

Hyperoxic Science (Review)

Introduction

Oxygen plays a key role in providing the energy needed for muscular contractions and oxygen supply has been identified as a limiting factor in the performance of sustained exercise. Researchers have demonstrated links between atmospheric oxygen levels, the delivery of oxygen to working muscles and exercise performance. When exercising subjects are exposed to low oxygen (hypoxic) environments, the delivery of oxygen to working muscle is compromised and exercise performance is reduced. In contrast, hyperoxic (high oxygen) environments have been shown to increase exercise capacity.

The following proposal was written to present scientific evidence in support of the concept of supplemental oxygen training. Following a physiological review of respiration and oxygen transport, evidence will be presented to support the efficacy of exercise training with the assistance of supplemental oxygen. Several models for the use of supplemental oxygen will be presented. Finally, safety issues surrounding the use of supplemental oxygen will be presented.

Oxygen Transport

Transporting oxygen from the atmosphere to the cells of the body is a process that involves two physiological processes: Respiration, which enables the transport of gasses (O₂ and CO₂) between the pulmonary tissues and the bloodstream; and circulation, which encompasses the transport of oxygen and CO₂ via the bloodstream to and from the tissues of the body.

During inspiration, oxygen is inhaled into the lungs from the atmosphere. Once in the lungs, the oxygen is transported across specialized tissues into the blood. As the oxygen enters the blood, it is bound by red blood cells. These tiny cells circulate throughout the body and deliver oxygen to the skeletal muscle and other tissues. Once in the tissues, oxygen is used in metabolic processes generating thermal (maintenance of body temperature) and mechanical (muscular work) forms of energy.

There are essentially three physiological points of control that determine the amount of oxygen that reaches the exercising muscle: the oxygen carrying capacity of the blood, the capacity of the lungs to transport oxygen into the blood and the density of the

capillary network in muscles. Experimental practice by athletes and scientific research has revealed a number of effective methods of manipulating these points of control. Furthermore, increasing the capacity of either of these systems has been shown to have a remarkable effect on exercise performance.

Increasing the oxygen carrying capacity of the blood is accomplished by increasing the numbers of red blood cells. This process can be successfully executed by a variety of methods including prolonged exposure to hypoxic environments, infusion of red blood cells, or the use of exogenous erythropoietin. Though the latter two methods are forbidden by most sports, the techniques still are used to improve the performance of athletes during competition. And while use of these methods is virtually undetectable, they can present significant risks to the health of the athlete.

Transport capacity of oxygen from the pulmonary system into the blood is primarily a function of oxygen pressure within the lungs which, in turn, is dictated by the oxygen pressure of the atmosphere. Total atmospheric pressure at sea level is 760 torr. Two gases combine to make up this pressure: nitrogen, which makes up approximately 79% of the earth's atmosphere, and oxygen, which makes up the remaining 21% of the atmosphere. Total oxygen pressure (also known as the "partial pressure of oxygen") in the atmospheric air is the product of the total atmospheric pressure multiplied by the percentage of oxygen found at that pressure ($.21 \times 760$ torr or 159 torr).

Changing in the partial pressure of atmospheric oxygen can have a remarkable effect on exercise performance. For instance, at an elevation of 6000 feet above sea level, the atmospheric pressure drops to approximately 600 torr. While the atmosphere still contains the same percentage of oxygen, the drop in atmospheric pressure causes a concurrent drop in the partial pressure of oxygen to 126 torr. This drop in the partial pressure of oxygen at 6000 feet causes a decrease in exercise performance of approximately 7-10% when compared to sea level performance.

Why does the atmospheric pressure of oxygen play such an important role in exercise performance? Laws that govern the flow of gases dictate that gases diffuse from areas of high pressure to those of relatively lower pressure.

