V}O_2max$, and PC_{20}, individual data of subjects in the Moderately trained group

SUBJECT	SEX	AGE years	HEIGHT cm	WEIGHT kg	$\dot{V}O_2max$ $ml \cdot kg \cdot min^{-1}$	PC_{20} $mg \cdot ml^{-1}$
MT group						
AB	M	23	192	87.0	57.0	11.2
GK	M	21	180	72.0	46.4	0.8
PK	M	23	187	85.1	57.3	8.9
RC	M	23	189	93.5	48.7	1.6
RF	M	23	175	71.4	53.1	9.4
SB	M	26	182	75.5	54.6	5.0
SM	M	23	200	96.0	48.6	15.9
CM	F	31	161	48.6	45.1	8.0
MEAN ±SD		24 ± 3	183 ± 12	78.6 ± 15.3	51.3 ± 4.9	7.6 ± 5.0

Table 9. $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 25 % $\dot{V}O_2$max with placebo, individual subject data (n = 17)

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l · min $^{-1}$	RER	HR bpm	PEFR l · sec-1	SaO_2
25%						
CL	33.2	1.16	0.89	96.0	500	96.0
JH	31.9	1.14	0.78	101.3	640	96.5
PMS	26.7	0.73	0.89	113.0	410	97.3
PH	32.5	1.20	0.80	105.8	600	97.3
PM	23.8	0.76	0.84	91.3	355	96.5
PR	34.8	1.49	0.78	114.5	520	96.5
RH	27.1	0.98	0.74	99.8	560	97.3
SH	24.6	0.83	0.71	110.5	545	97.8
SS	34.1	1.26	0.87	106.5	490	97.8
AB	39.4	1.67	0.77	117.8	730	97.3
GK	34.2	1.23	0.85	113.8	470	96.0
PK	29.2	1.29	0.78	85.5	600	96.8
RC	39.8	1.26	0.78	81.5	530	96.3
RF	28.4	1.17	0.72	101.8	670	
SB	32.2	1.23	0.89	97.8	620	97.3
SM	37.2	1.47	0.87	118.0	680	
CM	28.1	0.95	0.77	108.3	440	
MEAN ±SD	31.6 ± 4.8	1.16 ± .26	0.81 ± .06	103.7 ± 10.9	550 ± 102	96.9 ± 0.6

Table 10 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 25 % $\dot{V}O_2$max with salbutamol, individual subject data (n = 17)

SUBJECT	$\dot{V}E$ btps	$\dot{V}O2$ l · min $^{-1}$	RER	HR bpm	PEFR l · sec^{-1}	SaO2
25%						
CL	32.4	1.13	0.81	90.0	490	97.3
JH	36.5	1.31	0.85	106.0	630	97.3
PMS	36.0	1.09	0.86	117.3	420	98.3
PH	36.7	1.28	0.81	108.3	710	
PM	20.0	0.67	0.77	97.3	485	94.0
PR	30.8	1.32	0.72	102.8	590	96.5
RH	24.2	0.88	0.82	98.8	660	95.8
SH	30.6	1.01	0.73	116.3	565	99.3
SS	24.4	1.00	0.76	100.3	535	98.3
AB	31.0	1.47	0.74	106.8	710	95.5
GK	32.0	1.24	0.87	111.5	510	96.5
PK	35.3	1.37	0.91	89.0	640	96.0
RC	39.5	1.32	0.72	89.8	640	97.5
RF	26.3	1.03	0.78	104.8	650	97.8
SB	32.1	1.30	0.85	106.0	720	97.8
SM	38.6	1.55	0.87	125.5	710	95.8
CM	26.1	0.92	0.82	106.0	450	
MEAN ±SD	31.3 ± 5.6	1.17± .23	0.80± .06	104.5 ± 10.0	595 ± 98	96.9 ± 1.4

Table 11 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 50 % $\dot{V}O_2$max with placebo, individual subject data (n = 17)

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l · min $^{-1}$	RER	HR bpm	PEFR l · sec-1	SaO_2
50%						
CL	53.2	2.07	0.87	133.3	520	95.8
JH	59.2	2.20	0.88	136.5	640	95.5
PMS	48.7	1.49	0.95	149.3	440	96.3
PH	52.8	2.33	0.81	144.0	675	95.5
PM	39.2	1.51	0.85	126.8	370	96.8
PR	80.5	3.32	0.86	147.8	525	95.8
RH	45.5	1.81	0.75	136.0	610	96.5
SH	45.7	1.41	0.82	158.8	565	98.0
SS	47.6	1.84	0.92	125.5	480	96.5
AB	61.0	2.65	0.84	144.5	700	97.0
GK	59.7	2.03	0.96	145.8	480	96.3
PK	44.3	1.91	0.82	109.3	615	96.0
RC	70.1	2.43	0.91	114.3	585	96.8
RF	49.5	1.97	0.83	134.5	650	
SB	53.3	2.11	0.95	134.5	670	97.5
SM	50.7	2.19	0.90	142.3	705	97.0
CM	37.9	1.34	0.82	122.5	420	
MEAN ±SD	52.9 ± 10.8	2.03 ± .49	0.87 ± .06	135.6 ± 12.9	567 ± 104	96.5 ± 0.7

Table 12 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 50 % $\dot{V}O_2$max with salbutamol, individual subject data (n = 17)

SUBJECT	$\dot{V}E$ btps	$\dot{V}O2$ l · min $^{-1}$	RER	HR bpm	PEFR l · sec^{-1}	SaO2
50%						
CL	54.2	1.92	0.92	119.3	535	97.0
JH	64.2	2.32	0.98	138.0	660	97.0
PMS	46.5	1.56	0.90	138.3	490	97.3
PH	57.2	2.30	0.82	142.5	680	98.3
PM	39.8	1.45	0.88	123.5	420	94.5
PR	59.2	2.53	0.83	132.3	600	96.5
RH	45.0	1.75	0.86	134.0	675	96.0
SH	53.7	1.72	0.78	154.3	580	98.8
SS	39.6	1.64	0.85	122.3	540	95.5
AB	56.9	2.64	0.82	138.5	690	96.3
GK	52.7	1.83	1.03	145.3	510	96.8
PK	41.9	1.84	0.90	112.0	670	96.5
RC	69.4	2.42	0.77	120.0	700	97.3
RF	48.1	1.94	0.80	140.8	660	97.0
SB	54.6	2.12	0.92	141.0	710	97.3
SM	59.0	2.34	1.01	151.5	720	95.8
CM	38.5	1.33	0.90	132.3	460	
MEAN ±SD	51.8 ± 9.0	1.98 ± .39	0.88 ± .08	134.4 ± 11.8	606 ± 96	96.7 ± 1.0

Table 13 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 75 % $\dot{V}O_2$max with placebo, individual subject data (n = 17)

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l · min $^{-1}$	RER	HR bpm	PEFR l . sec-1	SaO_2
75%						
CL	107.3	3.31	0.99	170.5	550	95.0
JH	110.4	3.31	1.04	173.3	660	94.3
PMS	79.0	2.23	1.05	185.5	460	95.3
PH	115.3	3.86	1.02	180.3	690	96.5
PM	66.0	2.38	0.96	173.3	385	94.5
PR	128.0	4.30	1.00	175.0	580	94.5
RH	96.8	3.25	0.87	173.5	700	96.8
SH	114.6	2.61	1.09	191.8	600	95.8
SS	69.4	2.51	0.98	159.3	520	95.3
AB	110.6	3.99	0.98	172.3	715	96.8
GK	91.6	2.95	1.03	172.0	495	96.3
PK	71.8	3.44	0.90	150.0	620	94.3
RC	120.3	3.62	1.01	161.3	640	
RF	79.0	3.00	0.92	168.0	660	95.5
SB	90.5	3.25	1.04	171.3	730	96.3
SM	81.5	3.47	1.01	179.5	735	96.3
CM	63.0	1.95	0.90	160.8	510	
MEAN ±SD	93.8 ± 20.8	3.14 ± .65	0.99 ± .06	171.6 ± 10.1	602 ± 103	95.5 ± 0.9

Table 14 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 75 % $\dot{V}O_2$max with salbutamol, individual subject data (n = 17)

SUBJECT	$\dot{V}E$ btps	$\dot{V}O2$ l· min $^{-1}$	RER	HR bpm	PEFR l · sec^{-1}	SaO2
75 %						
CL	106.9	3.02	1.08	163.8	520	95.8
JH	115.4	3.55	1.07	170.8	690	96.3
PMS	71.7	2.21	0.99	170.0	485	95.3
PH	120.0	3.72	1.03	176.3	710	
PM	65.4	2.24	0.98	169.0	460	94.0
PR	95.7	3.72	0.92	160.5	610	96.5
RH	100.5	3.02	1.04	170.0	690	95.0
SH	113.3	2.98	0.94	186.3	590	97.0
SS	68.7	2.34	0.96	149.5	550	96.0
AB	102.0	4.16	0.95	171.5	720	96.0
GK	94.3	2.81	1.11	176.0	500	95.3
PK	70.7	3.28	0.97	154.3	680	95.5
RC	125.7	3.74	0.81	159.5	700	
RF	84.1	3.13	0.89	175.3	670	95.8
SB	88.9	3.23	1.01	173.8	730	97.0
SM	89.3	3.45	1.07	182.3	740	95.3
CM	66.5	1.89	1.03	165.3	470	
MEAN ±SD	92.9 ± 19.6	3.09 ± .63	0.99 ± .08	169.0 ± 9.5	618 ± 101	95.8 ± 0.8

Table 15 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 90 % $\dot{V}O_2$max with placebo, individual subject data (n = 17)

