REVIEW ARTICLE

Sports Medicine 16 (1): 14-22, 1993
0112-1642/93/0007-0014/$04.50/0

SPO1 256

Exercise-Induced Hypoxaemia in Elite Endurance Athletes

Incidence, Causes and Impact on $\dot{V}O_{2max}$

Scott K. Powers, Daniel Martin and *Stephen Dodd*
Center for Exercise Science, Departments of Exercise and Sport Sciences, Physical Therapy and Physiology, University of Florida, Gainesville, Florida, USA

Contents

Summary

Arterial oxygenation is well maintained in healthy untrained or moderately trained individuals during exercise. In contrast, approximately 40 to 50% of healthy elite endurance athletes (cyclists and runners) demonstrate a significant reduction in arterial oxygenation during exercise at work rates approaching $\dot{V}O_{2max}$. The mechanism(s) to explain this exercise-induced hypoxaemia (EIH) remain controversial. However, hypoventilation and venoarterial shunt do not appear to be involved. By elimination, this suggests that ventilation-perfusion inequality and/or pulmonary diffusion limitations must contribute to EIH in this population. Theoretical and direct experimental evidence exists to support the notion that both ventilation-perfusion inequality and diffusion disequilibrium contribute to EIH; however, the relative contribution of each factor remains to be determined. In athletes who exhibit a profound EIH, the exercise-induced decline in arterial oxygenation results in a limitation of $\dot{V}O_{2max}$. Further, athletes who exhibit EIH at sea level suffer more severe gas exchange impairments during short term exposure to altitude than athletes or nonathletes who do not exhibit EIH at sea level. This finding explains much of the observed variance in the decline in $\dot{V}O_{2max}$ among individuals during short term altitude or hypoxia exposure.

Historically, pulmonary gas exchange has not been considered a limiting factor in the maximal oxygen uptake ($\dot{V}O_{2max}$) of healthy individuals. Indeed, oxyhaemoglobin saturation and arterial oxygen tension (p_aO_2) are well maintained in healthy individuals during exercise at sea level (Powers et al. 1988, 1991) However, there is one exception to this rule. Several investigators have demonstrated that exercise-induced hypoxaemia (EIH) may occur in healthy elite endurance athletes at work rates approaching $\dot{V}O_{2max}$ (Dempsey et al. 1984; Holmgren & Linderholm 1958; Powers et al. 1992; Rowell et al. 1964; Williams et al. 1986). In those athletes who demonstrate EIH, p_aO_2 may decrease by 18 to 38mm Hg below resting values (Dempsey et al. 1984; Powers et al. 1992). The observation that EIH occurs in elite endurance athletes seems paradoxical and has been the topic of numerous recent investigations. In 1987, we summarised the literature on this issue (Powers & Williams 1987). Because of the large volume of new information on the EIH phenomenon, the current review is designed to provide the reader with an update on pulmonary gas exchange in healthy endurance athletes. In this review, we provide a discussion of the following: (a) a historical perspective on the discovery of EIH in athletes; (b) a debate on the physiological mechanisms to explain EIH in healthy subjects; (c) a discussion of exercise blood gas dynamics and the incidence of EIH in athletes; and (d) evidence that EIH may have a negative impact on exercise performance at both sea level and altitude.

1. Historical Perspective

Although widespread discussion of EIH in athletes did not begin until the 1980s, EIH in healthy people was observed in 1958 (Holmgren & Linderholm 1958). Indeed, Holmgren and Linderholm (1958) first reported a significant decline in p_aO_2 in elite 'junior' endurance athletes during heavy exercise. Of particular interest in this study was the variable blood gas response across subjects; some athletes demonstrated frank EIH (e.g. p_aO_2 = 57mm Hg; 44mm Hg below resting values), whereas others maintained p_aO_2 within 5 to 8mm Hg of resting values (e.g. p_aO_2 = 93mm Hg). Subsequently, Rowell et al. (1964) demonstrated that arterial oxyhaemoglobin saturation (%HbO_2) declined from a resting mean of approximately 98% to 85% during heavy exercise in highly trained endurance athletes. Surprisingly, scientific interest in EIH in athletes remained dormant until Gledhill et al. (1980) reported a 22mm Hg decline in p_aO_2 during heavy exercise in endurance athletes. Much of the current interest in EIH in athletes began after the classic publication of Dempsey et al. (1984) which provided careful documentation that the previously reported EIH in athletes was not an isolated case or measurement artifact. Dempsey et al. (1984) examined blood gas dynamics in 17 elite endurance athletes during high intensity exercise. Their findings confirmed the existence of EIH since p_aO_2 was reduced 21 to 35mm Hg below resting values in 8 of these athletes.