The interaction of the human respiratory system with the environment takes advantage of these physical laws to transport oxygen from the environment to the tissues

of the body. Pressure gradients are utilized to pull oxygen from the atmosphere into the lungs and to drive the oxygen from the lungs into the bloodstream. Thus, the atmosphere sits at the top of a pressure gradient that extends down to the body's peripheral tissues and higher oxygen pressures in the atmosphere result in higher blood oxygen levels and greater oxygen delivery to the working muscle.

Blood oxygen levels are usually expressed as saturation percent, which refers to the percentage of oxygen in the blood in comparison to its total oxygen holding capacity. Arterial blood is generally 98% saturated in healthy, resting individuals, while venous blood is only about 40% saturated as it has unloaded much of its oxygen at the peripheral tissues. During light to moderate-intensity exercise, more oxygen is removed from the blood to satisfy the increased oxygen needs of the working muscle. As a result, venous oxygen saturation usually falls into the low to mid 30% range during light to moderate exercise. However, arterial oxygen saturation typically is maintained at or near 98% as the pulmonary system is well equipped to handle the increases in O₂ demand brought on by moderate exercise.

During sustained, high-intensity exercise, the dramatic increase in oxygen need places incredible demands on the cardiopulmonary system. Because the working muscle requires such large amounts of oxygen during high intensity exercise, venous oxygen levels can slip into the 15-20% range. When venous oxygen reaches these low levels, the ability of the lungs to reoxygenate the blood is exceeded, and arterial oxygen saturation can drop into the high eighties to low nineties. This situation, commonly known as arterial desaturation, results in a decrease in oxygen delivery to the working muscle and limits exercise performance.

Maintaining Arterial Oxygen Levels and Improving Exercise Performance

Many well-controlled research studies have demonstrated that raising the partial pressure of inspired oxygen is an effective means of increasing arterial oxygen saturation and exercise performance during sustained, high-intensity work (1). An early study by Wilson and Welch (2) investigated the impact of breathing various hyperoxic gas mixtures on time to exhaustion during a maximal running tests.

Subjects performed five separate tests while breathing atmospheric air (21% O₂), 40%, 60%, 80% or 100% oxygen. Time to exhaustion was significantly increased by 22%, 29% and 38% percent during the 60%, 80% and 100% oxygen trials, respectively.

In a recent investigation at the U.S. Olympic Training Center, Wilber, et al. (3) studied the effects of breathing 60% oxygen on arterial oxygen saturation and power output during high intensity intervals. Competitive cyclists performed interval workouts consisting of six, 100 kJ efforts on bicycle ergometers while breathing either 21% or 60% oxygen. Arterial oxygen saturation were significantly higher during the hyperoxic trials when compared to the ambient condition (Hyperoxic = 99% saturation, Ambient = 91% saturation, Figure 1). Subjects also produced significantly more power during the hyperoxic (Hyperoxic = 290 W, Ambient = 265 W, increase = 9%) as opposed to the ambient condition (Figure 2).

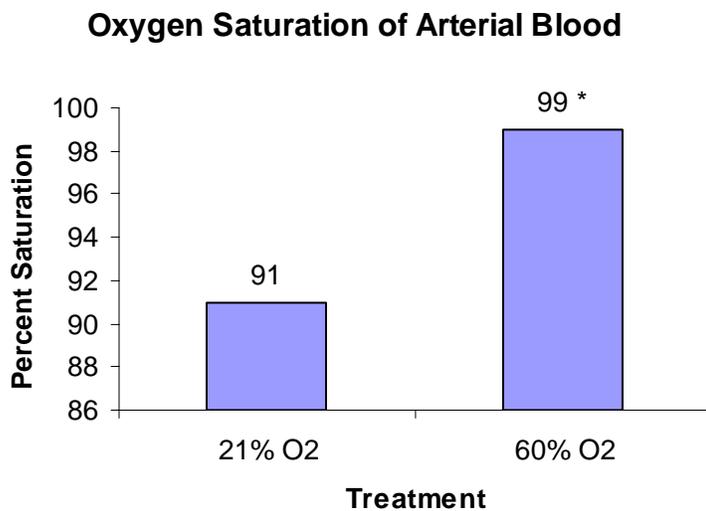


Figure 1. Oxygen saturation of arterial blood during 100 kJ intervals while breathing 21% or 60% oxygen (*Significantly higher than the 21% oxygen group).

