Eur J Appl Physiol (1986) 54:656–660

European Journal of
Applied Physiology
and Occupational Physiology

Sex difference in maximal oxygen uptake

Effect of equating haemoglobin concentration

Kirk Cureton, Phillip Bishop, Patricia Hutchinson, Hillary Newland, Susan Vickery, and Linda Zwiren

Human Performance Laboratory, University of Georgia, Athens, GA 30602, USA

Summary. Ten men and 11 women were studied to determine the effect of experimentally equating haemoglobin concentration ([Hb]) on the sex difference in maximal oxygen uptake ($\dot{V}_{O_{2max}}$). $\dot{V}_{O_{2max}}$ was measured on a cycle ergometer using a continuous, load-incremented protocol. The men were studied under two conditions: 1) with normal [Hb] (153 $g \cdot L^{-1}$) and 2) two days following withdrawal of blood, which reduced their mean [Hb] to exactly equal the mean of the women (134 $g \cdot L^{-1}$). Prior to blood withdrawal, $\dot{V}_{O_{2max}}$ expressed in $L \cdot min^{-1}$ and relative to body weight and ride time on the cycle ergometer test were greater ($p<.01$) in men by 1.11 $L \cdot min^{-1}$ (47%), 4.8 $ml \cdot kg^{-1} min^{-1}$ (11.5%) and 5.9 min (67%), respectively, whereas $\dot{V}_{O_{2max}}$ expressed relative to fat-free weight (FFW) was not significantly different. Equalizing [Hb] reduced ($p<.01$) the mean $\dot{V}_{O_{2max}}$ of the men by 0.26 $L \cdot min^{-1}$ (7.5%), 3.2 $ml \cdot kg^{-1} min^{-1}$ (6.9%) or 4.1 $ml \cdot kg\ FFW^{-1} min^{-1}$ (7.7%), and ride time by 0.7 min (4.8%). Equalizing [Hb] reduced the sex difference for $\dot{V}_{O_{2max}}$ less than predicted from proportional changes in the oxygen content of the arterial blood and arteriovenous oxygen content difference during maximal exercise. It was concluded that the sex difference in [Hb] accounts for a significant, but relatively small portion of the sex difference in $\dot{V}_{O_{2max}}$ ($L \cdot min^{-1}$). Other factors such as the dimensions of the oxygen transport system and musculature are of greater importance.

Key words: Aerobic capacity — Gender — Haemoglobin concentration — Oxygen transport — Sex difference

Offprint requests to: KJ Cureton, Stegeman Hall, University of Georgia, Athens, GA 30602, USA

Introduction

Men have, on average, higher maximal oxygen uptake ($\dot{V}_{O_{2max}}$) and physical work capacity (PWC) than women. Their $\dot{V}_{O_{2max}}$ is approximately 50% greater than that of women when expressed in $L \cdot min^{-1}$, 15 to 25% greater relative to body weight (BW), and 5 to 15% greater relative to fat-free weight (FFW) (Drinkwater 1973; Sparling 1980). Once factor suggested to contribute to these differences is the sex difference in blood haemoglobin concentration ([Hb]). Men, on the average, have a [Hb] that is approximately 20 $g \cdot L^{-1}$ (15%) higher than women. The lower [Hb] of women results in a lower arterial oxygen content (CaO_2) and arteriovenous oxygen content difference ($C(a-\bar{v})O_2$) during maximal exercise (Åstrand et al. 1964), and should contribute to their lower $\dot{V}_{O_{2max}}$.

The relationship between [Hb] and $\dot{V}_{O_{2max}}$ is inconsistent; there are indications that variations in [Hb] may be in part compensated for by changes in maximal cardiac output $\dot{Q}$ and/or $C(a-\bar{v})O_2$ (Hermansen 1973; Horstman et al. 1974, 1980; Rowell 1974). Thus, the portion of the sex difference $\dot{V}_{O_{2max}}$ that is due to the difference in [Hb] is unclear. The purpose of this study was to determine the effect of experimentally equating the [Hb] on the sex difference in $\dot{V}_{O_{2max}}$.