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l·min^{-1}	RER	HR bpm	PEFR l . sec-1	SaO_2
90 %						
CL	133.4	3.70	0.95	175.3	540	95.0
JH	167.6	3.98	1.16	189.0	680	93.5
PMS	107.7	2.60	1.12	195.0	480	94.8
PH	179.2	4.30	1.08	188.0	700	97.8
PM	95.4	2.91	1.05	195.8	450	92.5
PR	164.9	4.58	1.04	181.5	550	94.0
RH	184.4	4.33	0.92	188.5	650	95.0
SH	122.5	2.72	1.09	191.8	580	94.5
SS	99.2	3.01	1.04	175.8	525	94.3
AB	178.1	4.88	1.06	189.8	750	95.8
GK	135.9	3.51	1.03	187.3	490	95.5
PK	108.9	4.36	1.04	177.0	700	91.5
RC	163.6	4.41	1.05	184.5	675	96.3
RF	118.4	3.61	1.04	190.8	660	94.8
SB	147.2	3.97	1.17	190.8	740	96.0
SM	110.5	4.13	1.11	192.8	740	
CM	89.5	2.40	0.91	180.5	510	
MEAN ±SD	135.7 ± 32.2	3.73 ± .76	1.05 ± .07	186.7 ± 6.5	612 ± 102	94.7 ± 1.5

Table 16 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 90 % $\dot{V}O_2$max with salbutamol, individual subject data (n = 17)

SUBJECT	$\dot{V}E$ btps	$\dot{V}O2$ l · min $^{-1}$	RER	HR bpm	PEFR l · sec^{-1}	SaO2
90 %						
CL	116.0	3.24	1.03	171.8	515	93.3
JH	173.3	4.25	1.11	185.0	700	93.3
PMS	104.9	2.68	1.07	187.3	490	94.0
PH	162.0	4.08	1.05	182.5	725	98.0
PM	101.3	2.78	1.13	194.3	460	91.5
PR	130.0	4.43	1.00	175.0	600	94.5
RH	173.8	3.71	1.18	183.8	710	94.3
SH	130.4	3.25	0.91	190.8	560	95.5
SS	101.0	2.86	1.01	171.3	560	94.8
AB	147.4	5.06	1.04	185.0	690	95.8
GK	133.0	3.27	1.15	189.3	520	95.5
PK	105.1	4.22	1.08	178.3	700	93.3
RC	192.9	4.72	0.84	182.0	730	95.8
RF	133.7	4.17	1.01	192.5	670	93.8
SB	137.8	4.11	0.99	189.8	750	95.3
SM	112.0	4.06	1.12	192.0	760	94.8
CM	85.0	2.09	1.10	176.5	450	
MEAN ±SD	131.8 ± 30.2	3.70 ± .81	1.05 ± .09	183.9 ± 7.3	623 ± 108	94.6 ± 1.5

Table 17 $\dot{V}_E$, $\dot{V}O_2$, RER, PEFR, and SaO_2 at 25 % $\dot{V}O_2$max with placebo, individual subject data for HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l· min^{-1}	RER	HR bpm	PEFR l· sec^{-1}	SaO_2
25%						
CL	33.2	1.16	0.89	96.0	500	96.0
JH	31.8	1.14	0.78	101.3	640	96.5
PMS	26.7	0.73	0.89	113	410	97.3
PH	32.5	1.20	0.80	105.8	600	
PM	23.8	0.75	0.84	91.3	355	96.5
PR	34.8	1.49	0.78	114.5	520	96.5
RH	27.1	0.98	0.74	99.8	560	97.3
SH	24.6	0.82	0.71	110.5	545	97.8
SS	34.1	1.26	0.86	106.5	490	97.8
MEAN ±SD	29.8 ± 4.3	1.06 ± .26	0.81 ± .06	104.3 ± 7.9	513 ± 89	96.9 ± 0.7

Table 18 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 25 % $\dot{V}O_2$max with salbutamol, individual subject data for the HT group

SUBJECT	$\dot{V}_E$ BTPS	$\dot{V}O2$ l· min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
25%						
CL	32.4	1.13	0.81	90.0	490	97.3
JH	36.5	1.31	0.85	106.0	630	97.3
PMS	36.0	1.09	0.86	117.3	420	98.3
PH	36.7	1.28	0.81	108.3	710	
PM	20.0	0.67	0.77	97.3	485	94.0
PR	30.8	1.32	0.72	102.8	590	96.5
RH	24.2	0.88	0.82	98.8	660	95.8
SH	30.6	1.01	0.73	116.3	565	99.3
SS	24.4	1.00	0.76	100.3	535	98.3
MEAN ±SD	30.2 ± 6.1	1.08 ± .21	0.79 ± .05	104.1 ± 8.9	565 ± 93	97.1 ± 1.7

Table 19 $\dot{V}_E$, $\dot{V}O_2$, RER, PEFR, and SaO_2 at 50 %$\dot{V}O_2$max with placebo, individual subject data for HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l · min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
50%						
CL	53.2	2.07	0.87	133.3	520	95.75
JH	59.2	2.19	0.88	136.5	640	95.5
PMS	48.7	1.49	0.95	149.3	440	96.25
PH	52.8	2.33	0.81	144.0	675	
PM	39.2	1.51	0.85	126.8	370	96.75
PR	80.5	3.32	0.86	147.8	525	95.75
RH	45.5	1.81	0.75	136.0	610	96.5
SH	45.7	1.41	0.82	158.8	565	98
SS	47.6	1.84	0.92	125.5	480	96.5
MEAN ±SD	52.5 ± 11.9	2.00 ± .59	0.86 ±.06	139.8 ± 11.0	536 ± 98	96.4 ± .8

Table 20 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 50% $\dot{V}O_2$max with salbutamol, individual subject data for the HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ l· min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
50%						
CL	54.2	1.92	0.92	119.3	535	97.0
JH	64.2	2.32	0.98	138.0	660	97.0
PMS	46.5	1.56	0.90	138.3	490	97.3
PH	57.2	2.30	0.82	142.5	680	
PM	39.8	1.45	0.88	123.5	420	94.5
PR	59.2	2.53	0.83	132.3	600	96.5
RH	45.0	1.75	0.86	134.0	675	96.0
SH	53.7	1.72	0.78	154.3	580	98.8
SS	39.6	1.64	0.85	122.3	540	95.5
MEAN ±SD	51.0 ± 8.7	1.91 ± .38	0.87 ± .06	133.8 ± 11.1	575 ± 89	96.6 ± 1.3

Table 21 $\dot{V}_E$, $\dot{V}O_2$, RER, PEFR, and SaO_2 at 75 %$\dot{V}O_2$max with placebo, individual subject data for HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l· min^{-1}	RER	HR bpm	PEFR l· sec^{-1}	SaO_2
75%						
CL	107.3	3.31	0.99	170.5	550	95.0
JH	110.4	3.31	1.04	173.3	660	94.3
PMS	78.9	2.23	1.0475	185.5	460	95.3
PH	115.3	3.86	1.02	180.3	690	
PM	65.9	2.38	0.96	173.3	385	94.5
PR	128.0	4.30	0.99	175.0	580	94.5
RH	96.8	3.25	0.87	173.5	700	96.8
SH	114.6	2.61	1.09	191.8	600	95.8
SS	69.4	2.51	0.98	159.3	520	95.3
MEAN ±SD	98.5 ± 22.2	3.08 ± .71	1.00 ± .06	175.8 ± 9.3	571 ± 106	95.2 ± 0.8

Table 22 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 75 % $\dot{V}O_2$max with salbutamol, individual subject data for the HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ l· min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
75%						
CL	106.9	3.02	1.08	163.8	520	95.8
JH	115.4	3.55	1.07	170.8	690	96.3
PMS	71.7	2.21	0.99	170.0	485	95.3
PH	120.0	3.72	1.03	176.3	710	
PM	65.4	2.24	0.98	169.0	460	94.0
PR	95.7	3.72	0.92	160.5	610	96.5
RH	100.5	3.02	1.04	170.0	690	95.0
SH	113.3	2.98	0.94	186.3	590	97.0
SS	68.7	2.34	0.96	149.5	550	96.0
MEAN ±SD	95.3 ± 21.4	2.98 ± .61	1.00 ± .06	168.4 ± 10.2	589 ± 93	95.7 ± 0.9

Table 23 $\dot{V}_E$, $\dot{V}O_2$, RER, PEFR, and SaO_2 at 90 % $\dot{V}O_2$max with placebo, individual subject data for HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l min^{-1}	RER	HR bpm	PEFR l.· sec^{-1}	SaO_2
90%						
CL	133.4	3.70	0.95	175.3	540	95.0
JH	167.6	3.98	1.16	189.0	680	93.5
PMS	107.7	2.59	1.12	195.0	480	94.8
PH	179.2	4.29	1.08	188.0	700	
PM	95.4	2.91	1.05	195.8	450	92.5
PR	164.9	4.58	1.04	181.5	550	94.0
RH	184.4	4.33	0.92	188.5	650	95.0
SH	122.5	2.72	1.09	191.8	580	94.5
SS	99.2	3.01	1.04	175.8	525	94.3
MEAN ±SD	139.4 ± 35.2	3.57 ± .77	1.05 ± .08	186.7 ± 7.6	572 ± 87	94.2 ± 0.9

Table 24 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 90% $\dot{V}O_2$max with salbutamol, individual subject data for the HT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ l·min^{-1}	RER	HR bpm	PEFR l· sec^{-1}	SaO_2
90%						
CL	116.0	3.24	1.03	171.8	515	93.3
JH	173.3	4.25	1.11	185.0	700	93.3
PMS	104.9	2.68	1.07	187.3	490	94.0
PH	162.0	4.08	1.05	182.5	725	
PM	101.3	2.78	1.13	194.3	460	91.5
PR	130.0	4.43	1.00	175.0	600	94.5
RH	173.8	3.71	1.18	183.8	710	94.3
SH	130.4	3.25	0.91	190.8	560	95.5
SS	101.0	2.86	1.01	171.3	560	94.8
MEAN ±SD	132.5 ± 30.1	3.48 ± .66	1.05 ± .08	182.4 ± 8.2	591 ± 99	93.9 ± 1.2