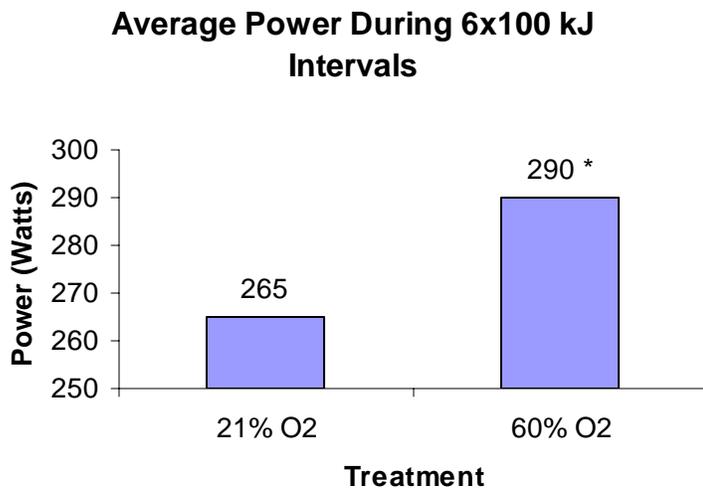


Figure 2. Power output during 100 kJ intervals while breathing 21% or 60% oxygen (*Significantly higher than the 21% oxygen group).

Peltonen, et al. (4) saw significant improvements in exercise performance during 2500 m maximum performance tests on rowing ergometers when subjects breathed a gas mixture containing 62% oxygen as opposed to performing the identical test while breathing ambient air. The increase in average power outputs during the hyperoxic trials were similar to those observed by Wilber.

Plet, et al. (5) compared maximal oxygen consumption and exercise time to exhaustion during cycling ergometry when subjects breathed either ambient air (21% O₂) or a 55% oxygen mixture. Maximal oxygen consumption increased significantly (12%) under the hyperoxic condition when compared to normoxic performance. In exercise tests to exhaustion, subjects worked at 80% of their ambient VO₂ max while breathing either 21% or 55% oxygen. Time to exhaustion increased significantly (41%) during the hyperoxic trials when compared to trials performed under the ambient condition.

Using Hyperoxic Training to Improve Competitive Performance

Success in endurance sports requires the ability to produce and sustain high power outputs. It is well documented that endurance exercise performance can be improved when training volume and intensity are increased (6,7,8). Moreover, maximum sustainable power output and performance in sustained, high-intensity competitions is highly correlated with training intensity (9,10,11) and athletes who maintain higher

training intensities typically achieve a greater training effect and perform better in competition

Evidence supporting the ergogenic effects of breathing hyperoxic gas during exercise has led some investigators to study the effects of using high-intensity, hyperoxic training to improve competitive performance. In an early study by Chick, et al. (12), trained endurance athletes perform six weeks of high intensity training while breathing a gas mixture consisting of 70% oxygen. Chick noted that training intensity was increased when the subjects breathed the hyperoxic mixture and endurance exercise performance was significantly improved following the training period.

In perhaps the most comprehensive hyperoxic training study to date, Morris, et al. (13), used 16 competitive cyclists to study the effects of hyperoxic training on cycling performance. During a three-week period of training at the United States Olympic Training Center, half of the subjects performed nine, high-intensity interval training sessions while breathing normal air, while the other eight subjects performed identical intervals while breathing hyperoxic mixture of 26% oxygen.

The results of the study showed that subjects who breathed the hyperoxic mixture were able to train at a 16% higher workload than were those who breathed normal air (Figure 3).