Methods

Subjects. Ten men and 11 women in good health served as subjects. Their physical characteristics are summarized in Table 1. Based on their reported physical activity and sport history, the two groups were similar in the amount of regular endurance exercise performed, although they individually, participated in a variety of recreational activities ranging from inactive to moderately trained. Nearly equal mean $\dot{V}_{O_{2max}}$ (ml·kg

Table 1. Subject physcial characteristics (Means ±SD)

Variable	Males	Females
Age (yr)	27.4±5.1	26.1±4.1
Height (cm)	176.0±7.0	166.2±7.0
Weight (kg)	74.3±9.1	56.0±7.3
Fat free weight (kg)	65.4±7.9	44.4±5.5
% Fat	11.6±4.9	20.7±3.1

FFW^{-1}min^{-1}) values indicated that men and women had similar cardiorespiratory capacities (Cureton 1981). Subjects were fully informed of the purpose of the study, experimental protocol and procedures, and risks involved in participating in the experiment. Each signed a statement of written informed consent approved by the Institutional Review Board concerned with the use of human subjects in research.

Procedures. $\dot{V}_{O_{2\,max}}$ was assessed on a cycle ergometer (Monarch) using a continuous, load-incremented protocol. Beginning at 123 watts, the work rate was increased by 25 watts every 2-min. Pedal rate remained constant at 50 rev · min^{-1}. Subjects pedaled as long as possible. The same protocol was used for men and women, with the duration of the test serving as a measure of PWC. A plateau in $\dot{V}_{O_{2\,max}}$ during the final minutes of the test or, a maximum heart rate within 10 bt · min^{-1} of the age-predicted maximum and an $R>1.1$ were used as criteria for attaining $\dot{V}_{O_{2\,max}}$.

Metabolic measurements were made using the semi-automated system described by Wilmore and Costill (1974). The volume of expired air was measured using a dry gas meter (Parkinson-Cowan CD-4). Concentrations of oxygen and carbon dioxide were measured using electronic gas analyzers (Beckman OM-11 and LB-2), calibrated with standard gases previously analyzed using the Lloyd-Gallenkamp apparatus. Heart rate was determined from ECG recordings.

Venous blood samples were collected in heparinized syringes. [Hb] was determined by the cyanmethemoglobin method and hematocrit (Hct) was calculated from measures of mean corpuscular volume and erythrocyte count using a Coulter counter. Individual blood volumes of the men were estimated from height and weight using an equation of Allen et al. (1956).

Body composition was estimated from body density measured using underwater weighing with simultaneous determination of residual lung volume. Percent fat was estimated from body density using the equation of Brozek et al. (1963), % fat=(4.57/D$_b$−4.142)100. FFW was calculated from BW and the estimate of % fat.

Experimental protocol. Prior to the experimental treatment, $\dot{V}_{O_{2\,max}}$ was determined twice, one week apart, in all subjects. The test-retest reliability was high (r=.95), with no significant difference between the two tests. Therefore, the mean of the two tests was used as the representative value. Resting [Hb] and Hct were also determined twice, prior to the work capacity tests, and the averages were used as the representative values. Following the completion of the work capacity tests, blood was withdrawn from the men by venesection on two occasions, three days apart. The total quantity of blood withdrawn from an individual was that estimated to decrease the subject's [Hb] by an amount equal to the mean difference between the groups of men and women (19 g · L^{-1}), as calculated from estimated blood volume, existing, and desired [Hb], assuming a constant plasma volume. The total volume of blood withdrawn varied from 650 to 1000 ml.

Two days were allowed for plasma volume to be restored. Subjects were encouraged to consume fluids liberally. In the third day following blood withdrawal, venous blood samples were obtained from the men following a 12-h fast and blood [Hb] and Hct were measured. On the same day, th $\dot{V}_{O_{2\,max}}$ of the men was reassessed. Because the test-retest reliability of $\dot{V}_{O_{2\,max}}$ for the initial two tests was high, a third test was not administered to the women.

