4 Physical Exercise Under Hyperbaric Conditions

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This chapter investigates the role of exercise under normoxic and hyperbaric conditions, as well as the impact of greatly reduced supplies of oxygen. These results help set the stage for later detailed analyses of the strengths and limits of HBO therapy itself. The main sections of this chapter are:

Introduction

Oxygen plays an important role in exercise physiology, and this extensive subject was discussed in an earlier book (Jain 1989b). The following brief account of what happens during exercise under normoxic conditions serves as an important introduction to the effects of hyperbaric conditions on physical exercise.

The dynamic transition among different metabolic rates of V O2 (V O2 kinetics), initiated, for example, at exercise onset, provides a unique window into understanding metabolic control. Because of interfiber type differences in O2 supply relative to V O2, the presence of much lower O2 levels in the microcirculation supplying fast-twitch muscle fibers, and the demonstrated metabolic sensitivity of muscle to O2, it is possible that fiber type recruitment profiles might help explain the slowing of V O2 kinetics at higher work rates and in chronic diseases (Poole *et al* 2008).

Oxygen demands on the body can of course increase dramatically during exercise. Our normal oxygen consumption of about 150 ml/min might rise to 1000 ml/min during moderate exercise, even though alveolar pO_2 is maintained at 104 mmHg. This situation is achieved by a fourfold increase of alveolar ventilation. During strenuous physical activity, such as a marathon race, the body's oxygen requirements may be 20 times normal, yet oxygenation of the blood does not suffer. There is, however, tissue hypoxia in some of the working muscles and strenuous exercise may be considered as a hypoxic episode. The response to physical exercise is outlined in Table 4.1. Physical activity, in the form of voluntary wheel running, induces gene expression changes in the brain. Animals that exercise show an increase in brain-derived neurotrophic factor, a molecule that increases neuronal survival, enhances learning, and protects against cognitive decline. Microarray analysis of gene expression provides further support that exercise enhances and supports brain function.

Exercise Under Hypoxia

Some decline in pO_2 may occur during intensive exercise, particularly in individuals with high $VO_{2\,max}$. Whether this can be termed "hypoxia" or not is controversial. Exercise is not considered to be hypoxia unless the pO_2 falls below the critical level of 40 mmHg. Exercise is hypoxic under the following circumstances:

- Exhausting exercise by normal individuals in normoxic environments
- Exercise at high altitudes
- Exposure to carbon monoxide in the atmosphere
- In patients with chronic obstructive pulmonary disease.

Table 4.1
Effects of Physical Exercise on the Human Body

System	Acute Effects (in untrained subjects)	Effects of Chronic Dynamic Exercise
Cardiovascular	Tachycardia Rise of cardiac output from 5 to 30 l/min	Bradycardia Increase of stroke volume of the heart Increase of heart size Increase of myocardial capillary to fiber ratio
Respiratory	Rise of alveolar ventilation linearly with rise of O_2 uptake Increased work of respiratory muscles, using up 10% of total O_2 uptake	Increase of number of alveoli available for O_2 exchange Increase of extraction fraction of (a-v) O_2 difference
Blood	Hemoconcentration due to fluid loss Reduction of O_2 saturation (5%) Rise of ammonia and lactate	Increase of hemoglobin Increase of 2,3-diphosphoglycerate Less accumulation of ammonia and lactate
Metabolism		Raised anaerobic thresholds Increased utilization of FFA Increased intracellular pools of ATP and phosphocreatine
Skeletal muscle		Increase of maximal blood flow rate Increase of mitochondrial volume and oxidative enzymes Increase of capillary density
Brain		Increase of cerebral blood flow Increase in brain-derived neurotrophic factor Enhances leaning and prevents cognitive decline.

Table 4.2
Effects on the Human Body of Exercise Under Hypoxic Conditions

Cardiovascular System
– Increase of cardiac output and muscle blood flow compared with normoxic conditions)

Respiratory System
– Increase of ventilation
– Increase in oxygen consumption
– No appreciable change in alveolar and arterial CO_2 transport

Metabolic
– Increase of "excess lactate"
– Increase of ammonia formation

The effects of physical exercise under hypoxic conditions are shown in Table 4.2.

The main changes in chronic hypoxia in relation to exercise are:

1. Decrease in arterial saturation (due to a fall of inspired oxygen pressure)
2. Decrease in maximal cardiac output (due to a fall of maximal heart rate)
3. Increase in hemoglobin concentration
4. Decrease in the maximal oxygen flow through muscle capillaries
5. Change in respiratory potential of the muscles due to loss of oxidative enzymes.

