INFLUENCE OF ALTITUDE TRAINING ON MUSCLE METABOLISM AND PERFORMANCE IN MAN*

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A good deal of information is available on the influence of hypoxia, or altitude, on physical performance, especially during prolonged exercise (2, 3, 4, 7, 8, 12, 18-22, 29, 33, 34-37, 41, 44, 45, 52). But, more than any other recent event, it was the Olympic Games in Mexico City that aroused so much interest in the problems surrounding altitude and sport performance. Four main questions were, at that time, asked.

1. To what extent is performance affected at moderate altitude (about 2,000m – 6,600 ft)?
2. Can the negative effects be overcome by the processes of adaptation; to what extent can they be overcome; and how long does adaptation take?
3. Can extremely hard training at this altitude lead to any bodily harm?
4. Can the performance at sea level be improved by training at altitude?

This last question is still of considerable interest as we are constantly confronted with athletes who want to carry out some portion of their training programme at altitude to improve their performance at sea level.

The Delivery of Energy

The two main energy delivering pathways in the resynthesis of adenosine triphosphate (ATP) should here be recalled to mind:

1. The breakdown of energy-yielding substrates without the participation of oxygen; that is, the anaerobic energy delivery.
2. The degradation of substrates in which oxygen is the ultimate hydrogen acceptor; that is, the aerobic process.

Figure 1 shows the shift of anaerobic to aerobic energy delivery in relation to the work time at sea level for individuals with high maximal power for both. For a maximal effort of less than two minutes duration, the anaerobic processes dominate, but for muscular work of more than two minutes duration the energy cost must be defrayed primarily through oxidative processes (29). The ability of the body to perform oxidative reactions is

Fig. 1. Absolute and relative contribution of total energy yield from aerobic and anaerobic energy production during maximal effort of up to 120 minutes duration. (On the abscissa, time is expressed logarithmically.) After two minutes of maximal exercise the relationships change owing to the increasing importance of the oxidative processes. This graph reflects the behaviour of persons with high aerobic and anaerobic powers.

reduced when the oxygen content in the inspired air, and therefore the oxygen content in the blood, is also reduced.

In the following discussion the influence of adaptive mechanisms on the aerobic and anaerobic processes during altitude training must be separated.

The values for arterial oxygen saturation, obtained under resting conditions at various altitudes, or using hypoxia-simulating gas mixtures, are reduced relative to those obtained at sea level (Fig. 2). In addition, it has been found that the arterial oxygen saturation at any given work load is reduced in relation to the altitude and that as the work is increased there is a greater reduction in oxygen saturation at the same altitude.

It is evident that at an altitude, for example, of 4,250m (14,000 ft) corresponding to a low hypoxic mixture of 12.7% oxygen, the arterial oxygen pressure and oxygen saturation are reduced – the oxygen

* Supported by Bundesinstitut für Sportwissenschaften

** Recipient of Humboldt Research fellowship

Fig. 2. Changes in the oxygen saturation (SO_2) of arterial blood during exercise at various altitudes. The arterial SO_2 drops during exercise at very high altitude; this drop is greater than the increase in the altitude or the working intensity, either alone or in combination.

1 = Banchemo et al, 1966 (5); 4 = Velasques, 1956 (55);
2 = Doll et al, 1967 (12); 5 = Vogel et al, 1962 (56);
3 = Doll et al, 1968 (13); 6 = West et al, 1962 (57).

saturation decreases additionally dependent on the work intensity (Fig. 3). The reduction in the arterial saturation at different oxygen diffusion capacities for an alveolar oxygen pressure of 80 mm Hg in the lungs — corresponding to that at Mexico City — has been calculated during increased oxygen consumption. When the oxygen consumption reaches a certain level, there is a steeper reduction of the arterial oxygen saturation (13, 29). The effect of this decreasing arterial oxygen saturation is to reduce the ability to perform prolonged work.

There is an actual diminution of the maximal oxygen uptake — or physical working capacity — for some days after arrival in Mexico City (Fig. 4). During residence at Mexico City (2,250 m — 7,382 ft) there is, however, an improvement as a result of various adaptive mechanisms; the maximal capacity as measured at sea level, nevertheless, was not reached even after prolonged residence. The measurements of different research groups show considerable variation in the degree both of diminution and of readjustment that can occur in maximal capacity (2, 18, 29, 44, 50, 52). There are three main reasons for this variation: length of residence before the first test (1 — 8 days); type of exercise and methods of oxygen-uptake measurement; and training status.

There is no doubt that the reduced physical performance is due to the decrease in oxygen supply.