Table 25 $\dot{V}_E$, $\dot{V}O_2$,RER, HR, PEFR, and SaO_2, at 25 % $\dot{V}O_2$max, individual subject data for the MT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l·min^{-1}	RER	HR bpm	PEFR l·sec^{-1}	SaO_2
25 %						
AB	39.4	1.67	0.77	117.8	730	97.25
GK	34.2	1.23	0.85	113.8	470	96
PK	29.2	1.29	0.78	85.5	600	96.75
RC	39.8	1.26	0.78	81.5	530	96.25
RF	28.4	1.17	0.72	101.8	670	
SB	32.2	1.23	0.89	97.8	620	97.25
SM	37.2	1.47	0.87	118.0	680	
CM	28.1	0.95	0.77	108.3	440	
MEAN±SD	33.6 ± 4.8	1.28 ± .21	0.80 ± .06	103.0±14.1	593 ± 103	96.9 ± 0.6

Table 26 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 25 % $\dot{V}O_2$max with salbutamol, individual subject data for the MT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ l·min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
25%						
AB	31.0	1.47	0.74	106.8	710	95.5
GK	32.0	1.24	0.87	111.5	510	96.5
PK	35.3	1.37	0.91	89.0	640	96
RC	39.5	1.32	0.72	89.8	640	97.5
RF	26.3	1.03	0.78	104.8	650	97.8
SB	32.1	1.30	0.85	106.0	720	97.8
SM	38.6	1.55	0.87	125.5	710	95.8
CM	26.1	0.92	0.82	106.0	450	
MEAN± SD	32.6 ± 5.0	1.27 ± .21	0.82 ± .07	104.9±11.7	628 ± 99	96.7 ± .9

Table 27 $\dot{V}_E$, $\dot{V}O_2$ RER, HR, PEFR, and SaO_2 at 50 % $\dot{V}O_2$max with placebo, individual subject data for MT group.

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l·min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
50%						
AB	61.0	2.65	0.84	144.5	700	97.0
GK	59.7	2.03	0.96	145.8	480	96.3
PK	44.3	1.91	0.82	109.3	615	96.0
RC	70.1	2.43	0.91	114.3	585	96.8
RF	49.5	1.97	0.83	134.5	650	97.3
SB	53.3	2.11	0.95	134.5	670	97.5
SM	50.7	2.19	0.90	142.3	705	97.0
CM	37.9	1.34	0.82	122.5	420	
MEAN ±SD	53.3 ± 10.1	2.08 ± .39	0.88 ± .06	130.9 ± 14.0	603 ± 104	96.8 ± 0.5

Table 28 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 50 % $\dot{V}O_2$max with salbutamol, individual subject data for the MT group

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O_2$ l · min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
50%						
AB	56.9	2.64	0.82	138.5	690	96.25
GK	52.7	1.83	1.03	145.3	510	96.75
PK	41.9	1.84	0.90	112.0	670	96.5
RC	69.4	2.42	0.77	120.0	700	97.3
RF	48.1	1.94	0.80	140.8	660	97
SB	54.6	2.12	0.92	141.0	710	97.3
SM	59.0	2.34	1.01	151.5	720	95.8
CM	38.5	1.33	0.90	132.3	460	
MEAN± SD	52.6 ± 9.8	2.06 ± .41	0.89 ± .09	135.2 ±13.2	640 ± 98	96.7 ± .6

Table 29 $\dot{V}_E$, $\dot{V}O_2$ RER, HR, PEFR, and SaO_2 at 75 % $\dot{V}O_2$max with Placebo, individual subject data for MT group.

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ l·min^{-1}	RER	HR bpm	PEFR l · sec^{-1}	SaO_2
75%						
AB	110.6	3.99	0.98	172.3	715	96.8
GK	91.6	2.95	1.03	172.0	495	96.3
PK	71.8	3.44	0.90	150.0	620	94.3
RC	120.3	3.62	1.01	161.3	640	
RF	79.0	3.00	0.92	168.0	660	95.5
SB	90.5	3.25	1.04	171.3	730	96.3
SM	81.5	3.47	1.01	179.5	735	96.3
CM	63.0	1.95	0.90	160.8	510	
MEAN ±SD	88.5 ± 19.2	3.21 ± .61	0.97 ± .06	166.9 ± 9.2	638 ± 94	95.9 ± 0.9

Table 30 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 75 % $\dot{V}O_2$max with salbutamol, individual subject data for the MT group

SUBJECT	$\dot{V}E$ btps	$\dot{V}O_2$ l·min^{-1}	RER	HR bpm	PEFR l·sec^{-1}	SaO_2
75%						
AB	102.0	4.16	0.95	171.5	720	96
GK	94.3	2.81	1.11	176.0	500	95.25
PK	70.7	3.28	0.97	154.3	680	95.5
RC	125.7	3.74	0.81	159.5	700	
RF	84.1	3.13	0.89	175.3	670	95.8
SB	88.9	3.23	1.01	173.8	730	97.0
SM	89.3	3.45	1.07	182.3	740	95.3
CM	66.5	1.89	1.03	165.3	470	
MEAN±SD	90.2 ± 18.5	3.21 ± .67	0.98± .10	169.7 ± 9.3	651 ± 106	95.8 ± .7

Table 31 $\dot{V}_E$, $\dot{V}O_2$ RER, HR, PEFR, and SaO_2at 90 % $\dot{V}O_2$max with placebo, individual subject data for MT group.

SUBJECT	$\dot{V}_E$ btps	$\dot{V}O2$ $l \cdot min^{-1}$	RER	HR bpm	PEFR $l \cdot sec^{-1}$	SaO_2
90%						
AB	178.1	4.88	1.06	189.8	750	95.8
GK	135.9	3.51	1.03	187.3	490	95.5
PK	108.9	4.36	1.04	177.0	700	91.5
RC	163.6	4.41	1.05	184.5	675	96.3
RF	118.4	3.61	1.04	190.8	660	94.8
SB	147.2	3.97	1.17	190.8	740	96.0
SM	110.5	4.13	1.11	192.8	740	95.8
CM	89.5	2.40	0.91	180.5	510	
MEAN ±SD	131.5 ± 30.1	3.91 ± .75	1.05 ± .07	186.7 ± 5.6	658 ± 103	95.1 ± 1.6

Table 32 $\dot{V}_E$, $\dot{V}O_2$, RER, HR, PEFR, and SaO_2 at 90 % $\dot{V}O_2$max with salbutamol, individual subject data for the MT group

SUBJECT	VE BTPS	VO2 $l \cdot min^{-1}$	RER	HR bpm	PEFR $l \cdot sec^{-1}$	SaO_2
90%						
AB	147.4	5.06	1.04	185.0	690	95.8
GK	133.0	3.27	1.15	189.3	520	95.5
PK	105.1	4.22	1.08	178.3	700	93.3
RC	192.9	4.72	0.84	182.0	730	95.8
RF	133.7	4.17	1.01	192.5	670	93.8
SB	137.8	4.11	0.99	189.8	750	95.3
SM	112.0	4.06	1.12	192.0	760	94.8
CM	85.0	2.09	1.10	176.5	450	
MEAN ±SD	130.9 ± 32.3	3.96 ± .92	1.04 ± .10	185.7 ± 6.2	658 ± 113	94.8 ± 1.0

Table 33 Pre and post medication and recovery PEFR measures with placebo, individual subject data (N = 17)

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
CL	525	503	530	520	510	500
JH	623	621	660	650	610	620
PMS	447	443	430	440	430	430
PH	630	633	700	665	635	660
PM	338	362	390	390	370	375
PR	520	500	540	520	470	480
RH	603	610	650	640	635	640
SH	545	533	565	540	540	540
SS	512	500	490	495	490	490
AB	673	673	710	710	700	660
GK	437	427	450	440	400	400
PK	602	613	650	620	610	620
RC	562	503	560	510	500	500
RF	640	632	660	660	640	640
SB	647	612	675	670	670	650
SM	687	667	670	660	640	550
CM	460	433	410	425	440	440
MEAN ±SD	556 ± 96	545 ± 95	573 ± 108	562 ± 103	546 103	541 ± 97

Table 34 Pre and post medication and recovery PEFR measures with salbutamol, individual subject data (N = 17)

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
CL	480	483	520	540	500	500
JH	615	630	640	610	570	630
PMS	427	443	450	465	475	475
PH	662	690	725	700	690	725
PM	342	403	440	425	420	415
PR	550	567	580	570	570	560
RH	637	667	700	675	670	665
SH	547	548	560	540	560	540
SS	500	533	540	530	550	535
AB	693	667	700	680	680	690
GK	473	500	510	510	505	470
PK	600	643	680	640	640	670
RC	622	670	690	660	680	680
RF	628	633	670	660	640	590
SB	653	663	720	700	700	700
SM	695	717	710	585	610	700
CM	460	433	460	430	440	435
MEAN ±SD	564 ± 102	582 ± 100	605 ± 103	584 ± 92	582 ± 91	587 ± 103

Table 35 Pre and post medication and recovery PEFR measures with placebo, individual subject data for the HT group

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
HT group						
CL	525	503	530	520	510	500
JH	623	621	660	650	610	620
PMS	447	443	430	440	430	430
PH	630	633	700	665	635	660
PM	338	362	390	390	370	375
PR	520	500	540	520	470	480
RH	603	610	650	640	635	640
SH	545	533	565	540	540	540
SS	512	500	490	495	490	490
MEAN ±SD	527 ± 92	523 ± 89	551 ± 105	540 ± 96	521± 93	526 ± 98