Exercise in Hyperbaric Environments

The study of human work performance in hyperbaric environments is important for evaluating the effects of diving on the human body. The effects of physical exercise while diving depend upon the following key factors:

1. Pressure to which the diver is subjected
2. Composition of the breathing mixture
3. Type of activity e.g., swimming, walking underwater, or operating a machine
4. Body posture, e.g., vertical or prone
5. Ambient temperature.

The increase of VO_2 under hyperbaric conditions corresponds to the rise in oxygen needs. The oxygen consumption during a standard exercise at 5 ATA of air is higher than at 1 ATA. The main reason for this is the increase of respiratory resistance due to a rise of gas density. Whereas the total oxygen consumption at 1 ATA comprises 81.5% of the total oxygen needs, this value decreases to 73.9% at 5 ATA. Factors that limit work capacity at depth include:

1. Increased respiratory resistance to breathing dense gases
2. Increased energy cost of ventilation
3. Carbon dioxide retention
4. Dyspnea
5. Adverse cardiovascular changes.

Exercise in hyperbaric environments depresses the heart rate. Part of this depression is due to the effects on the heart of a rise in the partial pressure of oxygen, both directly and via the parasympathetic efferents. In addition, other factors such as gas density, high inert gas pressure, or hydrostatic pressure may interfere with sympathetic stimulation of the heart.

A reduction of ventilation and bradycardia during exercise under 2 ATA in air has been attributed to the increase in gas density.

Hyperbaric conditions are known to increase the subjective feeling of fatigue in divers. there is a decrease of vigilance and a subjective feeling of change in the body functions of divers who undergo saturation dives to simulated pressures of 40 ATA. This feeling is more pronounced during compression and saturation, and decreased during compression.

Exercise Under Hyperoxia

Hyperoxia here refers to the use of raised oxygen fractions in the inspired air, but at a pressure not higher than 1 ATA.

The results may vary according to the method used to achieve hyperoxia, i.e., whether the hyperoxia is achieved

Table 4.3
Effect on the Human Body of Physical Exercise Under Hyperoxic Conditions

1. Cardiovascular response
   a) Variable decrease of heart rate
   b) Decrease of blood flow to the exercising limb to offset the raised O_2 tension
2. Pulmonary function
   a) Reduction of pulmonary ventilation
   b) Decrease of oxygen consumption compared with exercise under normoxia
3. Biochemical
   a) H^+ ion concentration is higher than during exercise under normoxia
   b) Reduction of excess lactate
4. Energy metabolism
   a) Decreased rate of glucose utilization and lactate production
   b) Shift of respiratory quotient toward fat metabolism, thus lowering RQ

by breathing a gas with high fractional concentration of oxygen at sea level, or by the study being carried out in a pressure chamber. The response to exercise at a given arterial pO_2 is not the same under these two conditions. Performance increases with increasing pO_2 under both conditions, but in hyperbaric studies performance levels were somewhere between 200 and 400 mmHg. In hyperoxia at 1 ATA, performance increases continuously as pO_2 increases. Increased gas density in the hyperbaric environment increases the work of breathing and compromises performance at high pressures. The effects of hyperoxia on exercise and the possible mechanisms involved are listed in Table 4.3. Cardiovascular function during exercise under hypoxia is described in Chapter 24.

Exercise studies on healthy volunteers have shown that leg $VO_{2\,max}$ is limited by oxygen supply during normoxia but it does not increase during hyperoxia in proportion to either the femoral venous pO_2 or mean leg capillary pO_2.

Physical Exercise Under Hyperbaric Conditions

General Effects

The effects of physical exercise under hyperbaric oxygenation (HBO) are often quite difficult to evaluate, due to the variable interaction of three factors: oxygen, pressure, and exercise. The effects of these factors are better known when applied individually. HBO at 1.5 ATA accentuates some of the effects of normobaric hyperoxia, but higher pressures may cancel some of the advantages of HBO such as reduction of the metabolic complications of exhausting physical exercise. Most of the studies on this topic have concentrated on the metabolic aspects, particularly the lactate accumulation in the blood, which can be easily measured.

A decrease of ventilation and some bradycardia is usually observed while exercising under HBO conditions. $VO_{2\,max}$ increases by 3% during exercise while breathing 100% O_2 at 1 ATA, but does not increase further when the pressure is raised to 3 ATA. There are no changes in oxygen consumption or oxygen extraction during exercise under HBO at 2 ATA, as compared with exercise while breathing normobaric air.