Since the work of Dempsey et al. (1984), only 4 studies have measured p_aO_2 directly during heavy exercise in highly trained endurance athletes (Martin et al. 1992b; Pedersen et al. 1992a; Powers et al. 1992; Warren et al. 1991). All of these studies reported EIH in 1 or more athletes. In contrast to the limited number of EIH studies involving measurement of p_aO_2, a large number of investigators have reported EIH in athletes using pulse oximetry to estimate %HbO_2 (Lawler et al. 1988; Martin & O'Kroy 1992; Powers et al. 1988, 1989a; Williams et al. 1986). Importantly, while some pulse oximeters have been validated for use during exercise (Martin et al. 1992b; Powers et al. 1989a), other models have been shown to provide erroneous estimates of exercise %HbO_2 (Smyth et al. 1986) and other pulse oximeters have not been evaluated during exercise. Therefore, interpretation of EIH studies using pulse oximeters should be examined carefully against the type of pulse oximeter used in the investigation; only those studies demonstrating EIH using exercise-validated pulse oximeters should be considered as evidence that EIH occurs in the population in question.

2. Mechanisms of Exercise-Induced Hypoxia

Clearly one of the most fascinating questions associated with the phenomenon of EIH in healthy athletes is: 'What is the physiological mechanism to explain this exercise-induced imperfection in pulmonary gas exchange?' Unfortunately, at present a definitive answer to this question is not available. Hypoxaemia during exercise can occur because of hypoventilation, venoarterial shunts, ventilation perfusion mismatch, or diffusion limitations across the blood-gas interface.

2.1 Hypoventilation

By definition, hypoventilation is an alveolar ventilation below the rate metabolically required to maintain arterial blood gases at normal values. A cardinal marker of hypoventilation is an increase in arterial carbon dioxide tension (p_aCO_2) above normal. The role that hypoventilation plays in mediating EIH at $\dot{V}O_{2max}$ has been investigated by Dempsey et al. (1984) and Powers et al. (1992). Both investigators reported that p_aCO_2 is decreased during heavy exercise in athletes exhibiting EIH; these observations demonstrate that frank hypoventilation is not responsible for EIH in athletes.

Despite this finding, Dempsey et al. (1984, 1987) have suggested that an inadequate hyperventilatory response may contribute to the differences in the magnitude of EIH between athletes. A lack of hyperventilation during heavy exercise would result in a relatively low alveolar oxygen tension (p_AO_2) and a reduction in the driving force for oxygen transfer across the blood-gas interface. To test the hypothesis that the degree of EIH in athletes is related to the hyperventilatory response, Powers et al. (1992) examined the relationship between exercise ventilatory responses and p_aO_2 in elite endurance athletes. The data revealed a low correlation between p_aO_2 and p_AO_2 during maximal exercise. We interpret this finding as an indication that the magnitude of the hyperventilatory response is not a key factor in determining the magnitude of EIH in athletes.

2.2 Venoarterial Shunt

Even in the normal circulatory system there are areas where venous blood is not circulated through ventilated areas of the lung (Bachofen et al. 1973). This venoarterial shunt results in induction of poorly oxygenated blood into the arterial circulation and, therefore, causes a decline in p_aO_2. At rest, shunt accounts for about 50% of the alveolar-arterial oxygen tension difference (A-a pO_2 diff) [Gledhill et al. 1977; Whipp & Wasserman 1969] and it has been postulated that venoarterial shunt could account for approximately 49% of the A-a pO_2 diff during moderate exercise (Asmussen & Nielson 1960). In contrast, several investigators have demonstrated that venoarterial shunt does not play an important role in increasing the A-a pO_2 diff in athletes during heavy exercise. A simple test to determine the role of venoarterial shunts in mediating EIH is to allow individuals to breathe a hyperoxic gas mixture when hypoxaemic. If shunt is responsible for EIH, breathing the hyperoxic gas mixture would have limited effect on p_aO_2. Both Dempsey et al. (1984) and Powers et al. (1992) have demonstrated that a switch from breathing a normoxic gas mixture (e.g. room air at sea level) to a mild hyperoxic gas mixture (i.e. 24 to 26% O_2) results in increasing p_aO_2 back to normal levels in hypoxaemic athletes exercising at near $\dot{V}O_{2max}$. Therefore, venoarterial shunt is not a major factor mediating EIH in healthy endurance athletes.