Statistical analysis. A 't' test for independent samples was used to test the significance of the differences between the women's and men's means for the physiological and performance variables. A 't' test for dependent samples was used to test the significance of mean changes in the men resulting from blood withdrawal. An alpha level of .01 was used for the significance tests to compensate for the effect of multiple comparisons on the probability of making a Type 1 error. All mean percentage differences between the men and women were computed as $(\bar{X}_M - \bar{X}_F)/\bar{X}_F)100$.

Results

The means and standard deviations for the physiological responses to maximal exercise and the hematological measures are presented in Table 2.

[Hb] and Hct. Prior to blood withdrawal, the men had significantly higher [Hb] (14.2%) and Hct (13.6%) than the women. Blood withdrawal significantly reduced the mean [Hb] of the men to equal that of the women. Individual changes in [Hb] varied from 12 to 27 g · L^{-1}. The mean sex difference in Hct was also reduced to nonsignificance.

$\dot{V}_{O_{2\,max}}$ and PWC. Prior to blood withdrawal, $\dot{V}_{E_{max}}$, $\dot{V}_{O_{2\,max}}$ in L · min^{-1} or relative to BW, and ride time were significantly greater in men by 52%, 47%, 12% and 67%, respectively; $\dot{V}_{O_{2\,max}}$ (ml · kg FFW^{-1}min^{-1}), HR$_{max}$, and R$_{max}$ did not differ significantly. Withdrawal of blood significantly reduced all three $\dot{V}_{O_{2\,max}}$ expressions by 7–8%, and ride time by 5%, but did not significantly affect $\dot{V}_{E_{max}}$, HR$_{max}$, or R$_{max}$. With [Hb] equated, mean $\dot{V}_{E_{max}}$, $\dot{V}_{O_{2\,max}}$ (L · min^{-1}) and ride time were significantly above the corresponding mean values for women by 48%, 36% and 59%, respectively; whereas $\dot{V}_{O_{2\,max}}$ (ml · kgmin^{-1}), $\dot{V}_{O_{2\,max}}$ (ml · kg FFW^{-1}min^{-1}), HR$_{max}$ and R$_{max}$ were not significantly different.

Discussion

Blood withdrawal and reinfusion has been widely used as an experimental approach for altering

Table 2. Physiological responses to maximal exercise and hematological data (Means ±SD)

Variable	Men			Women	Male-Female Differences	
	Before Blood Withdrawal	After Blood Withdrawal	Mean Change		Before Blood Withdrawal	After Blood Withdrawal
$\dot{V}_E$ (L · min^{-1})	121.7 ±19.6	118.8 ±17.8	2.9	80.3 ± 8.8	41.4*	38.5*
$\dot{V}_{O_2}$ (L · min^{-1})	3.47± 0.40	3.21± 0.35	0.26*	2.36± 0.36	1.11*	0.85*
$\dot{V}_{O_2}$ (ml · kg^{-1}min^{-1})	46.4 ± 4.5	43.2 ± 4.1	3.2*	41.6 ± 3.7	4.8*	1.6
$\dot{V}_{O_2}$ (ml · kg FFW^{-1}min^{-1})	53.4 ± 5.1	49.3 ± 4.6	4.1*	53.1 ± 5.1	0.3	−3.8
HR (bt · min^{-1})	189 ±10	186 ±10	3	185 ± 6	4	1
R	1.28± 0.05	1.30± 0.07	−0.02	1.25± 0.05	0.03	0.05
Ride time (min)	14.7 ± 3.3	14.0 ± 2.9	0.7*	8.8 ± 2.4	5.9*	5.2*
Hb (g · L^{-1})	153 ± 6	134 ± 6	19*	134 ± 7	19*	0
Hct (%)	44.4 ± 2.0	39.5 ± 2.0	4.9*	39.1 ± 1.8	5.3*	0.4

* Significant at $p<.01$

[Hb] and CaO_2 to determine the effects on $\dot{V}_{O_{2max}}$ and PWC (Gledhill 1985). The present study was not designed to look specifically at these effects, but to create groups of men and women with equal [Hb]. The unique aspect of this study was the direct comparison of $\dot{V}_{O_{2max}}$ in groups of men and women before and after equalizing [Hb]. The difference between the comparisons was used to indicate the portion of the sex difference in $\dot{V}_{O_{2max}}$ determined by [Hb].