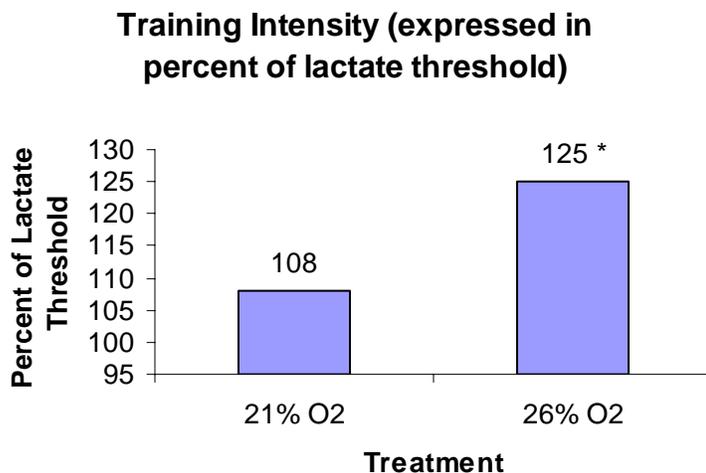


Figure 3. Training intensity of subjects performing intervals while breathing 21% or 26% oxygen (*Significantly higher than the 21% oxygen group).

This increased training intensity appeared to have positive effects on performance, as subjects who trained with the hyperoxic mixture saw significant improvements in their performance of a 120 kJ cycling test (Figure 4) and in power output at lactate threshold (Figure 5), while the subjects who breathed normal air saw no improvements in these measurements.

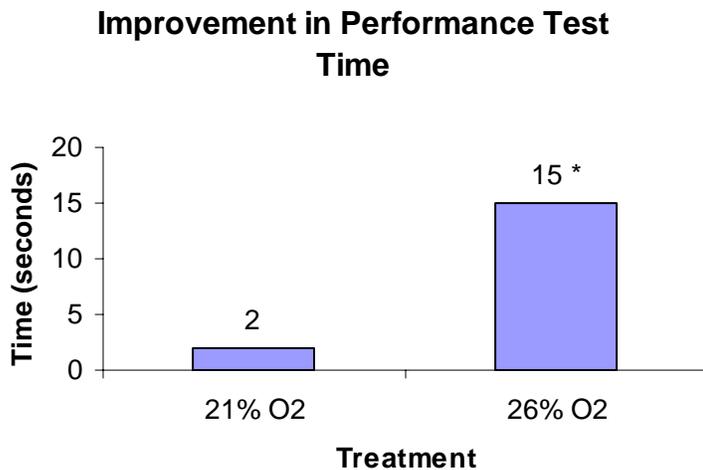


Figure 4. Improvement in performance test time pre vs. post-training (*Significantly different from the 21% oxygen group).

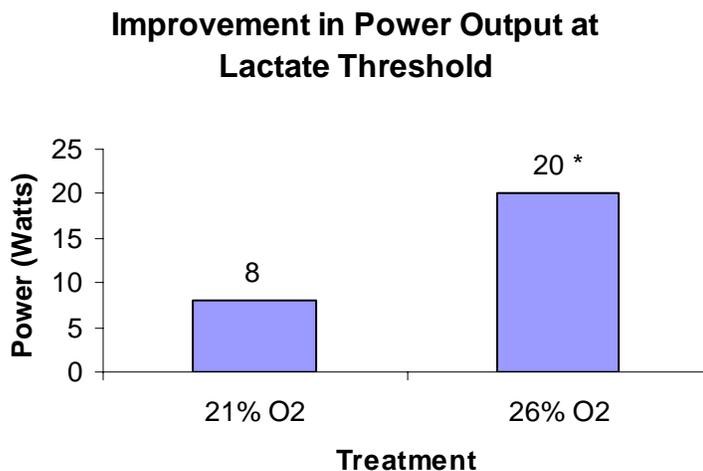


Figure 5. Improvement in power output at lactate threshold pre vs. post-training (*Significantly different from the 21% oxygen group).