Table 36 Pre and post medication and recovery PEFR measures with salbutamol, individual subject data for the HT group

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
HT group						
CL	480	483	520	540	500	500
JH	615	630	640	610	570	630
PMS	427	443	450	465	475	475
PH	662	690	725	700	690	725
PM	342	403	440	425	420	415
PR	550	567	580	570	570	560
RH	637	667	700	675	670	665
SH	547	548	560	540	560	540
SS	500	533	540	530	550	535
MEAN ±SD	529 ± 104	552 ± 99	573 ± 100	562 ± 89	556 ± 86	560 ± 97

Table 37 Pre and post medication and recovery PEFR measures with placebo, individual subject data for the MT group

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
MT group						
AB	673	673	710	710	700	660
GK	437	427	450	440	400	400
PK	602	613	650	620	610	620
RC	562	503	560	510	500	500
RF	640	632	660	660	640	640
SB	647	612	675	670	670	650
SM	687	667	670	660	640	550
CM	460	433	410	425	440	440
MEAN ±SD	589 ± 95	570 ±101	598 ± 113	587 ± 112	575 113	558 ± 101

Table 38 Pre and post medication and recovery PEFR measures with salbutamol, individual subject data for the MT group

SUBJECT	Pre- med. PEFR	Post-med. PEFR	3 min PEFR	5 min PEFR	10 min PEFR	15 min PEFR
MT group						
AB	693	667	700	680	680	690
GK	473	500	510	510	505	470
PK	600	643	680	640	640	670
RC	622	670	690	660	680	680
RF	628	633	670	660	640	590
SB	653	663	720	700	700	700
SM	695	717	710	585	610	700
CM	460	433	460	430	440	435
MEAN ±SD	603 ± 91	616 ± 97	643 ± 99	608 ± 94	612 ± 92	617 ± 108

Table 39 Blood lactates ($mmol \cdot l^{-1}$) at 25, 50, 75, and 90 % $\dot{V}O_2max$ with placebo, individual subject data (n = 17)

Lactate ($mmol \cdot l^{-1}$) Subjects	Placebo 25 %	50 %	75 %	90 %
CL	1.30	1.53	6.34	7.27
JH	1.23	1.91	6.46	19.04
PMS	1.42	1.87	6.13	9.07
PH	0.97	1.55	8.86	14.83
PM	1.83	1.47	3.66	13.48
PR	1.26	2.05	8.12	8.79
RH	0.82	0.82	4.84	18.15
SH	0.63	1.02	8.90	11.76
SS	0.56	1.46	4.45	9.72
AB	1.69	2.08	5.85	15.16
GK	2.77	3.40	7.73	11.93
PK	1.06	1.34	2.17	6.86
RC	0.93	0.88	3.33	7.24
RF	0.87	1.08	4.24	11.95
SB	1.83	2.42	5.90	11.61
SM	0.56	1.07	3.43	6.72
CM	0.75	0.93	1.79	5.61
MEAN ± SD	1.20 ± .58	1.58 ± .67	5.42 ± 2.20	11.13 ± 4.02

Table 40 Blood lactate ($mmol \cdot l^{-1}$) measures at rest and recovery conditions with placebo, individual subject data (n = 17)

Lactate ($mmol \cdot l^{-1}$)	Rest Placebo	1 min	3 min	5 min	10 min
Subjects					
JH	0.94	17.22	16.03	18.15	15.69
PH	0.84	13.61	13.19	12.22	10.08
PR	1.34	9.18	7.84	6.07	6.46
RH	1.11	15.68	15.34	13.36	12.05
AB	1.00	13.47	15.41	13.94	10.26
GK	1.13	10.96	8.78	10.33	8.69
PK	1.18	7.37	7.80	7.49	6.07
RC	0.44	7.53	7.43	7.43	3.33
RF	0.56	13.38	11.26	12.21	7.53
SB	1.36	12.58	16.16	14.95	14.91
SM	0.37	8.71	7.18	7.83	4.68
CL	0.93	7.36	6.90	10.33	7.41
PMS	1.47	12.36	10.13	7.15	6.64
PM	1.22	13.22	12.00	10.58	10.48
SH	0.87	15.05	12.10	12.34	8.08
SS	0.64	8.34	9.35	6.92	5.24
CM	0.64	3.52	4.6	4.64	3.89
MEAN ± SD	0.94 ± .33	11.15 ± 3.66	10.68 ± 3.62	10.35 ± 3.63	8.32 ± 3.57

Table 41 Blood lactates (mmol·l^{-1}) at 25, 50, 75, and 90 % $\dot{V}O_2$max with salbutamol, individual subject data (n = 17)

Lactate (mmol · l^{-1})	Salbutamol 25 %	50 %	75 %	90 %
Subjects				
CL	0.39	1.17	7.97	8.26
JH	0.76	2.42	8.73	17.62
PMS	1.18	1.39	4.28	8.86
PH	0.57	1.50	6.03	7.74
PM	0.91	1.77	3.29	12.67
PR	0.27	0.22	2.49	4.28
RH	2.85	2.59	8.85	16.63
SH	1.08	1.43	8.57	11.52
SS	0.95	1.73	3.74	7.64
AB	1.02	1.74	5.99	7.95
GK	0.97	1.63	5.59	9.98
PK	0.49	0.80	2.45	8.95
RC	1.57	2.13	6.58	9.73
RF	3.18	1.21	4.14	13.48
SB	1.93	2.08	9.93	16.42
SM	0.59	0.83	3.81	6.55
CM	0.60	0.95	3.78	6.72
MEAN ± SD	1.14 ± 0.82	1.51 ± 0.62	5.66 ± 2.42	10.29 ± 3.87

Table 42 Blood lactate ($mmol \cdot l^{-1}$) measures at rest and recovery conditions with salbutamol, individual subject data (n = 17)

Lactate ($mmol \cdot l^{-1}$)	Rest Salbutamol	1 min	3 min	5 min	10 min
Subjects					
CL	9.10	10.47	9.05	6.60	0.20
JH	16.66	19.31	18.88	19.04	0.66
PMS	8.99	6.09	7.06	5.50	0.80
PH	10.51	8.49	6.42	5.50	1.06
PM	12.16	12.87	9.48	7.09	0.91
PR	4.94	8.28	3.88	3.07	0.36
RH	21.46	17.39	18.31	15.10	2.14
SH	12.17	13.51	11.69	9.53	0.87
SS	8.75	8.00	7.80	7.33	0.75
AB	9.14	7.06	6.84	4.21	1.23
GK	9.15	10.51	7.30	9.19	0.22
PK	9.93	9.09	8.70	7.53	0.36
RC	9.26	8.43	9.08	6.21	1.34
RF	12.57	12.07	11.71	8.94	0.91
SB	16.72	13.68	14.95	14.34	1.17
SM	9.63	8.66	8.02	6.31	0.29
CM	7.71	7.66	7.22	4.68	0.65
MEAN ± SD	11.11 ± 3.97	10.68 ± 3.67	9.79 ± 4.14	8.24 ± 4.24	0.82 ± 0.49

Table 43 Blood lactates (mmol·l^{-1}) at 25, 50, 75, and 90 % $\dot{V}O_2$max with placebo, individual subject data for the HT group

Lactate (mmol·l^{-1})	Salbutamol 25 %	50 %	75 %	90 %
Subjects				
CL	1.30	1.53	6.34	7.27
JH	1.23	1.91	6.46	19.04
PMS	1.42	1.87	6.13	9.07
PH	0.97	1.55	8.86	14.83
PM	1.83	1.47	3.66	13.48
PR	1.26	2.05	8.12	8.79
RH	0.82	0.82	4.84	18.15
SH	0.63	1.02	8.90	11.76
SS	0.56	1.46	4.45	9.72
MEAN ± SD	1.11 ± 0.41	1.52 ± 0.40	6.42 ± 1.91	12.46 ± 4.22

Table 44 Blood lactate (mmol·l^{-1}) measures at rest and recovery conditions with placebo, individual subject data for the HT group

Lactate (mmol·l^{-1})	Rest Placebo	1 min	3 min	5 min	10 min
Subjects					
CL	0.93	7.36	6.90	10.33	7.41
JH	0.94	17.22	16.03	18.15	15.69
PMS	1.47	12.36	10.13	7.15	6.64
PH	0.84	13.61	13.19	12.22	10.08
PM	1.22	13.22	12.00	10.58	10.48
PR	1.34	9.18	7.84	6.07	6.46
RH	1.11	15.68	15.34	13.36	12.05
SH	0.87	15.05	12.10	12.34	8.08
SS	0.64	8.34	9.35	6.92	5.24
MEAN ± SD	1.04 ± 0.27	12.45 ± 3.45	11.43 ± 3.16	10.79 ± 3.81	9.12 ± 3.29

Table 45 Blood lactates (mmol·l^{-1}) at 25, 50, 75, and 90 % $\dot{V}O_2$max with salbutamol, individual subject data for the HT group

Lactate (mmol · l^{-1})	Salbutamol 25 %	50 %	75 %	90 %
Subjects				
CL	0.39	1.17	7.97	8.26
JH	0.76	2.42	8.73	17.62
PMS	1.18	1.39	4.28	8.86
PH	0.57	1.50	6.03	7.74
PM	0.91	1.77	3.29	12.67
PR	0.27	0.22	2.49	4.28
RH	2.85	2.59	8.85	16.63
SH	1.08	1.43	8.57	11.52
SS	0.95	1.73	3.74	7.64
MEAN ± SD	1.00 ± 0.76	1.58 ± 0.70	5.99 ± 2.59	10.58 ± 4.42