The $(a–v)O_2$ difference is the same in healthy young volunteers whether they exercise breathing normal air or under HBO at 3 ATA (pAO_2 1877 mmHg). It appears probable, therefore, that the maximum oxygen uptake in active muscles does not increase when the arterial oxygen content is increased. Thus, the maximum oxygen uptake in an active muscle seems not to be limited by the blood flow to the muscle or the oxygen diffusion from the blood to the interior of the muscle cell, but rather by the oxygen utilization system inside the cell.

Effect on Lactate Production and Clearance

Studied of the effect of HBO (3 ATA) on excess lactate production during exercise in dogs show that the values of excess lactate are much lower than those observed during previous exercise by the same animals at 1 ATA while breathing air. If exercise is conducted under HBO first, not only is the excess lactate low, but it remains so during subsequent exercise at 1 ATA breathing air 45 min later. Three mechanisms for this effect are:

- Oxygen provided to the exercising muscles during hyperoxia is sufficient to lower the excess lactate formation. It counteracts the hypoxia that usually results while exercising at atmospheric pressure, and is responsible for the production of lactic acid.
- There is increased removal of excess lactate as a result of stimulation of the oxidative enzymatic process.
- HBO produces inhibition of glycolytic sulfhydryl enzymes. This results in an improvement of glycolysis, and therefore in lowered lactate formation. Such an inhibitory effect could well persist for up to 45 min and explain the continual decrease of excess lactate after HBO exposure when exercise under atmospheric air followed.

The myocardium and liver of dogs exercised under 3 ATA HBO can eliminate the increased amount of lactate at the expense of glucose consumption.

Studies of the blood chemistry parameters in healthy adult volunteers who exercised while breathing air, normobaric oxygen, and oxygen at 1.5 ATA revealed that in the rest period following exercise, uric acid, lactate, and pyruvate decreased significantly compared with the levels after exercise without HBO. The drop in the level of ammonia was less. However, the ammonia levels 1 min and 15 min after exercise under HBO were much lower than the corresponding values during exercise while breathing normobaric oxygen (see Figure 4.1). Lactate levels immediately after exercise (1–20 min) were lower during exercise while breathing oxygen than during exercise in room air. Lactate levels were lower during exercise under HBO than they had been 1, 5, 10, and 15 min previously after exercise, breathing normobaric oxygen. The rise of excess lactate was less after ergometry under HBO than after ergometry under oxygen breathing. The excess lactate (XL) was calculated according to the formula:

$$XL = (Ln - Lo) - (Pn - Po)\frac{Lo}{Po}$$

where Lo is the resting and Ln the exercise blood lactate, and Po and Pn are the resting and exercise blood pyruvate values, respectively. There was a fall of glucose during exercise under HBO, suggesting inhibition of glycolysis, which is a contributory factor to the rise in the level of ammonia. Inhibition of glycolysis should lead to diminu-

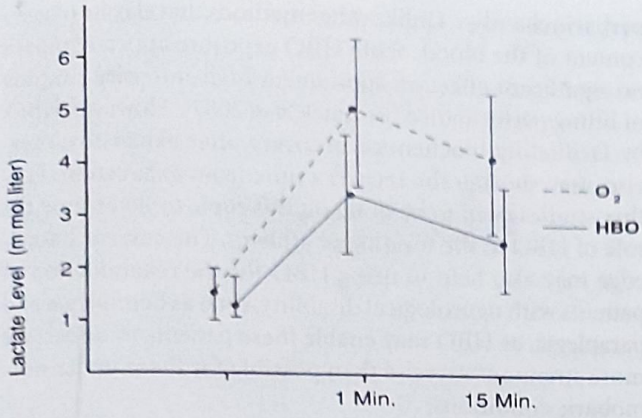

Figure 4.1
Effect of physical exercise on lactate levels under normobaric oxygenation (---O_2) and hyperbaric oxygenation (—HBO). Arterial blood lactate levels were determined before treadmill exertion as well as 1 min and 15 min following the completion of exercise.

tion of uricemia. Whether there is stimulation or depression of the Krebs cycle at 1.5 ATA HBO remains to be determined. But in any case, the tendency of ammonia levels to fall is striking. These findings tend to support the hypothesis that more glycogenic amino acids go into the citric acid cycle than does α-ketoglutaric acid.