Blood withdrawal reduced the mean [Hb] of the men to equal that of the women. The fact that the mean [Hb] was reduced by exactly the amount predicted provides support for the assumption that plasma volume was restored during the two-day interval following blood withdrawal; others have observed restoration within one day of withdrawing 500—1000 ml blood (Ekblom et al. 1976; Fortney et al. 1981).

The magnitude of change in $\dot{V}_{O_{2max}}$ in the men agrees closely with a number of other studies in which a similar volume of blood was withdrawn or in which a similar reduction in [Hb] was produced through blood withdrawal (Ekblom et al. 1972, 1976; Freedson 1981; Horstman et al. 1974, 1980; Rowell 1964). In those studies, $\dot{V}_{O_{2max}}$ declined 4—10% and work time on maximal-effort constant-rate endurance tests decreased 20—35%. The smaller percentage change in our performance measure may have been a reflection of the nature of the test, which was graded rather than constant-load. Balke (1954) observed a 7.8% reduction in the time required to reach a heart rate of 184—188 bt · min^{-1} on a graded walking treadmill test 2—3 days following withdrawal of 500 ml blood in 14 men. Freedson (1981) obtained a small, nonsignificant (1.2%) reduction in maximal work rate on a graded cycle ergometer test 4 days following blood withdrawal and reduction of [Hb] by 18.6% in 6 men. The changes in $\dot{V}_{O_{2max}}$ and PWC in this study were also very similar in magnitude (but opposite in direction) to increases observed following increased [Hb] due to reinfusion of approximately 800 ml blood (Gledhill 1985).

In the present study, the decrease in $\dot{V}_{O_{2max}}$ (L · min^{-1}) in the men resulting from the decrease in [Hb] was only about 60% as large as that expected if [Hb] reduction had produced proportional changes in CaO_2, $C(a-\bar{v})O_2$, and $\dot{V}_{O_2}$ during maximal exercise. Since other research has shown that [Hb] reduction is accompanied by a proportional change in CaO_2 (Ekblom et al. 1976; Woodson et al. 1978), this suggests that compensatory alterations occured in maximal $C\bar{v}O_2$ or $\dot{Q}$. Previous studies have found $\dot{Q}_{max}$ may be increased (Horstman et al. 1980; Woodson et al. 1978) or unchanged (Ekblom et al. 1976) following blood withdrawal. Horstman et al. (1974, 1980) have argued that the compensatory increase in $\dot{Q}_{max}$ that may accompany [Hb] and Hct reduction is due to reduced blood viscosity. In the perfused dog hindlimb, blood viscosity has been shown to be directly related to Hct (Levy and Share 1953), and blood flow inversely related to Hct (Gaehtgens et al. 1979). During electrical stimulation, increased blood flow due to reduced Hct is associated with increased O_2 delivery up to an optimal hematocrit of 0.5 or 0.6 (Gaehtgens et al. 1979).

Considerable additional evidence indicates maximal $\dot{Q}$ is proportionately higher in individuals with low [Hb], including women (Hermansen 1973). For example, Åstrand et al. (1964) found the $\dot{Q}_{max}/\dot{V}_{O_{2max}}$ ratio to be 7.1 in a group of young women with a mean [Hb] of 137 $g \cdot L^{-1}$ compared to 5.9 in young men with a mean [Hb] of 156 $g \cdot L^{-1}$. Thus, it is possible that the lower [Hb] of women compared to men does not result in a proportionately lower $\dot{V}_{O_{2max}}$ because lower blood viscosity results in proportionately higher $\dot{Q}_{max}$. If this is the case, the overall effect of a lower [Hb] on $\dot{V}_{O_{2max}}$ is less than that represented by the effect on maximal $C(a-\bar{v})O_2$.