Table 46 Blood lactate (mmol·l^{-1}) measures at rest and recovery conditions with salbutamol, individual subject data for the HT group

Lactate (mmol·l^{-1})	Rest Salbutamol	1 min	3 min	5 min	10 min
Subjects					
CL	0.20	9.10	10.47	9.05	6.60
JH	0.66	16.66	19.31	18.88	19.04
PMS	0.80	8.99	6.09	7.06	5.50
PH	1.06	10.51	8.49	6.42	5.50
PM	0.91	12.16	12.87	9.48	7.09
PR	0.36	4.94	8.28	3.88	3.07
RH	2.14	21.46	17.39	18.31	15.10
SH	0.87	12.17	13.51	11.69	9.53
SS	0.75	8.75	8.00	7.80	7.33
MEAN ± SD	0.86 ± 0.55	11.64 ± 4.88	11.69 ± 4.69	10.57 ± 5.75	8.75 ± 5.12

Table 47 Blood lactates (mmol·l^{-1}) at 25, 50, 75, and 90 % $\dot{V}O_2$max with placebo, individual subject data for the MT group

Lactate (mmol·l^{-1})	Placebo 25 %	50 %	75 %	90 %
Subjects				
GK	2.77	3.40	7.73	11.93
PK	1.06	1.34	2.17	6.86
RC	0.93	0.88	3.33	7.24
RF	0.87	1.08	4.24	11.95
SB	1.83	2.42	5.90	11.61
SM	0.56	1.07	3.43	6.72
CM	0.75	0.93	1.79	5.61
MEAN ± SD	131 ± .74	1.65 ± 0.90	4.30 ± 2.04	9.63 ± 3.45

Table 48 Blood lactate (mmol·l^{-1}) measures at rest and recovery conditions with placebo, individual subject data for the MT group

Lactate (mmol·l^{-1})	Rest Placebo	1 min	3 min	5 min	10 min
subjects					
AB	1.00	13.47	15.41	13.94	10.26
GK	1.13	10.96	8.78	10.33	8.69
PK	1.18	7.37	7.80	7.49	6.07
RC	0.44	7.53	7.43	7.43	3.33
RF	0.56	13.38	11.26	12.21	7.53
SB	1.36	12.58	16.16	14.95	14.91
SM	0.37	8.71	7.18	7.83	4.68
CM	0.64	3.52	4.60	4.64	3.89
MEAN ± SD	0.84 ± 0.38	9.69 ± 3.53	9.83 ± 4.12	9.85 ± 3.61	7.42 ± 3.86

Table 49 Blood lactates (mmol·l^{-1}) at 25, 50, 75, and 90 % VO_2max with salbutamol, individual subject data for the MT group

Lactate	Salbutamol			
(mmol·l^{-1})	25 %	50 %	75 %	90 %
Subjects				
AB	1.02	1.74	5.99	7.95
GK	0.97	1.63	5.59	9.98
PK	0.49	0.80	2.45	8.95
RC	1.57	2.13	6.58	9.73
RF	3.18	1.21	4.14	13.48
SB	1.93	2.08	9.93	16.42
SM	0.59	0.83	3.81	6.55
CM	0.60	0.95	3.78	6.72
MEAN ± SD	1.29 ± .91	1.42 ± .55	5.28 ± 2.32	9.97 ± 3.40

Table 50 Blood lactate (mmol·l^{-1}) measures at rest and recovery conditions with salbutamol, individual subject data for the MT group

Lactate	Rest	1 min	3 min	5 min	10 min
(mmol·l^{-1})	Salbutamol				
Subjects					
AB	1.23	9.14	7.06	6.84	4.21
GK	0.22	9.15	10.51	7.30	9.19
PK	0.36	9.93	9.09	8.70	7.53
RC	1.34	9.26	8.43	9.08	6.21
RF	0.91	12.57	12.07	11.71	8.94
SB	1.17	16.72	13.68	14.95	14.34
SM	0.29	9.63	8.66	8.02	6.31
CM	0.65	7.71	7.66	7.22	4.68
MEAN ± SD	.77 ± .45	10.52 ± 2.85	9.64 ± 2.28	9.23 ± 2.78	7.68 ± 3.24

Table 51 The duration of exercise test with salbutamol and placebo, individual subject data (n = 17)

Subjects	Salbutamol	Placebo
CL	16.2	15.5
JH	19.2	20.0
PMS	19.1	16.5
PH	15.3	17.2
PM	20.0	20.0
PR	20.0	16.5
RH	20.0	20.0
SH	16.1	16.3
SS	20.0	20.0
AB	20.0	20.0
GK	17.1	17.1
PK	20.0	20.0
RC	17.3	17.3
RF	20.0	20.0
SB	20.0	20.0
SM	17.1	17.1
CM	16.4	20.0
MEAN ± SD	18.5 ± 1.8	18.4 ± 1.8

Table 52 The duration of exercise test with salbutamol and placebo, individual subject data for the HT and MT groups

Subjects	Placebo Time (min)	Salbutamol	Subjects	Placebo Time (min)	Salbutamol
HT group			MT group		
CL	15.5	16.2	AB	20.0	20.0
JH	20.0	19.2	GK	17.1	17.1
PMS	16.5	19.1	PK	20.0	20.0
PH	17.2	15.3	RC	17.3	17.3
PM	20.0	20.0	RF	20.0	20.0
PR	16.5	20.0	SB	20.0	20.0
RH	20.0	20.0	SM	17.1	17.1
SH	16.3	16.1	CM	20.0	16.4
SS	20.0	20.0			
MEAN ±SD	18.0 ± 1.9	18.4 ± 2.0		18.9 ± 1.46	18.5 ± 1.7

Table 53 RMANOVA Summary (N= 17)

Effect	DEPENDENT VARIABLES				
	$\dot{V}O_2$ $l \cdot min^{-1}$	$\dot{V}_E$ $l \cdot min^{-1}$	HR bpm	RER	SaO_2
Sex (S)	p = .000 *	p =.008*	p = .843	p = .903	p = .950
Drug (D)	p = .531	p = .492	p= .138	p = .936	p = .747
Trained (T)	p = .902	p = .786	p = .137	p = .971	p = .574
condition (C)	p = .000	p = .000	p = .000	p = .000	p = .000
D X S	p = .927	p = .738	p = .209	p = .764	p = .994
D X T	p = .439	p = .482	p =.003*	p = .851	p = .777
D X C X T	p = .454	p = .283	p = .007*	p = .553	p = .422
D X C X S	p = .578	p = .786	p= .289	p = .274	p = .332

α^* $p < 0.05$

Table 54 RMANOVA Summary for PEFR and Blood lactate measurements

Effect	DEPENDENT VARIALBLES	
	PEFR $l \cdot sec^{-1}$	LACTATE $(mmol \cdot l^{-1})$
Drug(D)	p = .002*	p = .688
Sex(S)	p = .000*	p = .259
Trained(T)	p = .215	p = .342
Condition(C)	p = .000*	p = .000*
D X S	p = .334	p = .816
D X T	p = .875	p = .517
D X C	p = .001*	p = .838
D X C XT	p = .247	p = .369
D X C X S	p = .392	p = .947

$\alpha = p < 0.05$

Table 55 RMANOVA summary for the HT group

Effect	DEPENDENT VARIABLES				
	$\dot{V}O_2$ $l \cdot min^{-1}$	$\dot{V}_E$ $l \cdot min^{-1}$	HR bpm	RER	SaO_2
Drug (D)	p=.429	p=.345	p=.010*	p=1.00	p=.699
Condition (C)	p=.000*	p=.000*	p=.000*	p=.000*	p=.000*
D X C	p=.436	p=.243	p=.002*	p=.740	p=.322

Effect	DEPENDENT VARIABLES	
	PEFR $l \cdot sec^{-1}$	Lactate $mmol \cdot l^{-1}$
Drug (D)	p=.009*	p=.463
Condition (C)	p=.000*	p=.000*
D X C	p= .031*	p=.382

* $p < 0.05$

Table 56 RMANOVA summary for the MT group

Effect	DEPENDENT VARIABLES				
	$\dot{V}O_2$ $l \cdot min^{-1}$	$\dot{V}_E$ $l \cdot min^{-1}$	HR bpm	RER	SaO_2
Drug (D)	p=.869	p=.945	p=.146	p=.819	p=.955
Condition (C)	p=.000*	p=.000*	p=.000*	p=.000*	p=.015*
D X C	p=.825	p=.915	p=.075	p=.749	p=.762

Effect	DEPENDENT VARIABLES	
	PEFR $l \cdot sec^{-1}$	Lactate $mmol \cdot l^{-1}$
Drug (D)	p=.078	p=.836
Condition (C)	p=.000*	p=.000*
D X C	p=.806	p=.027*

* $p < 0.05$

Table 57 RMANOVA summary for subjects with a PC_{20} < 4.0 mg/ml

EFFECT	DEPENDENT VARIABLES				
	$\dot{V}O_2$ $l \cdot min^{-1}$	$\dot{V}E$ $l \cdot min^{-1}$	HR bpm	RER	SaO_2
Drug (D)	p =.058	p =.717	p =.206	p =.806	p =.336
Condition(C)	p =.000*	p =.000*	p =.000*	p =.000*	p =.000*
D X C	p =.395	p =.663	p =.477	p =.110	p=.983

	DEPENDENT VARIABLES	
Effect	PEFR $l \cdot sec^{-1}$	Lactate $mmol \cdot l^{-1}$
Drug (D)	p =.031*	p =.477
D x C	p =.047*	p =.470