In addition to the scientific data, there have been a growing number of athletes who have successfully used supplemental oxygen training over the last seven years. Since 1995, supplemental oxygen training has been used extensively by athletes at the

United States Olympic Training Center in Colorado Springs, Colorado. In 1996, cyclist Jane Quigley began incorporating supplemental oxygen training into her overall preparation for the 1996 World Track Championships. At the world championships, Jane set a personal record in the women's individual pursuit and won a silver medal in the points race (the best placing of her career). Additionally, Mari Holden and Alison Dunlap both utilized supplemental oxygen training in their preparation to win the 2000 World Time Trial Championship and the 2001 World Mountain Bike Championship, respectively.

In other endurance sports, the U.S. Olympic Speed Skating Team began using supplemental oxygen training in 2001 in preparation for the 2002 Winter Olympic Games in Salt Lake City. At the Olympic Games, the team surpassed even the most optimistic expectations by winning three gold, and four bronze medals. Many skaters who typically placed in the top 20 in other international competitions were suddenly winning medals in Salt Lake City. When asked about the success of the team, the coaches stated that the only thing they changed about their preparation was the addition of supplemental oxygen training before the Olympic Games.

In addition to the success in preparing athletes for traditional endurance sports, researchers at the Olympic Training Center have used supplemental oxygen training to improve performance in sports that feature numerous and repeated bouts of high intensity exercise (Morris, unpublished research findings). Thus, athletes participating in sports such as soccer, basketball and hockey could use supplemental oxygen training to improve their stamina and increase the quality and quantity of their playing time.

Other Uses for Supplemental Oxygen Training

Treatment of Obesity

Approximately 40% of the adult population of western nations suffer from obesity. Health problems associated with excess body fat are numerous. In addition to lowering the quality of life, obesity is recognized as either the primary cause or as a contributing factor for a variety of maladies including cardiovascular disease, hypertension, diabetes, arthritis and some forms of cancers. Many health professionals currently recognize obesity as the number one health concern facing the population of the United States.

While there are many contributing factors that give rise to the development of obesity, the most prevalent cause is excessive caloric consumption in combination with inadequate physical exercise. In most individuals, these energy imbalances are small, and the process of becoming obese occurs over a process of several years. Thus, preventing obesity can be accomplished with minor adjustments in daily eating or exercise habits.

For those individuals afflicted with obesity, treatment strategies include dietary restriction, increased levels of exercise and various surgical techniques. Unfortunately, many methods of weight control offer only temporary relief as permanent reduction of excess body fat cannot be attained until the individual achieves a proper balance between caloric consumption and caloric expenditure. Preventing and treating obesity through the development of more effective methods of maintaining proper caloric balance will be a major challenge for health professionals in the coming years.

Supplemental oxygen training is emerging as a potentially useful tool for increasing caloric expenditure. A recent study at the United States Olympic Training Center, revealed that subjects increased their rate of caloric expenditure by 13% during exercise when breathing 60% oxygen as opposed to exercising under ambient conditions (Morris, unpublished research findings). In addition to the increase in caloric expenditure, Morris also noticed that exercising under the 60% oxygen condition resulted in a significant increase fat utilization of 21% when compared to the ambient trials.

Other research data also suggest an increase in fat burning during exercise in hyperoxia. Adams, et al. (14), had subjects exercise for 30 minutes at an intensity that elicited 75% of their maximal oxygen consumption while breathing either ambient air or a 61% oxygen mixture. Because exercise intensity was kept consistent for both treatments, caloric expenditure did not change with a change in gas concentrations. However, metabolic markers indicated that fat consumption did increase during the 61% oxygen trial.

Cardiovascular Disease

The primary cause of heart disease and heart attacks is a buildup of fat and cholesterol deposits in the coronary arteries. These deposits will harden over time leading to atherosclerosis and eventually to congestive heart failure – a disease that is responsible for nearly half of all deaths in the United States and Western Europe.