Effect of Exercise on Ammonia Metabolism

Lactate accumulation is well known as a factor in causing fatigue and limiting the capacity for physical exertion. However, the role of ammonia in causing fatigue is not quite so clear.

At rest skeletal muscle is consistently an ammonia consumer with a clearance of approximately 0.3 mmol/kg wet wt/min by resting muscle. Assuming that the body is 40% muscle, there is 8 mmol/min uptake by the resting muscle. Ammonia levels are known to rise steeply following muscular exertion, but they decline spontaneously in a short time in healthy adults. Hyperammonemia of exercise is due mainly to a release of ammonia from muscles during the recovery phase. As muscle pH returns to the resting level, more ammonia diffuses from the muscle into the blood. If the ammonia levels do not subside promptly, untoward effects may be experienced by a person doing exhaustive physical exercise. This is likely to happen in untrained persons with neurological disorders. Healthy young athletes usually do not suffer from "ammonia hangover."

Ammonia levels are lower in those exercising under HBO compared with those exercising under normobaric conditions. The mechanism by which HBO lowers ammonia levels in the blood is not clear. Ammonia is formed in the body by deamination of amino acids where the amino group is transferred to α-ketoglutaric acid, which becomes glutamic acid and may release ammonia again. Most of the ammonia is removed from the blood by conversion to urea in the liver. HBO has been shown to lower blood ammonia in hepatic encephalopathy (see Chapter 26). Blood urea can be lowered in volunteers exercising under HBO, an effect attributed to inhibition of glycolysis.

Effect of HBO on Antioxidant Enzyme Skeletal Muscle

In skeletal muscle the activity of the enzymatic antioxidants superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT) is regulated in response to generation of reactive oxygen species (ROS). Increased activity of these enzymes is observed after repeated bouts of aerobic exercise, a potent stimulus for intracellular ROS production. Although ROS formation in response to vigorous physical exertion can result in oxidative stress, ROS also play an important role as signaling molecules (Niess and Simon 2007). ROS modulate contractile function in unfatigued and fatigued skeletal muscle. Furthermore, involvement of ROS in the modulation of gene expression via redox-sensitive transcription pathways represents an important regulatory mechanism, which has been suggested to be involved in the process of training adaptation.

HBO inhalation also stimulates intracellular ROS production although the effects of HBO on skeletal muscle SOD, GPx and CAT activity have not been studied. In adult male rats acute HBO inhalation at 3 ATA reduced catalase activity by approximately 51% in slow-twitch soleus muscles (Gregorevic *et al* 2001). Additionally, repeated HBO inhalation (twice daily for 28 days) increased Mn^{2+}-superoxide dismutase activity by approximately 241% in fast-twitch extensor digitorum longus muscles. Thus both acute and repeated HBO inhalation can alter enzymatic antioxidant activity in skeletal muscles.

Physical Exercise in Relation to Toxic Effects of HBO

The toxic effects of oxygen are not usually seen during HBO below pressures of 3 ATA. Concern has been expressed that physical exercise may predispose patients to oxygen toxicity.

Breathing oxygen at 2 ATA during exercise lowered ventilation and restores arterial pH and pCO_2 toward resting levels. There is either a slight elevation of cerebral blood flow or a diminished rate of cerebral oxygen consumption during exercise while breathing oxygen at 2 ATA, without gross elevation of cerebral venous pO_2.

Physical exercise is accompanied by a rise in body temperature that may increase the possibility of oxygen toxicity. In the hyperbaric chamber, the temperature is usually

controlled and this factor is eliminated. Peripheral vasoconstriction usually limits blood flow and oxygen delivery under hyperoxia, but exercise may have a vasodilating effect which might allow exposure of the tissues to high oxygen concentrations.

Conclusions

Although HBO reduces the biochemical disturbances resulting from physical exertion, it has not been shown that HBO extends human physical performance. The duration of time to physical exhaustion does not decrease in the hyperbaric chamber. Unlike other methods that elevate oxygen content of the blood, acute HBO exposure appears to have no significant effect on subsequent high-intensity running or lifting performance (Rozenek *et al* 2007). However, HBO, by facilitating biochemical recovery after exhaustive exercise, may shorten the recovery time from exhaustion. Further studies need to be done on this topic to determine the role of HBO in the training of athletes. The current knowledge may also help in using HBO for the rehabilitation of patients with neurological disability, such as hemiplegia and paraplegia, as HBO may enable these patients to undertake more strenuous exercise than possible for them under normobaric conditions.