It is also possible that a smaller change in $\dot{V}_{O_{2max}}$ than expected occurred following blood withdrawal in the men in this study due to a compensatory decrease in $C\bar{v}O_2$. This could have occurred if red blood cell 2,3-DPG increased in response to blood loss. Although not measured in the present investigation, in other studies blood 2,3-DPG has either increased (Freedson 1981) or not changed significantly (Ekblom et al. 1976; Woodson et al. 1978) 1 to 3 days following blood withdrawal and reduction in [Hb]. In studies on blood doping in which red blood cell 2,3-DPG was measured, no significant changes were observed 24 h after blood reinfusion (Buick et al. 1980; Ekblom et al. 1976; Williams et al. 1981). Thompson et al. (1982) found no change in maximal $C\bar{v}O_2$ following induced erythrocythemia, in which [Hb] was increased by an amount similar to the decrease in the present study. Therefore, it seems unlikely, although possible, that alterations in 2,3-DPG and a compensatory decrease in $C\bar{v}O_2$ accounted for the smaller than expected change in $\dot{V}_{O_{2max}}$ in the present study.

The physiological differences responsible for the sex difference in $\dot{V}_{O_{2max}}$ have been a topic of interest for many years (Åstrand 1952; Drinkwater 1973; von Dobeln 1956). The sex difference in [Hb] is always mentioned as one contributing factor, but its importance relative to other differences has not been clear. Differences in the size of the oxygen transport organs and musculature appear to be of primary importance since the percentage difference in $\dot{V}_{O_{2max}}$ between groups of men and women is reduced dramatically when $\dot{V}_{O_{2max}}$ is expressed relative to BW or FFW. Based on an analysis of 13 studies in the literature in which $\dot{V}_{O_{2max}}$ of men and women was directly compared, Sparling (1980) reported average mean differences of 56%, 28%, and 15% for $\dot{V}_{O_{2max}}$ expressed in $L \cdot min^{-1}$, relative to BW and relative to FFW, respectively. These differences were independent of test mode. However, the groups of men and women in most studies were not matched on level of physical condition and Sparling concluded that differences in physical activity probably contributed to the magnitude of sex differences observed. In two studies on relatively large groups of male and female runners and swimmers carefully matched on training history (Sparling and Cureton 1983; Zwiren et al. 1983), the differences for the BW and FFW $\dot{V}_{O_{2max}}$ expressions were smaller, 18% and 3—5%, respectively. The small sex difference in $\dot{V}_{O_{2max}}$ expressed relative to FFW suggests that all but a very small portion of the sex difference in $\dot{V}_{O_{2max}}$ ($L \cdot min^{-1}$) is related to dimensional differences between the sexes, if men and women are equally-trained. The findings of the present study are in agreement with this deduction and suggest that the portion of the sex difference in $\dot{V}_{O_{2max}}$ ($L \cdot min^{-1}$) not related to dimensional differences could be due to the sex difference in [Hb].

We conclude that sex difference in [Hb] accounts for a significant, but small portion of the sex difference in $\dot{V}_{O_{2max}}$ ($L \cdot min^{-1}$). Other factors such as the dimensions of the oxygen transport system and musculature are of greater importance.

Acknowledgements. This study was supported in part by Athens General Hospital. The authors thank Joyce Edwards and Cathy Critter for their technical assistance.