2.3 Ventilation-Perfusion Mismatch

Ventilation-perfusion (V_A/Qc) inequality is a mismatching of ventilation and perfusion in the lung and may result in significant impairments of pulmonary gas exchange in various lung diseases (West 1982, 1985; West & Wagner 1991). In contrast, in the healthy lung, V_A/Qc is generally well matched and does not have a negative impact on pulmonary gas exchange during rest (West & Wagner 1991). While V_A/Qc equality is more than ad-

equate for almost complete pulmonary gas exchange at rest, the key question is whether heavy exercise results in V_A/Qc inequality and contributes to the incomplete pulmonary gas exchange in athletes who exhibit EIH. Unfortunately, a definitive answer to this question is not available. To-date, there are limited studies of V_A/Qc relationships during heavy exercise and no studies that evaluate V_A/Qc in elite endurance athletes during maximal exercise. To further complicate this issue, exercise studies evaluating V_A/Qc relationships provide conflicting results. Studies using radiotracer techniques to evaluate V_A/Qc during moderate to heavy work suggest that exercise promotes a more regional V_A/Qc homogeneity (Bake et al. 1968; Bryan et al. 1964). However, these findings must be evaluated with the knowledge that radioactive tracer techniques have limited spatial resolution and may not sample the entire lung (Gale et al. 1985).

In contrast to the abovementioned studies suggesting that regional V_A/Qc equality improves during exercise, several studies using the multiple inert gas washout technique have demonstrated V_A/Qc inequality increases during heavy exercise and that this V_A/Qc mismatch explains at least a portion of the widening of the A-a pO_2 diff (Gale et al. 1985; Gledhill et al. 1977, 1978; Hammond et al. 1986). Of particular interest is the study by Hammond et al. (1986) which demonstrated that V_A/Qc mismatch increased with exercise intensity up to an oxygen consumption of approximately 3 L/min. At higher work rates, V_A/Qc equality remained constant but the A-a pO_2 diff increased. The exclusion of frank hypoventilation and shunts as causes of EIH, and the demonstration that V_A/Qc inequality alone does not explain the widening of the A-a pO_2 diff at higher exercise intensities, suggest the development of pulmonary diffusion limitations.

2.4 Diffusion Limitations

A final possible mediator of EIH in endurance athletes is diffusion limitations resulting in an incomplete pulmonary gas exchange. Exercise presents a special challenge for pulmonary diffusion because of decreases in both the partial pressure of oxygen in mixed venous blood (p_vO_2) and red blood cell (RBC) transit time in the pulmonary capillary. Indeed, owing to an increased extraction of oxygen in the contracting muscle, the blood presented to the lung for gas exchange (i.e. p_vO_2) has a reduced oxygen tension. Because of the increase in cardiac output with increasing exercise intensity, the RBC transit time also decreases. Clearly, these conditions could result in pulmonary diffusion limitations and hypoxaemia if the lung did not make physiological adjustments to improve the conditions for diffusion. Two key adjustments are made during exercise to improve the conditions for diffusion: (a) hyperventilation results in an increase in p_aO_2 which increases the 'driving force' for oxygen diffusion into the blood; and (b) the pulmonary capillary blood volume rises, which increases the surface area available for diffusion and also prolongs the RBC transit time in the pulmonary capillaries. As a result of these changes, p_aO_2 in untrained individuals remains near resting levels and therefore, no significant exercise diffusion disequilibrium exists.

In contrast to this conclusion concerning pulmonary diffusion in untrained individuals, Dempsey et al. (1984, 1987) has argued that the demand placed on pulmonary diffusion during heavy exercise in the elite endurance athlete is ideal to promote diffusion disequilibrium. Their reasoning is as follows. The major determinants of alveolar-capillary diffusion are: (a) the surface area available for diffusion (varies with pulmonary capillary blood volume); (b) the distance required for diffusion from the alveolar membrane to the RBC; (c) RBC transit time (time available for gas equilibration in the pulmonary capillary); and (d) the rate of equilibration of mixed venous blood with alveolar gas. The high metabolic demand of the endurance athlete during heavy exercise could result in diffusion disequilibrium by negatively affecting at least 2 and perhaps 3 of these determinants (Dempsey 1987). First, as hydrostatic pressures increase in the pulmonary artery with increases in cardiac output, there is an increased transcapillary fluid flux (Wagner et al. 1986). This

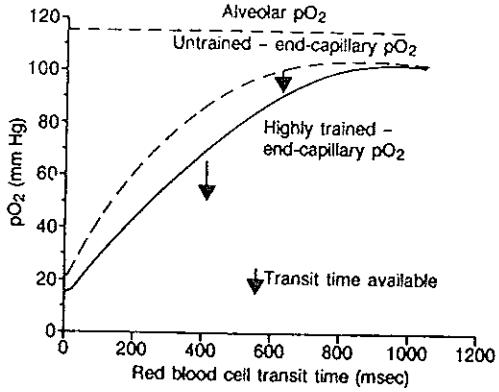

Fig. 1. Theoretical model examining the relationship between end-capillary pO_2, mixed pO_2 and red blood cell (RBC) transit time in untrained and highly trained endurance athletes during maximal exercise. 'Transit time available' is the mean RBC transit time in the untrained and highly trained athletes. This model illustrates how pulmonary diffusion limitations might occur in highly trained endurance athletes at work rates approaching $\dot{V}O_{2max}$ (data from Dempsey 1987 and Wagner 1982).

could result in a low-grade oedema and increase the diffusion distance from the alveolar membrane to the RBC (Wagner 1992). Secondly, the high cardiac output of the athlete during heavy exercise results in a decrease in RBC transit time. Thirdly, the rate of equilibrium of alveolar and end-capillary gas is increased because of the reduction in p_vO_2 (Wagner 1982).