Regular physical exercise is recognized as an effective means of reducing blood cholesterol and preventing the genesis of atherosclerosis in healthy individuals. However, to be effective, exercise must be frequent, prolonged and vigorous. Cardiologists routinely prescribe physical exercise to cardiac patient as part of the rehabilitative process following heart attacks and heart surgery. Cardiac rehabilitation units designed to provide supervised exercise opportunities for these cardiac patients are numerous and generate a great deal of revenue for the health care industry. However, despite their widespread use there is little evidence that these supervised exercise programs make a significant impact on the quality of life for cardiac patients, reduce their chances of having a second heart attack, or extend lifespan.

One reason for this apparent dichotomy is that the physical condition of most patients recovering from heart attacks limit their ability to perform vigorous exercise. Atherosclerosis develops as a result of many years of sedentary living and other unhealthy activities. As a result, victims of congestive heart failure are typically in very poor physical condition at the time of the event. Poor physical conditioning combined with the heart attack itself and subsequent open heart surgery severely compromises a patient's ability to perform physical exercise. Specific problems experienced by cardiac patients include low cardiac output, reduced arterial oxygen saturation and poor vascularization of peripheral musculature. All of these physiological shortcomings combine to reduce the flow of oxygen to the working muscle. As a result, these patients often are unable to perform exercise of sufficient intensity to make a significant impact on their recovery. Breathing hyperoxic gas during exercise would promote an increase in oxygen flow to the working muscle and increase exercise performance of cardiac patients. The increase in exercise intensity may lead to a more complete recovery of these patients, thus reducing their chances of experiencing future heart attacks and improve their quality of life.

Potential Dangers of Hyperoxic Training

Exposure to high levels of oxygen poses two main threats to the health of human subjects. The first and most serious threat is oxygen toxicity to the central nervous system. Lengthy exposures to high levels of oxygen have been shown to cause temporary reductions in coordination and mental capacity and continued exposure eventually leads to unconsciousness and death. Secondly, a less serious problem associated with oxygen exposure is the development of free-oxygen radicals, which can result in cell and tissue damage.

Central nervous system oxygen toxicity was first noticed in deep-sea divers. In the early years of oxygen assisted diving, individuals would breathe normal oxygen concentrations in high-pressure underwater environments. This combination exposed divers to extremely high oxygen pressures and sometimes had a negative impact on the nervous system. The degree of oxygen toxicity experienced is dependant on the degree of oxygen pressure and the duration of exposure. Scientists have used a number of animal models to test the tolerance of mammalian nervous system to extreme doses of oxygen, and while many have been successful in inducing oxygen toxicity, (Arieli and Hershko Harabin, et al.) most utilized models that exposed animals to oxygen pressures in the range of 2000 – 6000 torr for time periods ranging from several hours to days (15,16,17,18). These levels of exposure are far above those proposed by the TrainXtreme system where typical exposures would consist of oxygen pressures of approximately 450 torr for two to three, 45-min training sessions per week. By comparison, this level of exposure is roughly half of that used currently in therapeutic settings to treat burns and chronic wounds with no harmful side-effects.

Hyperoxia and Free Oxygen Radicals

The production of free oxygen radicals (FOR) occurs as a normal part of aerobic metabolism (19,20). While FOR can damage healthy cells, the human body is generally well protected from FOR by antioxidant enzymes and antioxidant agents found in foods. During heavy exercise, however, rates of aerobic metabolism increase exponentially, giving rise to unusually high levels of free oxygen radicals that may result in increased cellular damage (21). Hyperoxia also appears to stimulate the production of free oxygen radicals in resting animals, presumably by increasing the rate aerobic metabolism (22).

Interestingly, exposure to high levels of FOR via hyperoxia or heavy exercise has been shown to increase antioxidant capacity and tolerance to FOR stress in human and animal models (23,24,25). Dietary strategies have also been effective in reducing or eliminating damage caused by free oxygen radicals (26).

Like CNS toxicity studies, researchers who have investigated the effects of hyperoxia on cellular damage caused free oxygen radicals typically have utilized exposures to high levels of oxygen over extended periods of time. Ahotupa et al. (22) subjected rats to 100% oxygen and observed the first measurable signs of FOR damage only after 12 hours of continuous exposure. Others (27,28) have reported the development of pulmonary edema (a sign of FOR damage) after 60-66 hours of continuous exposure to 95% oxygen mixtures.