References

Allen T, Peng M, Chen K, Huang T, Chang C, and Fang H (1956) Prediction of blood volume and adiposity in man from body weight and the cube root of height. Metabolism 5:328—345

Åstrand P-O (1952) Experimental studies of physical working capacity in relation o sex and age. Munksgaard, Copenhagen, pp 103—115

Åstrand P-O, Cuddy T, Saltin B, Stenberg J (1964) Cardiac output during submaximal and maximal work. J Appl Physiol 19:268—274

Balke B, Brillo P. Konecci E, Luft U (1954) Work capactiy after blood donation. J Appl Physiol 7:231—238

Brozek J, Grande F, Anderson J, Keys A (1963) Densitometric analysis of body composition: revision of some quantitative assumptions. Ann NY Acad Sci (USA) 110:113—140

Buick F, Gledhill N, Froese A, Spriet L, Myers E (1980) Effect of induced erythrocythemia on aerobic work capacity. J Appl Physiol 48:636—642

Cureton K (1981) Matching male and female subjects using $\dot{V}_{O_{2max}}$. Res Q Exerc Sport 52:264—268

Drinkwater B (1973) Physiological responses of women to exercise. In: Wilmore J (ed) Exercise and sport sciences reviews, vol. 1. Academic Press, New York, pp 125—154

Ekblom B, Goldberg A, Gullbring B (1972) Response to exercise after blood loss and reinfusion. J Appl Physiol 33:175—180

Ekblom B, Wilson G, Åstrand P-O (1976) Central circulation during exercise after venesection and reinfusion of red blood cells. J Appl Physiol 40:379—383

Fortney S, Nadel E, Wegner C, Bove J (1981) Effect of acute alterations in blood volume on circulatory performance in humans. J Appl Physiol 50:292—298

Freedson P (1981) The influence of hemoglobin concentration on exercise cardiac output. Int J Sports Med 2:81—86

Gaehtgens P, Kreutz F, Albrecht K (1979) Optimal hematocrit for canine skeletal muscle during rhythmic isotonic exercise. Eur J Appl Physiol 41:27—39

Gledhill N (1985) The influence of altered blood volume and oxygen transport capacity on aerobic performance. In: Turjung R (ed) Exercise and sport sciences reviews, vol. 13. Macmillan, New York, pp 75—94

Hermansen L (1973) Oxygen transport during exercise in human subjects. Acta Physiol Scand [Suppl] 399:76—80

Horstman D, Gleser M, Wolfe D, Tryon T, Dalehut J (1974) Effects of hemoglobin reduction on $\dot{V}_{O_{2\,max}}$ and related hemodynamics in exercising dogs. J Appl Physiol 37:97—102

Horstman D, Weiskopf R, Jackson R (1980) Work capacity during 3-week sojourn at 4,300 m: effects of relative polycythemia. J Appl Physiol 49:311—318

Levy M, Share L (1953) The influence of erythrocyte concentration upon the pressure-flow relationships in the dog's hind limb. Circ Res 1:247—255

Rowell L, Taylor H, Wang T (1964) Limitations to prediction of maximal oxygen intake. J Appl Physiol 19:919—927

Rowell L (1974) Human cardiovascular adjustments to exercise and thermal stress. Physiol Rev 54:75—159

Sparling P (1980) A meta-analysis of studies comparing maximal oxygen uptake in men and women. Res Q Exerc Sport 51:542—552

Sparling P, Cureton K (1983) Biological determinants of the sex difference in 12-min run performance. Med Sci Sports Exerc 15:218—223

Thompson J, Stone J, Ginsberg A, Hamilton P (1982) O_2 transport during exercise following blood reinfusion. J Appl Physiol 53:1213—1219

Von Dobeln W (1956) Human standard and maximal metabolic rate in relation to fat-free body mass. Acta Physiol Scand [Suppl] 126:1—78

Williams M, Wesseldine S, Somma T, Schuster R (1981) The effect of induced erythrocythemia upon 5-mile treadmill run time. Med Sci Sports Exerc 13:169—175

Wilmore J, Costill D (1974) Semiautomated Systems approach to the assessment of oxygen uptake during exercise. J Appl Physiol 36:618—620

Woodson R, Wills R, Lenfant C (1978) Effect of acute and established anemia on O_2 transport at rest, submaximal and maximal work. J Appl Physiol 44:36—43

Zwiren L, Cureton K, Hutchinson P (1983) Comparison of circulatory responses to submaximal exercise in equally-trained men and women. Int J Sports Med 4:255—259

Accepted September 19, 1985