In theory, the combined effects of 2 or all 3 factors could result in EIH in athletes (Dempsey 1987; Powers & Williams 1987). To illustrate this hypothesis, the combined effects of an exercise-induced low p_vO_2 and rapid RBC transit time on diffusion equilibrium can be considered. The relationship between p_vO_2, RBC transit time and end-capillary pO_2 for an untrained and a highly trained individual during maximal exercise is illustrated in figure 1. The 2 key factors are the individual differences in p_vO_2 and the RBC transit time. Indeed, p_vO_2 (indicated by the y-intercept in figure 1) and RBC transit time are significantly lower in the highly trained athlete than in the untrained individual. The low p_vO_2 in the trained athlete means that the 'effective slope' of the oxyhaemoglobin dissociation curve is shifted and that the time required for alveolar-capillary equilibrium is increased (Wagner 1982). Further, the reduction in mean RBC transit time in the athlete to approximately 400 msec (RBC transit time range approximately 100 to 600 msec) is significantly lower than the estimated average time required (approximately 600 msec) for gas equilibration (Dempsey 1987). Theoretically, these 2 factors alone could result in incomplete pulmonary gas exchange in athletes.

The above discussion is theoretical and based on data demonstrating that venoarterial shunt and V_A/Qc mismatching together do not account for all of the widening of the A-a pO_2 diff during exercise in endurance athletes. What direct evidence exists to support the theory that a pulmonary diffusion limitation exists in athletes? Hammond et al. (1986) have demonstrated that diffusion limitations exist during heavy exercise in moderately trained individuals. Further, Turner et al. (1992) have demonstrated that intense exercise results in a decrease in post-exercise pulmonary diffusion in athletes. To date, there is only 1 investigation that has attempted to examine pulmonary diffusion during heavy exercise in highly trained endurance athletes. Warren et al. (1991) estimated cardiac output, pulmonary capillary blood volume and pulmonary diffusion capacity during heavy exercise in male athletes. They concluded that a decrease in mean transit time alone could not explain the EIH observed in athletes. However, these data did not rule out the possibility that pulmonary diffusion limitation exists during heavy exercise in this population. There is a clear need for additional research in this area to resolve this issue.

In summary, direct evidence that hypoventilation and venoarterial shunt do not contribute to EIH in athletes has been provided by several authors (Dempsey et al. 1984; Powers et al. 1992). By elimination, V_A/Qc mismatching and/or diffusion limitations must account for the widening of the A-a pO_2 diff during exercise in endurance athletes who exhibit EIH. The relative individual contribution of V_A/Qc mismatch and diffusion limitation to EIH is still to be determined. This remains an interesting area for further research.

3. Incidence of Exercise-Induced Hypoxia in Endurance Athletes

It is clear that EIH in healthy subjects occurs only in those athletes with a high $\dot{V}O_{2max}$ (elite endurance athletes: $\dot{V}O_{2max}$ 68 to 70 ml/kg/min) [Williams et al. 1986]. Of particular interest is the finding that EIH is not universal among elite endurance athletes. When discussing the incidence of EIH in athletes, a key issue is the criterion used to define hypoxaemia. Powers et al. (1992) proposed that EIH be defined as a reduction in resting p_aO_2 of 18mm Hg. The rationale for this criterion is that an exercise-induced decline in resting p_aO_2 of 18mm Hg is >4 SD away from the mean maximal exercise-induced change in p_aO_2 in healthy untrained people (Powers et al. 1991). Using this criterion, Powers et al. (1992), Martin et al. (1992a) and Dempsey et al. (1984) reported that between 40 and 47% of endurance athletes studied (elite cyclists and runners) exhibited EIH.

Further, using a physiologically significant decline in $\%HbO_2$ (i.e. reduction in $\%HbO_2$ to 4% below resting levels) as the criterion to define EIH, Powers et al. (1988) and Martin et al. (1992a) reported that between 46 and 52% of elite cyclists studied exhibited EIH during heavy exercise. Collectively, these investigations suggest that 40 to 50% of elite endurance athletes exhibit EIH and that the incidence of EIH does not differ between elite cyclists and runners. At present, no data exist concerning the incidence of EIH in endurance athletes in sports other than cycling and running; hence, exercise blood gas data are needed on other endurance athletes (e.g. cross-country skiers, swimmers, triathletes). Also lacking is an estimate of the incidence of EIH, based on arterial blood samples, in female endurance athletes.