Fig. 3. Oxygen pressure, saturation, pH, and carbon dioxide pressure in arterial blood during breathing of normal air and a 12.7 vol% O_2 in N_2 hypoxic mixture (4,250 m altitude) (13) oxygen in nitrogen hypoxic mixture — equivalent to 4,250 (14,000 ft) altitude (13).

The oxygen pressure (pO_2) and the oxygen saturation of the femoral venous blood are lower at altitude than at sea level. During maximal exercise under different hypoxic conditions the venous pO_2 is respectively 2 and 5 mm Hg lower than when breathing normal air (Fig. 5). The absolute values for the average pO_2 under these hypoxic conditions are 15.9 and 12.6 mm Hg during heavy steady-state exercise. In individual cases, values of 8.5 and 9.0 mm Hg were observed with 12.7% oxygen in the inspired air; thus, in these cases the critical venous pO_2 values given by Stainsby (54) were surpassed.

The lower arterial oxygen saturation under hypoxic conditions cannot be compensated by the higher oxygen extraction by the muscle. The femoral arterio-venous oxygen difference is reduced by 7% and 26% during exercise when breathing hypoxic mixtures of 15.9% and 12.7% oxygen — corresponding respectively to altitudes of 2,500 m (8,250 ft) and 4,250 m (14,000 ft).

During steady-state exercise breathing a 15.9% oxygen

Fig. 4. Effect of altitude on physical working capacity. At the altitude of Mexico City (2,250m – 7,382 ft) there is a marked reduction in the maximal oxygen intake capacity; the situation improves as the adaptive mechanisms come into play. (Note the variation in measurements between the different research groups).

1 = Asahina et al, 1960 (2); 4 = Roskmann et al, 1968 (50);
2 = Faulkner et al, 1968 (18); 5 = Saltin, 1966 (52);
3 = Pugh, 1964 (45); 6 = Scharf et al, 1969 (see 29).

Fig. 5. Left: oxygen pressure (pO_2), oxygen saturation (SO_2), pH, and carbon dioxide pressure (pCO_2) in femoral venous blood during breathing of normal air and a 15.9 vol% oxygen in nitrogen hypoxic mixture. Right: pO_2 , SO_2 , pH, and pCO_2 in femoral venous blood during breathing of normal air and a 12.7 vol% oxygen in nitrogen hypoxic mixture (13).

mixture there is no alteration in the proportions of energy produced by aerobic and anaerobic substrate metabolism. By lowering the oxygen content of the inspired air to 12.7%, however, changes in metabolism are observed which indicate that a larger proportion of anaerobic energy is required. But under conditions of maximal exercise at this altitude the oxygen supply to

muscle probably also limits the capacity to work, since lactic acid in blood is significantly higher than at sea level (29, 33, 34). Skeletal muscle simply cannot sufficiently increase its blood volume per unit time to cover its oxygen requirement, so at maximal work loads it must rely on the venous oxygen reserves.

Fig. 6. Coronary arterio-venous differences for oxygen content at rest, during exercise, and in the recovery phase while breathing normal air or 15.9% oxygen (above) and while breathing normal air or 12.7% oxygen (below) (29).

As a result of the lower arterial oxygen supply due to breathing a 15.9% hypoxic mixture under the same conditions of exercise, the coronary arterio-venous oxygen difference is reduced by about 10%. With a 12.9% oxygen mixture there is a 30% reduction in the coronary arterio-venous oxygen difference (Fig. 6). As against this, there is only a small or non-existent drop in the coronary venous oxygen pressure itself (Fig. 7) the lowest values observed were 16 mm Hg the critical coronary venous pO_2 of 5 mm Hg given by Bretschneider (6, 7) and Lochner and Nasser (42) for the heart is not reached during exercise under hypoxic conditions. Thus, we expect there to be no deficiency of myocardial oxygen due to the decreased arterial oxygen pressure. The significant rebound in the coronary venous oxygen pressure during maximal exercise possibly indicates that the hypoxic stimulus provoked a maximal vasodilatation. The increased coronary blood flow should provide sufficient contact between the blood and muscle tissue (23, 32).

After a training period at altitude the physical performance capacity increases, but there are no changes in the arterial pO_2 or oxygen saturation (Fig. 8) and no

Other Mechanisms Affecting Physical Capacity

What other important mechanisms can result in a greater physical capacity after altitude training?

Haemoglobin

During maximal exercise, the reductions in arterial pO_2 and, thereby, arterial oxygen saturation are associated with a reduction in the oxygen content of arterial blood; relative to sea-level values, this reduction is about 2 vol % at an altitude of 2,500m (8,200 ft) and 4.6 vol % at 4,250m (14,000 ft). This means that during maximal exercise, with cardiac output of 30 l/min, less oxygen can be transported in arterial blood at altitude than at sea level; that is, approximately 600 and 1,400 ml oxygen min less during the same work loads at 2,500m and 4,250m respectively. Since the effective draining of oxygen from the blood is fixed by the critical venous pO_2 -limit, a lack of oxygen in arterial blood cannot be

Fig. 7. Oxygen pressure (pO_2) in coronary venous blood during breathing of normal air and 15.9 vol% and 12.7% oxygen in nitrogen mixtures (29).