*p < 0.05

Table 58 Baseline Spirometry for the HT group

HT GROUP	FVC	FEV_1	$FEV_1/FVC\%$
CL	5.09	4.34	85
JH	6.32	5.22	83
PMS	4.19	3.49	83
PH	4.53	3.84	85
PM	3.77	2.54	67
PR	5.00	3.53	71
RH	5.31	4.91	92
SH	4.15	3.62	87
SS	4.34	3.71	85
MEAN ± SD	4.74 ± 0.78	3.91 ± 0.81	82 ± 7.9

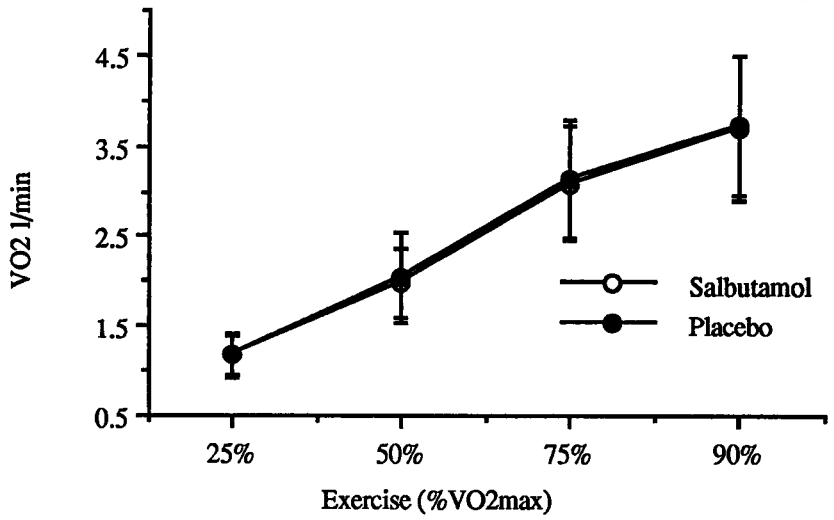
Table 59 Baseline Spirometry for the MT group

MT GROUP	FVC	FEV_1	$FEV_1/FVC\%$
AB	8.37	6.24	75
GK	5.61	4.05	72
PK	6.56	5.17	78
RC	6.30	4.06	64
RF	5.91	4.96	83
SB	6.00	4.96	83
SM	6.94	6.20	89
CM	3.91	3.30	82
MEAN ± SD	6.20 ± 1.26	4.87 ± 1.04	78 ± 7.7

APPENDIX C

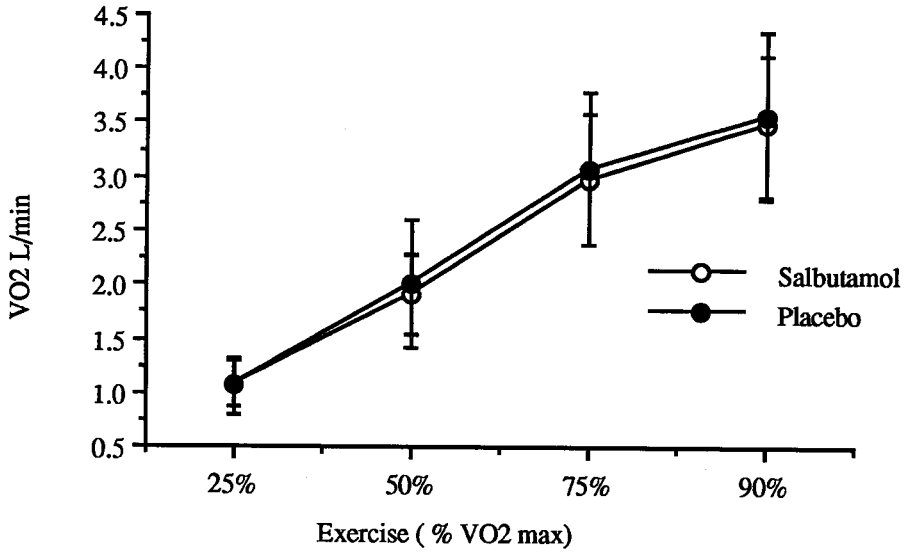
Figures

Figure 7. $\dot{V}O_2$ ($l \cdot min^{-1}$) responses at various exercise intensities (% $\dot{V}O_2max$), all subjects data (n = 17)



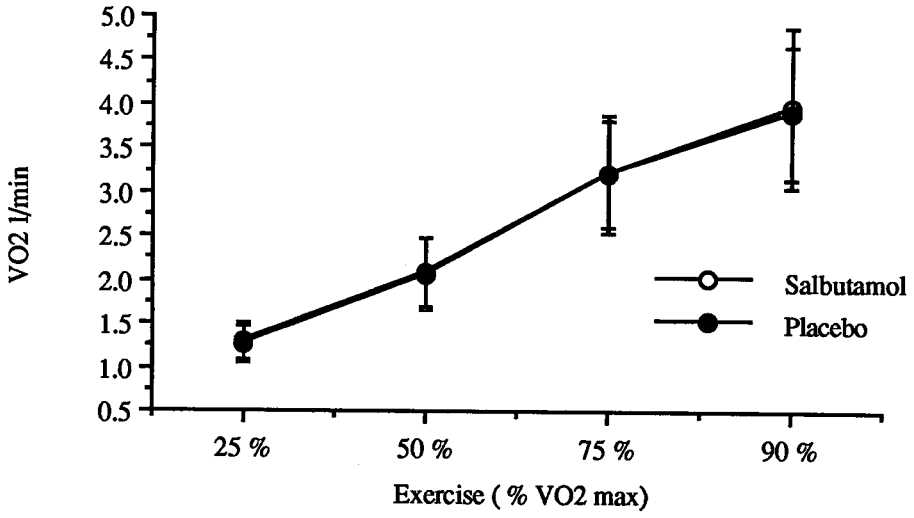
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p=0.531

Figure 8. $\dot{V}O_2$ ($l \cdot min^{-1}$) responses at various exercise intensities ($\%\dot{V}O_2max$), HT subjects data



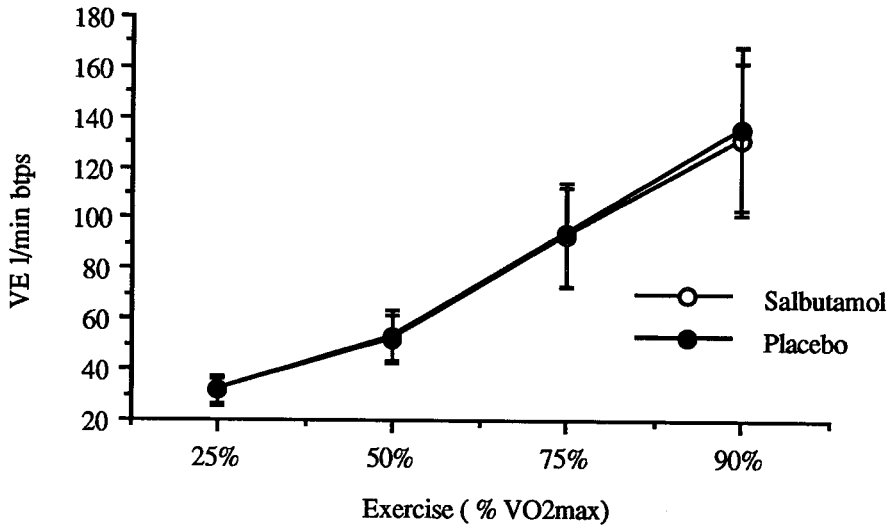
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .429

Figure 9. $\dot{V}O_2$ ($l \cdot min^{-1}$) responses at various exercise intensities (%$\dot{V}O_2max$), MT subjects data



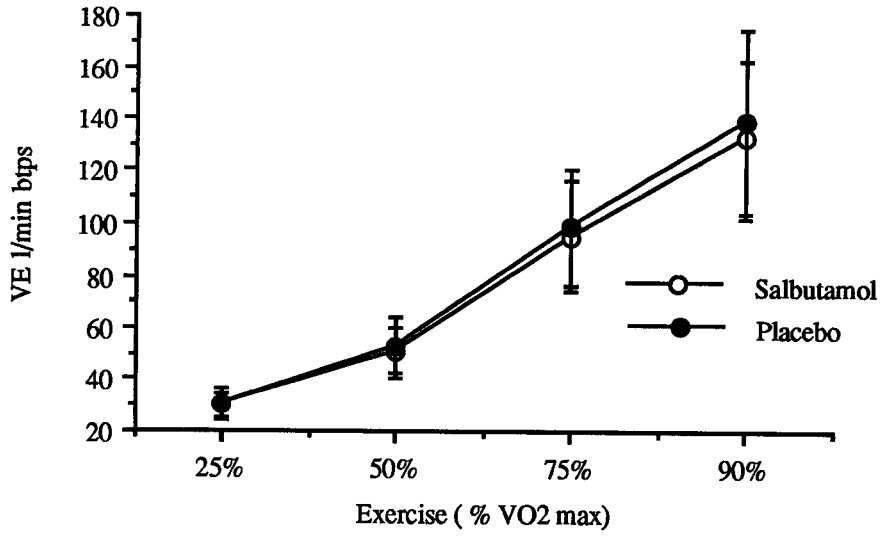
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .869

Figure 10. $\dot{V}E$ ($l \cdot min^{-1}$)responses at various exercise intensities (%$\dot{V}O_2max$), all subject data (n = 17)