Although the above studies clearly demonstrate that EIH occurs in a significant number of elite male endurance athletes, the explanation why only some of these athletes demonstrate EIH is unclear. In general, we do not believe that an inadequate hyperventilatory response can explain these large intersubject differences (Powers et al. 1992). However, in those athletes who exhibit severe EIH (i.e. $p_aO_2 \leq 70$mm Hg), inadequate hyperventilation may play an 'accessory' role in determining the degree of EIH. Additional studies that evaluate intersubject differences in maximal pulmonary capillary blood volume, V_A/Qc inequality and pulmonary artery pressures during exercise would be useful in explaining why only some endurance athletes exhibit EIH.

4. Exercise Blood Gas Dynamics in Elite Athletes

Examining the dynamics of arterial blood gas during exercise in elite athletes reveals several interesting points. Figure 2 illustrates the changes in p_aO_2 and the A-a pO_2 diff during an incremental exercise test in 3 elite cyclists ($\dot{V}O_{2max}$ = 72 to 77 ml/kg/min). Note the interindividual variation in the p_aO_2 nadir and the A-a pO_2 diff zenith at $\dot{V}O_{2max}$. The variation in p_aO_2 at $\dot{V}O_{2max}$ across athletes illustrates that the exercise-induced decline in p_aO_2 in elite athletes is not 'all or none' but is a continuum. Also, in general, there is little change in p_aO_2 or A-a pO_2 diff until the athlete reaches high work rates $\geq$70% $\dot{V}O_{2max}$. In short, these observations demonstrate that exercise-induced imperfections in pulmonary gas exchange occur only at relatively high work rates.

5. Exercise-Induced Hypoxia and $\dot{V}O_{2max}$

Another key question in the area of EIH in athletes is whether the exercise-induced decline in p_aO_2 results in a significant reduction in arterial O_2 content resulting in a limitation of $\dot{V}O_{2max}$. Given the belief that O_2 transport to the working muscle is the limiting factor in determining $\dot{V}O_{2max}$ (Ekblom et al. 1975; Robertson et al. 1982), any reduction in O_2 transport across the blood-gas barrier could result in a reduction in $\dot{V}O_{2max}$. Consider the following theoretical prediction of the change in $\dot{V}O_{2max}$ in a person exhibiting a significant exercise reduction in $\%HbO_2$ (i.e. $\%HbO_2$ decreasing 6% below resting levels) versus the same person maintaining $\%HbO_2$ within 2% of resting values.

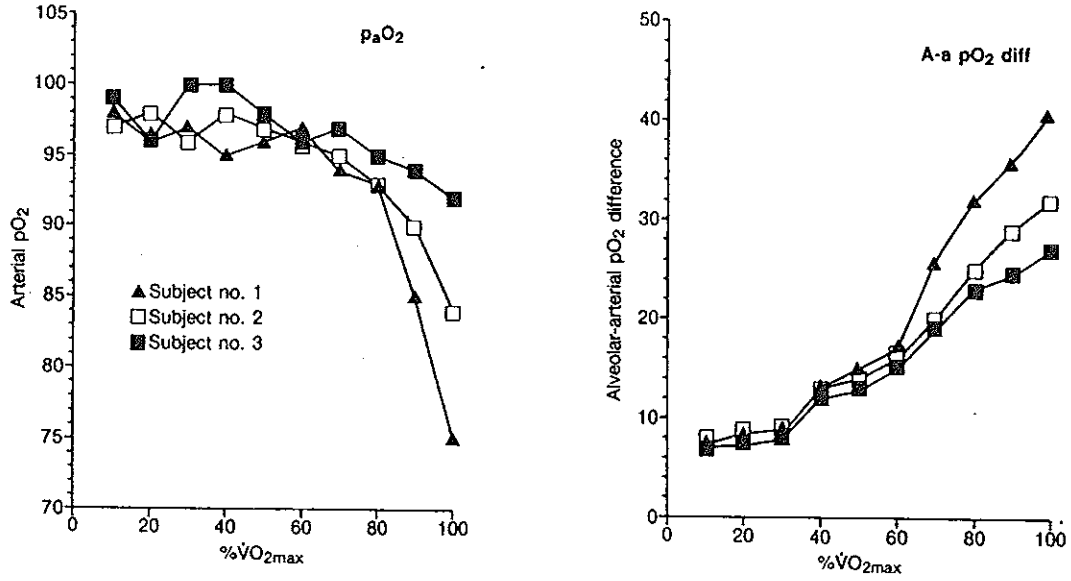

Fig. 2. Changes in arterial partial pressure of oxygen (p_aO_2) and alveolar-arterial pO_2 differences (A-a pO_2 diff) in 3 highly trained endurance athletes during an incremental exercise test. The range of exercise p_aO_2 and A-a pO_2 diff in these 3 athletes illustrates the wide range of responses to heavy exercise in this population (data from Powers et al. 1992).