In a study performed at the United States Olympic Training Center, researchers investigated the effects of supplemental oxygen training on free oxygen radicals in exercising humans. Competitive cyclists completed high-intensity training sessions consisting of six, 100 kJ work intervals while breathing either ambient air or a 60% oxygen mixture. Total duration of exposure to the hyperoxic mixture was approximately 36 minutes. No differences were observed between the two trials with respect to markers of FOR damage or ostensive symptoms of oxygen toxicity (Morris, unpublished research findings). The results of this study provide strong evidence that the supplemental oxygen training approach proposed by the TrainXtreme system does not promote oxygen toxicity or submit its users to extraordinary health risks.

Summary

Scientific research has produced strong evidence to support the breathing of hyperoxic gas mixtures as a safe method of increasing power output, work tolerance, rate of caloric expenditure and fat usage during single exercise events. Furthermore, when supplemental oxygen is used regularly to increase training intensity, performance is improved in competitive events that feature single, prolonged, steady efforts and in those that require numerous, short, high-intensity periods of exertion. Thus, supplemental oxygen training could be used effectively to improve the performance capacity of endurance athletes such as cyclists, long-distance runners and swimmers and in athletes participating in traditional team sports such as basketball, soccer and hockey.

Another potential area of use would be in the promotion of public health. The increase in the rate of caloric expenditure and fat utilization while exercising in hyperoxia could provide a useful tool in preventing atherosclerosis and heart disease, and in the prevention and treatment of obesity. The prevalence of these maladies in the populations of western nations could provide a large market for the trainXtreme system.

References

1. Welch, H.G. (1987). Effects of hypoxia and hyperoxia on human performance. *Exercise and Sports Science Review* 15: 191-220.
2. Wilson, G.D. & H.G. Welch (1975). Effects of hyperoxic gas mixtures on exercise tolerance in man. *Medicine and Science in Sports and Exercise* 7: 46-52.
3. Wilber, R.L., P.L. Holm, D.M. Morris, G.M. Dallam, & S.D. Callan (2002). Effect of $F_{I}O_2$ on physiological responses and power output in trained cyclists at moderate altitude. *Medicine and Science in Sports and Exercise* 34(5): S1509.
4. Peltonen, J.E., J. Rantamaki, S.P.T. Niittymaki, K. Sweins, J.T. Viitasalo, & H.K. Rusko (1995). Effects of oxygen fraction in inspired air on rowing performance. *Medicine and Science in Sports and Exercise* 27(4): 573-579.
5. Plet, J., P.K. Pedersen, F.B. Jensen, & J.K. Hansen (1992). Increased working capacity with hyperoxia in humans. *European Journal of Applied Physiology* 65: 171-177.
6. Esbjornsson-Liljedahl, M., C.J. Sundberg, B. Norman, & E. Jansson (1999). Metabolic response in type I and type II muscle fibers during a 30-s cycle sprint in men and women. *Journal of Applied Physiology* 87(4): 1326-1332.
7. Martin, D.T., J.C. Scifres, S.D. Zimmerman, & J.G. Wilkinson (1994). Effects of interval training and a taper on cycling performance and isokinetic leg strength. *International Journal of Sports Medicine* 15(8): 485-491.
8. Sands, W.A. (1992). Periodization and planning of training. *American Ski Coach* Fall: 9-17.