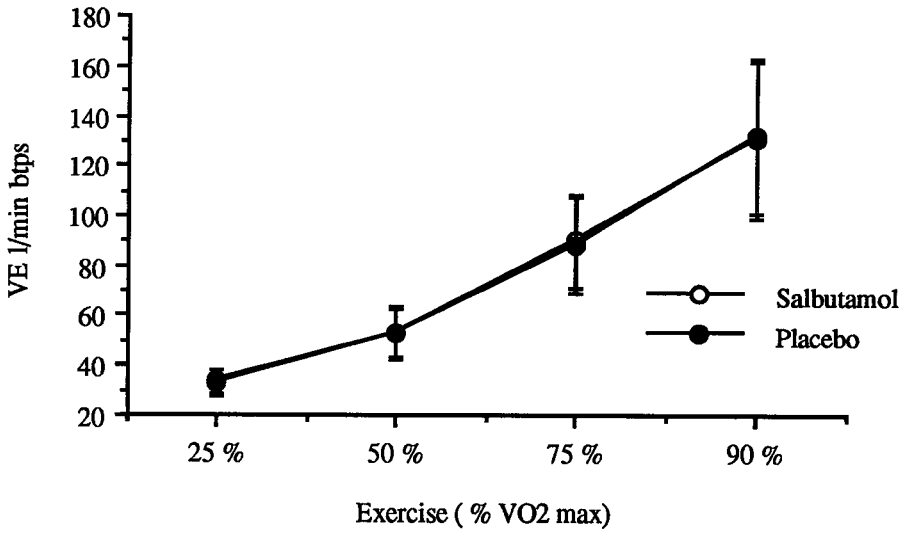
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .492

Figure 11. $\dot{V}_E$ ($l \cdot min^{-1}$)responses at various exercise intensities (%$\dot{V}O_2max$), HT subject data



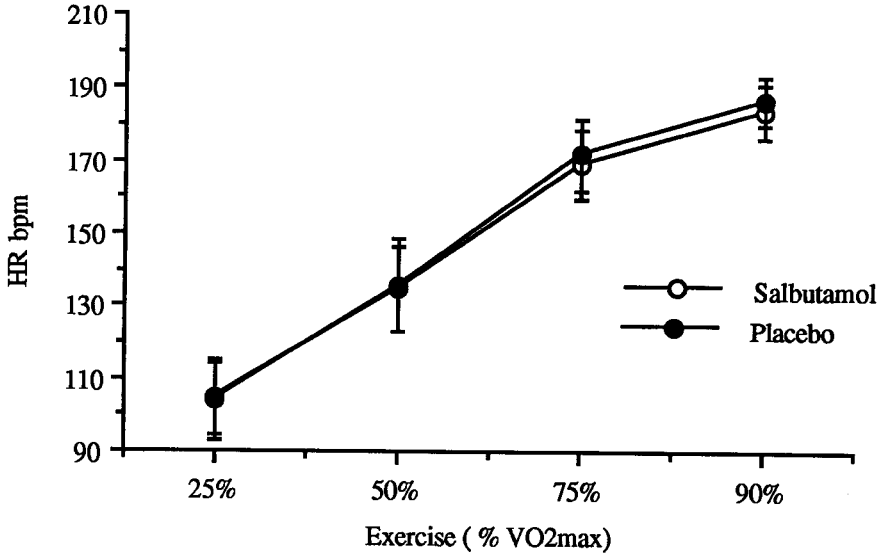
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .345

Figure 12. $\dot{V}_E$ ($l \cdot min^{-1}$)responses at various exercise intensities (%$\dot{V}$ O_2max), MT subject data



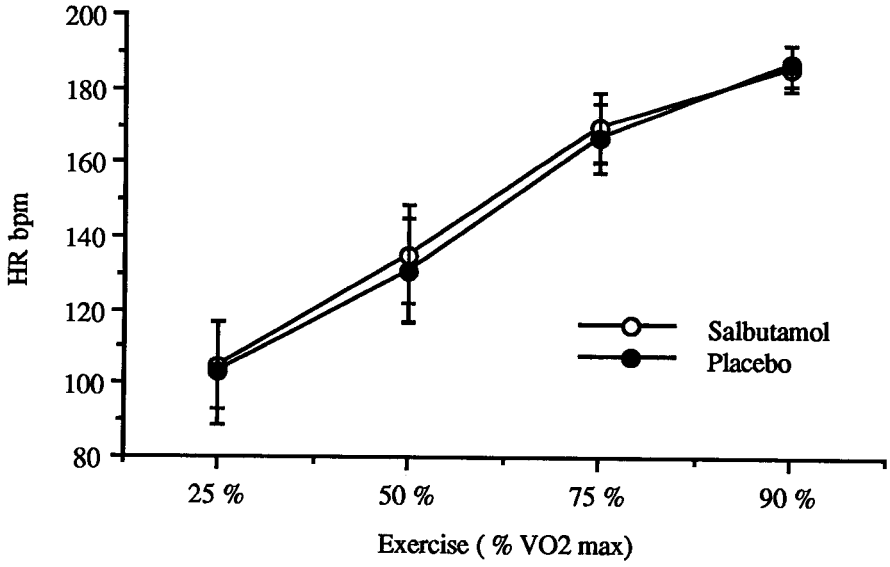
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .945

Figure 13. HR (bpm) responses at various exercise intensities (%$\dot{V}O_2$max), all subject data (n = 17)



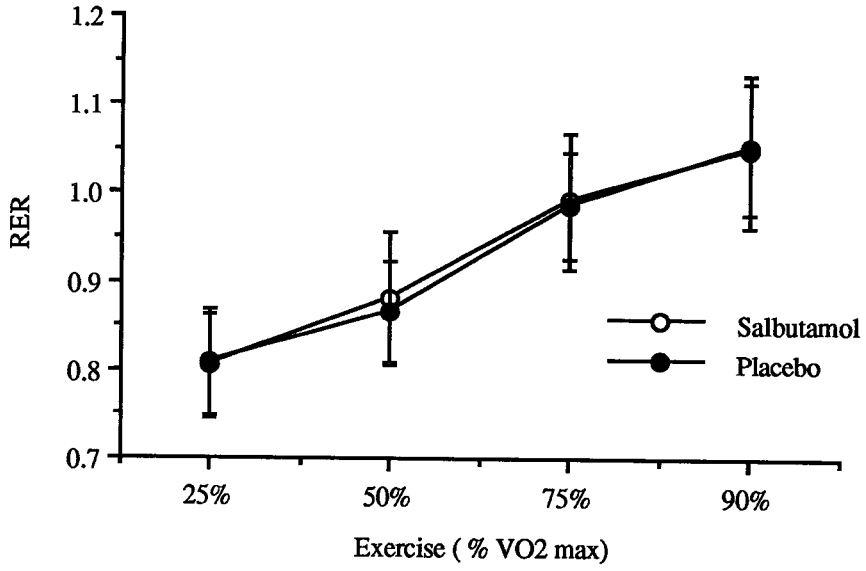
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .138

Figure 14. HR (bpm) responses at various exercise intensities (%$\dot{V}O_2$max), MT subject data



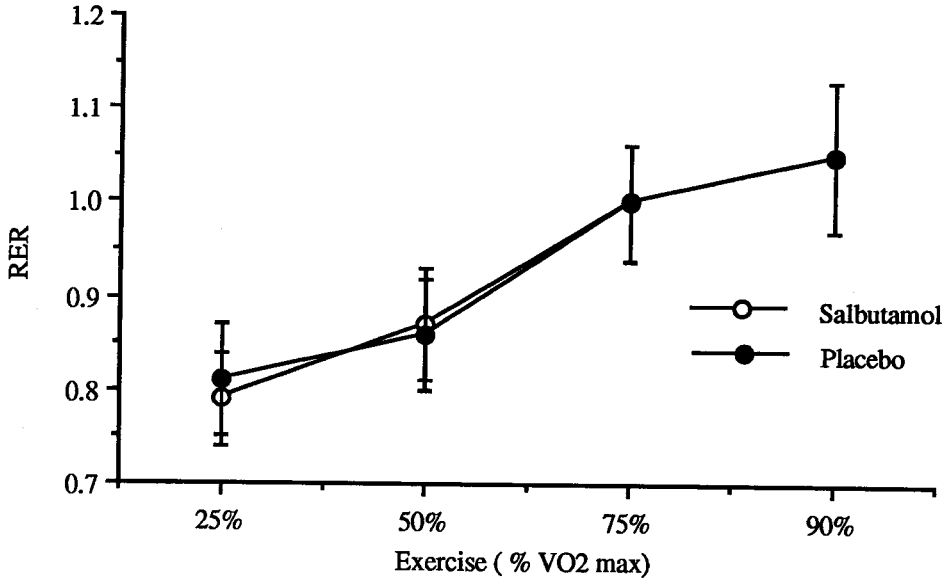
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p =.146

Figure 15. RER responses at various exercise intensities (%$\dot{V}O_2$max), all subject data (n = 17)



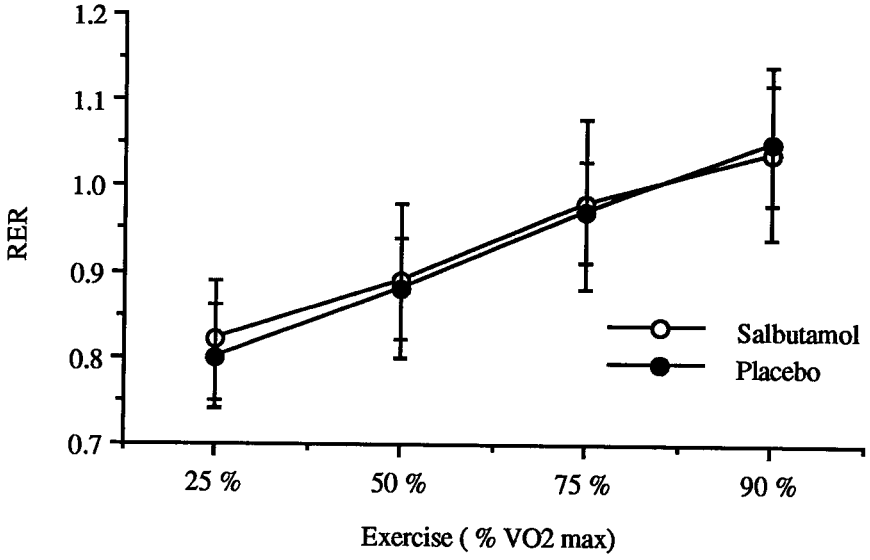
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p =.936