Table I contains oxygen transport data during maximal exercise for this highly trained athlete under 2 theoretical conditions: (a) EIH present during exercise at $\dot{V}O_{2max}$, i.e. $\%HbO_2$ decreased by 6% below resting values; (b) EIH not present during exercise at $\dot{V}O_{2max}$ and $\%HbO_2$ decreased by only 2% below resting values. To estimate the impact of EIH on $\dot{V}O_{2max}$, the differences in maximal oxygen transport in the 2 conditions must be computed. If we assume a haemoglobin concentration of 150 g/L of blood and that haemoglobin that is 100% saturated with oxygen can transport 1.34ml O_2/g haemoglobin (Slonin & Hamilton 1981), we can compute the maximal oxygen transport per minute in the 2 conditions. The values for maximal cardiac output, $\%HbO_2$, and the arterial-mixed venous oxygen difference (a-$\bar{v}$ O_2 diff) contained in table I are taken from published values (Ekblom

Table I. Influence of arterial oxyhaemoglobin desaturation on maximal oxygen transport in an elite endurance athlete. The values represent parameters measured at $\dot{V}O_{2max}$ with exercise-induced hypoxia (EIH) present ($\%HbO_2$ = 92%) and absent ($\%HbO_2$ = 96%)

Condition	$\%HbO_2$ (%)	$\dot{Q}$ (L/min)	Maximum a-$\bar{v}$ O_2 diff (ml/L)	Maximum O_2 transport (L/min)	$\dot{V}O_{2max}$ (L/min)
EIH absent	96	30	180	5.79	5.40
EIH present	92	30	155	5.55	5.16[a]

a EIH-mediated reduction in $\dot{V}O_{2max}$ = 0.24 L/min or ≈4.4%.

Abbreviations and symbols: $\%HbO_2$ = arterial oxyhaemoglobin saturation; $\dot{Q}$ = cardiac output (L/min); a-$\bar{v}$ O_2 diff = arterial-mixed venous oxygen difference.

t al. 1975; Powers et al. 1989b). As illustrated in able I, a difference in $\%HbO_2$ of 4% at $\dot{V}O_{2max}$ etween the 2 conditions (i.e. EIH *vs* normal exrcise gas exchange) results in a reduction in $\dot{V}O_{2max}$ of approximately 4.4%. This reduction in $\dot{V}O_{2max}$ is predicted by differences in maximal oxygen transport in these 2 conditions.

To-date, 3 investigators have provided direct experimental evidence to support these theoretical calculations that EIH results in a significant limitation of $\dot{V}O_{2max}$. The first published study in this area demonstrated that an exercise-induced reduction in $\%HbO_2$ to 92 to 93% is sufficient to cause a measurable effect on $\dot{V}O_{2max}$ in elite endurance athletes (Powers et al. 1989b). In this study, the incomplete pulmonary gas exchange observed in athletes approximates a 1% decrement in $\dot{V}O_{2max}$ for each 1% decrement in $\%HbO_2$. These findings have recently been corroborated by O'Kroy and Martin (1989) and Pedersen et al. (1992). Collectively, these data provide direct experimental support for theoretical data presented in table I.

It seems possible that gas exchange limitations might be exacerbated during exercise at altitude in elite endurance athletes who exhibit EIH at sea level compared with healthy untrained individuals. That is, if $\dot{V}O_{2max}$ is limited by O_2 delivery to the working muscle, then individuals experiencing a large reduction in $\%HbO_2$ during intense exercise during altitude exposure would be likely to exhibit a greater decrement in $\dot{V}O_{2max}$ compared with individuals with a smaller reduction in $\%HbO_2$ at altitude. This postulate has been experimentally tested by Lawler et al. (1988) who demonstrated that endurance athletes who exhibit EIH at sea level suffer more gas exchange impairments at altitude than healthy untrained individuals. The authors concluded that their findings may explain a large portion of the observed variance in sea level versus altitude $\dot{V}O_{2max}$ (i.e. $\Delta\dot{V}O_{2max}$) among a group of heterogeneous individuals. These findings have been corroborated by Martin and O'Kroy (1992).