9. Jeukendrup, A.E., M.K.C. Hesselink, A.C. Snyder, H. Kuipers, & H.A. Keizer (1992). Physiological changes in competitive cyclists after two weeks of intensified training. *International Journal of Sports Medicine* 13(7): 534-541.
10. Keith, S.P., I. Jacobs, & T.M. McLellan (1992). Adaptations to training at the individual anaerobic threshold. *European Journal of Applied Physiology* 65: 316-323.
11. Martin, D.T. (1994). Stress hormones following intense cycling exercise: insights into overtraining. Unpublished Doctoral Dissertation. University of Wyoming, Laramie, WY.
12. Chick, T.W., D.M. Stark, & G.H. Murata (1993). Hyperoxic training increases work capacity after maximal training at moderate altitude. *Chest* 104:1759-1762.
13. Morris, D.M., J.T. Kearney, & E.R. Burke (2000). The effects of breathing supplemental oxygen during altitude training on cycling performance. *Journal of Science and Medicine in Sport* 3(2): 165-175.
14. Adams, R.P., P.A. Cashman, & J.C. Young (1986). Effect of hyperoxia on substrate utilization during intense submaximal exercise. *Journal of Applied Physiology* 61(2): 523-529.
15. Arieli, R. (1994). Oxygen toxicity as a function of time and PO₂. *Journal of Basic & Clinical Physiology & Pharmacology* 5(1): 67-87.
16. Arieli, R., & G. Hershko (1994). Prediction of central nervous system oxygen toxicity in rats. *Journal of Applied Physiology* 77(4): 1903-1906.
17. Butler, F.K. & E.D. Thalmann (1986). Central nervous system oxygen toxicity in closed circuit scuba divers II. *Undersea Biomedical Research* 13(2): 193-223.
18. Harabin, A., S. Survanshi, P. Weathersby, J. Hays, & L. Homer (1988). The modulation of oxygen toxicity by intermittent exposure. *Toxicology and Applied Pharmacology* 93: 298-311.
19. Dekkers, J.C., L.J.P. van Doornen, & H.C.G. Kemper (1996). The role of antioxidant vitamins and enzymes in the prevention of exercise-induced muscle damage. *Sports Medicine* 21(3): 213-238.
20. Lawler, J.M., & S.K. Powers (1998). Oxidative stress, antioxidant status, and the contracting diaphragm. *Canadian Journal of Applied Physiology* 23(1): 23-55.

21. Alessio, H.M., A.E. Hagerman, B.K. Fulkerson, J. Ambrose, R.E. Rice, & R.L. Wiley (2000). Generation of reactive oxygen species after exhaustive aerobic and isometric exercise. *Medicine and Science in Sports and Exercise* 32(9): 1576-1581.
22. Ahotupa, M., E. Mantyla, V. Peltola, A. Puntala, & H. Toivonen (1992). Pro-oxidant effects of normobaric hyperoxia in rat tissues. *Acta Physiologica Scandinavica* 145: 151-157.
23. Harabin, A.L., J.C. Braisted, & E.T. Flynn (1990). Response of antioxidant enzymes to intermittent and continuous hyperbaric oxygen. *Journal of Applied Physiology* 69(1): 328-335.
24. Ho, Y.S., M.S. Dey, & J.D. Crapo (1996). Antioxidant enzyme expression in rat lungs during hyperoxia. *American Journal of Physiology* 270(14): L810-L818.
25. Powers, S.K., L.L. Ji, & C. Leeuwenburgh (1999). Exercise training-induced alterations in skeletal muscle antioxidant capacity: a brief review. *Medicine and Science in Sports and Exercise* 31(7): 987-997.
26. Cao, G., B. Shukitt, P. Bickford, J. Joseph, J. McEwen, & R. Prior (1999). Hyperoxia-induced changes in antioxidant capacity and the effect of dietary antioxidants. *Journal of Applied Physiology* 86(6): 1817-1822.
27. Crapo, J., B. Barry, H. Foscue, & J. Shelburne (1980). Structural and biochemical changes in rat lungs occurring during exposure to lethal and adaptive doses of oxygen. *American Review of Respiratory Disease* 122: 123-143.
28. Olivera, W., K. Ridge, & J. Sznajder (1995). Lung liquid clearance and Na^+-K^+ -ATPase during acute hyperoxia and recovery in rats. *American Journal of Respiratory Critical Care Medicine* 152: 1229-1234.