Figure 16. RER responses at various exercise intensities (%$\dot{V}O_2$max), HT subject data



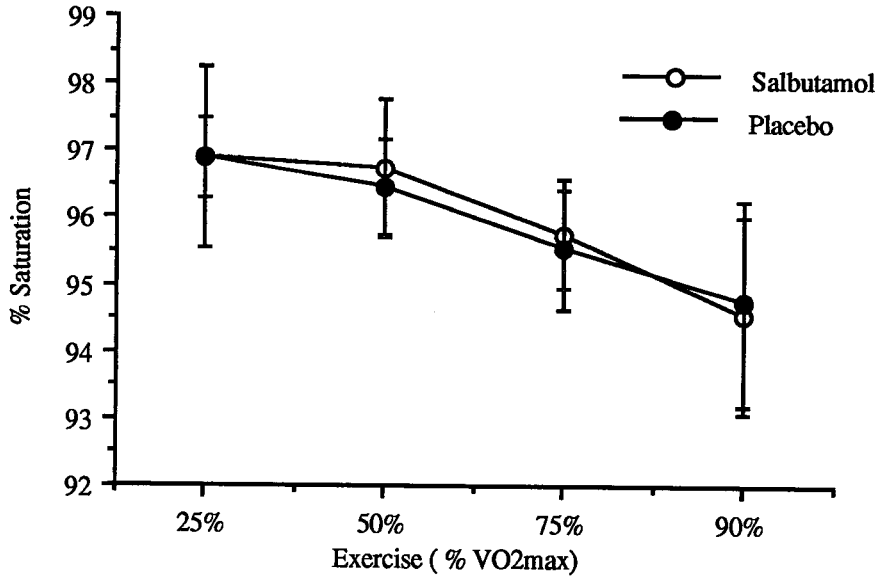
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p =1.00

Figure 17. RER responses at various exercise intensities (%$\dot{V}O_2$max), MT subject data



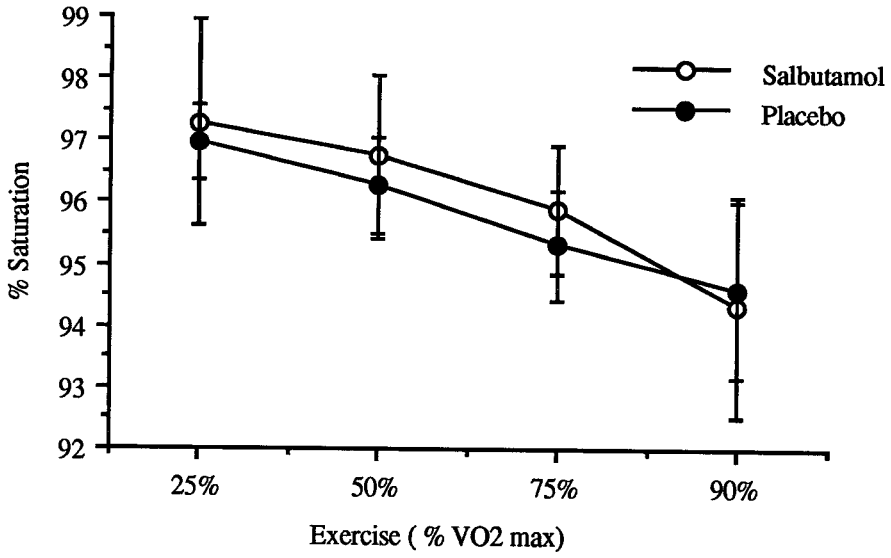
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .819

Figure 18. SaO_2 measures at various exercise intensities (%$\dot{V}O_2$max), all subject data (n = 17)



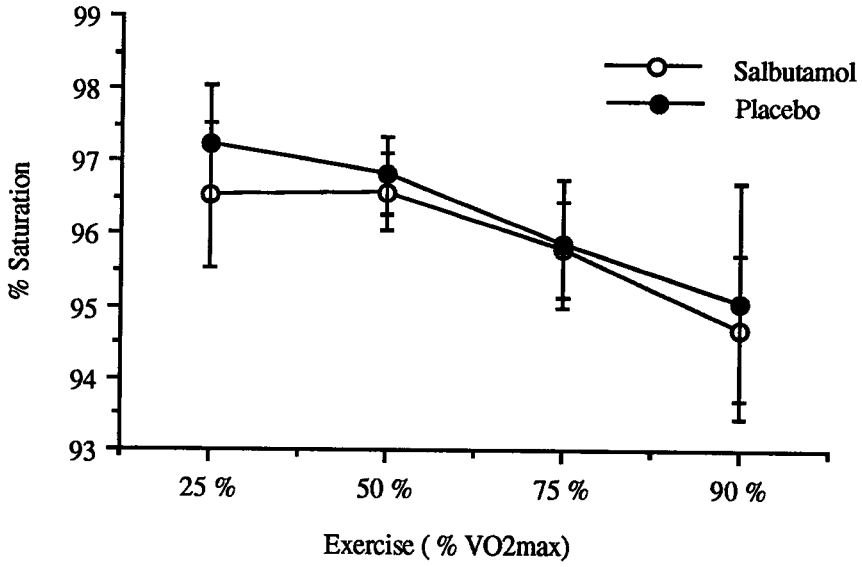
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p= .747

Figure 19. SaO_2 measures at various exercise intensities (%$\dot{V}O_2$max), HT subject data



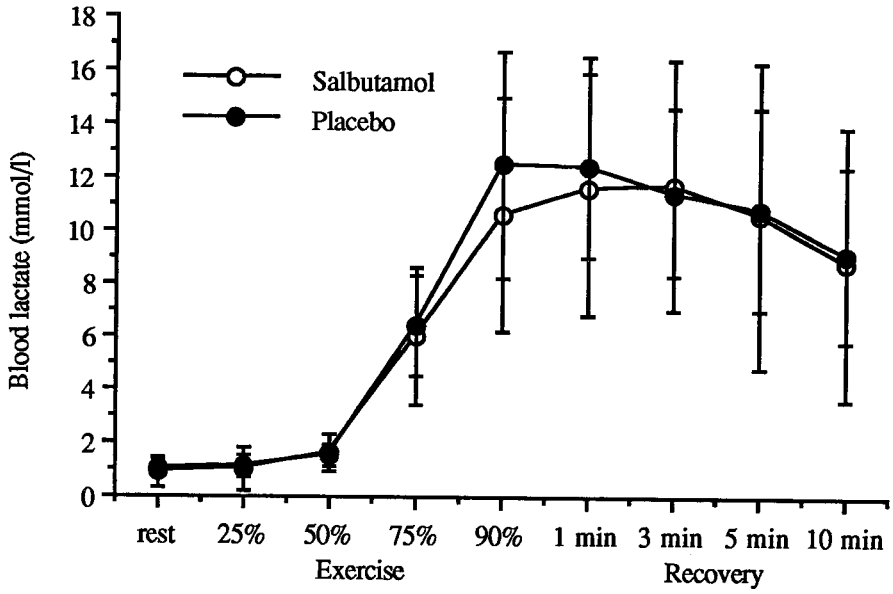
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p= .699

Figure 20. SaO_2 measures at various exercise intensities (%$\dot{V}O_2max$), HT subject data



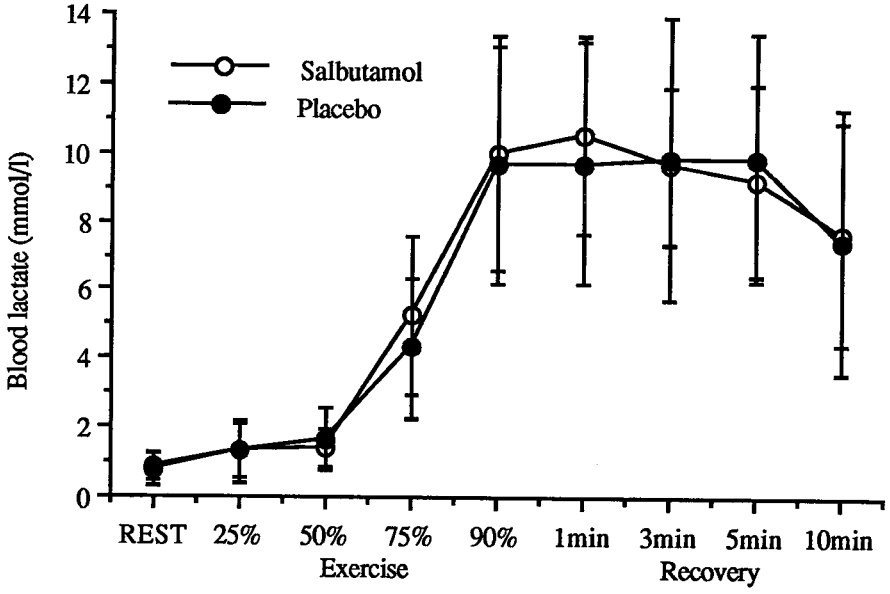
Values are means ± SD; open circles, salbutamol; closed circles, placebo : p= .955

Figure 21. Blood lactate (mmol·l^{-1}) at various exercise intensities (% $\dot{V}O_2max$) and 1 to 10 minutes into recovery, HT subject data



Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .463

Figure 22. Blood lactate (mmol·l^{-1}) at various exercise intensities (% $\dot{V}O_2max$) and 1 to 10 minutes into recovery, MT subject data



Values are means ± SD; open circles, salbutamol; closed circles, placebo : p = .836