6. Conclusions

While it is generally accepted that the pulmonary system does not limit $\dot{V}O_{2max}$ in healthy humans, a possible exception to this rule is elite endurance athletes. Indeed, in athletes exhibiting frank EIH, the exercise-induced imperfections in pulmonary gas exchange (i.e. resulting in a reduction in $\%HbO_2$) limit $\dot{V}O_{2max}$. Further, endurance athletes who exhibit EIH at sea level suffer greater gas exchange impairments during exercise at altitude than do athletes or nonathletes who do not exhibit EIH at sea level. This observation may explain much of the observed variance in $\dot{V}O_{2max}$ among individuals during short term altitude or hypoxia exposure. It is now well established that 40 to 50% of elite male highly trained endurance athletes (i.e. cyclists or runners) exhibit EIH at work rates near $\dot{V}O_{2max}$. The exercise-induced imperfections in pulmonary gas exchange are not 'all or none' but represent a continuum, with athletes exhibiting a wide range of response. Although the physiological mechanisms to explain frank EIH in pulmonary gas exchange continues to be debated, it seems likely that both V_A/Qc inequality and pulmonary diffusion limitations play a role.

References

Asmussen E, Nielson M. Alveolar-arterial gas exchange at rest and during work at different oxygen tensions. Acta Physiologica Scandinavica 50: 153-166, 1960

Åstrand P, Rodahl K. Textbook of work physiology, p. 238, McGraw-Hill, New York, 1986

Bachofen H, Hobi H, Scherrer M. Alveolar-arterial nitrogen gradients at rest and during exercise in healthy men of different ages. Journal of Applied Physiology 34: 137-142, 1973

Bake B, Bjure J, Widimsky J. The effect of sitting and graded exercise on the distribution of pulmonary blood flow in healthy subjects studied with the ^{133}Xenon technique. Scandinavian Journal of Clinical and Laboratory Investigation 22: 99-106, 1968

Barr P, Beckman M, Bjurstedt H, Brismar J, Hesser C. Time courses of blood gas changes provoked by light and moderate exercise in man. Acta Physiologica Scandinavica 60: 1-17, 1964

Brooks G, Fahey T. Exercise physiology: human bioenergetics and its applications, p. 271, John Wiley and Sons, New York, 1984

Bryan A, Bentivoglio L, Beerd F, MacLeish H, Zudulka A, et al. Factors affecting regional distribution of ventilation and perfusion in the lung. Journal of Applied Physiology 19: 395-402, 1964

Dempsey J. Exercise-induced imperfections in pulmonary gas exchange. Canadian Journal of Applied Sports Sciences 12: 66s-70s, 1987

Dempsey J, Hanson P, Henderson K. Exercise-induced arterial hypoxemia in healthy persons at sea level. Journal of Physiology 355: 161-175, 1984

Ekblom B, Huot R, Stein E, Thorstensson A. Effect of changes in arterial oxygen content on circulation and physical performance. Journal of Applied Physiology 39: 71-75, 1975

Gale G, Torre-Bueno J, Moon R, Saltzman H, Wagner P. Ventilation-perfusion inequality in normal humans during exercise

at sea level and simulated altitude. Journal of Applied Physiology 58: 978-988, 1985
Gledhill N, Froese A, Buick F, Bryan A. V_A/Q inhomogeneity in man during exercise: the effects of SF6 breathing. Journal of Applied Physiology 45: 512-515, 1978
Gledhill N, Froese A, Dempsey J. Ventilation to perfusion distribution during exercise in health. In Dempsey & Reed (Eds) Muscular exercise and the lung, pp. 325-343, University of Wisconsin Press, Madison, 1977
Gledhill N, Spriet L, Froese A, Wilkes D, Meyers E. Acid-base status with induced erythrocemia and its influence on arterial oxygenation during heavy exercise. Abstract. Medicine and Science in Sports and Exercise 12: 122, 1980
Hansen J, Casaburi R. Validity of ear oximetry in clinical exercise testing. Chest 91: 333-337, 1987
Holmgren A, Linderholm H. Oxygen and carbon dioxide tensions of arterial blood during heavy and exhaustive exercise. Acta Physiologica Scandinavica 44: 203-215, 1958
Lawler J, Powers S, Thompson D. Linear relationship between maximal oxygen uptake and $\dot{V}O_{2max}$ decrement during exposure to acute hypoxia. Journal of Applied Physiology 64: 1486-1492, 1988
Martin D, Cicale M, Huang D, Mengelkoch L, Powers S. Incidence of exercise-induced hypoxemia in male endurance athletes. Abstract. Medicine and Science in Sports and Exercise 24: S69, 1992a
Martin D, O'Kroy J. Effects of acute hypoxia on $\dot{V}O_{2max}$ of trained and untrained subjects. Journal of Sports Sciences 11: 37-42, 1992
Martin D, Powers S, Cicale M, Collop N, Huang D, et al. Validity of pulse oximetry during exercise in elite endurance athletes. Journal of Applied Physiology 72: 544-458, 1992b
McClusker M, Brilla L. Exercise induced hypoxemia in female athletes. Abstract. Medicine and Science in Sports and Exercise 24: S70, 1992
Murray J. The normal lung, pp. 170-171, 344-348, Saunders Co, Philadelphia, 1986
O'Kroy J, Martin D. Effect of acute hypoxia and hyperoxia on maximal oxygen uptake of trained and untrained subjects. Abstract. Medicine and Science in Sports and Exercise 21: S21, 1989
Pedersen P, Andersen C, Madsen K, Jensen K. Role of pulmonary oxygen diffusion for arterial oxygen saturation and $\dot{V}O_{2max}$. Abstract. Physiologist 35: 234, 1992b
Pedersen P, Madsen K, Andersen C, Secher N, Jensen K. Arterial oxygen saturation during dynamic exercise. Abstract. Medicine and Science in Sports and Exercise 24: S69, 1992a
Powers S, Dodd S, Criswell D, Lawler J, Martin D, et al. Evidence for an alveolar-arterial pO_2 gradient threshold during incremental exercise. International Journal of Sports Medicine 12: 313-318, 1991
Powers S, Dodd S, Freeman J, Ayer SG, Samson H, et al. Accuracy of pulse oximetry to estimate HbO_2 fraction of Hb during exercise. Journal of Applied Physiology 67: 300-304, 1989a
Powers S, Dodd S, Woodyard J, Beadle R, Church G. Alterations in hemoglobin saturation during incremental arm and leg exercise. British Journal of Sports Medicine 18: 212-216, 1984
Powers S, Lawler J, Dempsey J, Dodd S, Landry G. Effects of incomplete pulmonary gas exchange on $\dot{V}O_{2max}$. Journal of Applied Physiology 66: 2491-2495, 1989b
Powers S, Lawler J, Dodd S, Kirtley M, Landry G, et al. Incidence of exercise-induced hypoxemia in elite athletes at sea level. European Journal of Applied Physiology and Occupational Physiology 58: 298-302, 1988
Powers S, Martin D, Cicale M, Collop N, Huang D, et al. Exercise-induced hypoxemia in athletes: role of inadequate hyperventilation. European Journal of Applied Physiology and Occupational Physiology 65: 37-42, 1992
Powers S, Williams J. Exercise induced hypoxemia in highly trained athletes: a review. Sports Medicine 4: 46-53, 1987
Riley R, Lilienthal J, Proemmel D, Frankee R. On the determination of the physiologically effective pressure of oxygen and carbon dioxide in alveolar air. American Journal of Physiology 147: 191-198, 1946
Rowell L, Taylor H, Wang V, Carlson Y. Saturation of arterial blood with oxygen during maximal exercise. Journal of Applied Physiology 19: 284-286, 1964
Saltin B. Cardiovascular and pulmonary adaptation to physical activity. In Bouchardet al. (Eds) Exercise, fitness, and health, pp. 187-204, Human Kinetics Press, Champaign, 1990
Severinghaus J. Blood gas calculator. Journal of Applied Physiology 21: 1108-1116, 1966
Turner S, McKenzie D, Coutts K, Wilcox P, Jespersen D, et al. The effects of intense exercise on DLCO and $\%SaO_2$ in competitive athletes. Abstract. Physiologist 35: 231, 1992
Wagner P. Influence of mixed venous pO_2 on diffusion across the pulmonary blood-gas barrier. Clinical Physiology 2: 105-115, 1982
Wagner P. Ventilation-perfusion matching during exercise. Chest 101: 192S-198S, 1992
Wagner P, Gale G, Moon R, Torre-Bueno J, Stolp B, et al. Pulmonary gas exchange in humans exercising at sea level and simulated altitude. Journal of Applied Physiology 60: 260-270, 1986
Warren G, Cureton K, Middendorf W, Ray C, Warren J. Red blood cell pulmonary capillary transit time during exercise in athletes. Medicine and Science in Sports and Exercise 23: 1353-1361, 1991
Wasserman K, Van Kessel A, Burton G. Interactions of physiological mechanisms during exercise. Journal of Applied Physiology 22: 71-85, 1967
West J. Pulmonary pathophysiology, pp. 33-34, Williams and Wilkins, Baltimore, 1982
West J. Ventilation/blood flow and gas exchange, pp. 12-14, Blackwell Scientific Publications, London, 1985
West J, Wagner P. Ventilation-perfusion relationships. In Crystal et al. (Eds) The lung: scientific foundations, pp. 1289-1306, Raven Press, New York, 1991
Whipp B, Wasserman K. Alveolar-arterial gas tension difference during graded exercise. Journal of Applied Physiology 27: 361-365, 1969
Williams J, Powers S, Stuart M. Hemoglobin desaturation in highly trained athletes during heavy exercise. Medicine and Science in Sports and Exercise 18: 168-173, 1986

Correspondence and reprints: Dr *Scott K. Powers*, Center for Exercise Science, Room 33-FLG, University of Florida, Gainesville, FL 32611, USA.