Fig. 8. Oxygen saturation (SO_2) and oxygen pressure (pO_2) in arterial blood on different days in 1966 at Freiburg (260m – 850 ft) and at Mexico City (2,250m – 7,382 ft) of 14 well-trained athletes. Blood samples were taken under resting conditions, during exercise to exhaustion on a bicycle ergometer (sitting) and in the third minute after exercise (12).

change in the ventilation, either. This fact is surprising because Cerny, Dempsey, and Reddan (9) have recently found an increased diffusion capacity in man after longer residence at high altitude.

Fig. 9. Changes in haemoglobin erythrocytes, and haemoglobin content per erythrocyte of 41 athletes at the Olympic Games in Mexico City. These high values were observed after administration of iron vitamin preparations (35).

indefinitely balanced by an increase in the amount of oxygen extracted. During exercise at altitude the increase in the haemoglobin level through *haemoconcentration* also plays a role in oxygen transport; the effect is an increased oxygen carrying capacity during exercise. Of primary importance during prolonged residence at altitude is the increase in haemoglobin (Fig. 9) which is produced by an *increase in the total blood volume*.

In this regard, there was an increase in haemoglobin content of more than 2 g/100 ml after three weeks altitude training. Similar high levels were found in top athletes from Kenya and in untrained native residents at altitude (35). This corresponds to a rise in oxygen content of arterial blood of 3 vol % at sea level, and means that the oxygen transport capacity of arterial blood was considerably improved at the altitude of 2,500m. There was even over-compensation: the increased viscosity of blood containing more than six million erythrocytes per cu. mm during maximal exercise reduced the heart minute volume, mainly by slowing the rate.

Fig. 10. Level of glucose, lactate, pyruvate, free fatty acids, amino acids, and ammonia in arterial blood at rest, and during and after exercise while breathing normal air (20.9% oxygen at an altitude of 260m - 850 ft) and hypoxic mixture of 15.9%

Lactic Acid Production

A further compensation for the decrease in available oxygen is possible through the increased lactic acid production. This lowers the pH of the blood leaving the working muscles (12 - 15) and has the effect of shifting the oxygen dissociation curve to the right. This shift aids oxygen "off loading" at the muscle without a change in pO₂; the equivalent gain in pO₂ is 2 to 4 mm Hg.

With steady-state exercise (Fig. 10) at altitudes up to 2,500m (8,200 ft), there appears to be no particular change in metabolic substrates in blood when compared to sea level. With steady-state exercise at altitudes up to 4,250m (14,000 ft) a higher lactate production is found, and with maximal exercise (Fig. 11) the lactate level is significantly increased both during and after exercise. This is an indication of the increased anaerobic energy production during this type of exercise (Fig. 12).

Calculations show that the potential increase in energy production through the increased glycolytic turnover -

oxygen (left) and 12.7% oxygen (right). Significant differences were seen only for glucose, lactate, free fatty acids, and ammonia while breathing an hypoxic mixture of 12.7% oxygen (33).

Fig. 11. Femoral arterio-venous differences for glucose, lactate, and free fatty acids ($\mu\text{Val} = \mu\text{Eq}$) at rest, and during and after exercise while breathing normal air and hypoxic mixtures of 15.9 and 12.7% oxygen. While breathing the 12.7% oxygen

mixture, more glucose was extracted and increased levels of lactate were released. There was a markedly reduced extraction of free fatty acids during maximal work (29).

as compared with the aerobic capacity — is about 6%. This is found, however, for only a short while on arrival at altitude, after which the lactate levels fall. Whether this is a result of a decreased energy delivery or of increased lactate metabolism is undecided at present. In support of the latter possibility is the fact that with altitude training, the glycolytic capacity of muscle tissue is sharply increased compared with the results obtained at sea level (48, 49).

Diphosphoglycerate

Residence at altitude (16, 39, 40) or training (10, 46, 53) produce a higher concentration of 2-3-diphosphoglycerate in the erythrocytes with a resultant shift in the oxygen dissociation curve to the right (5, 51). Although, residence at altitude or training *alone* may not have a significant effect on performance capacity, together they may.

Iron metabolism

Interesting information on altitude acclimatization and de-acclimatization may be obtained by studying the various aspects of iron metabolism. As is well known, iron turnover is affected both by altitude and by exercise. Preliminary investigation on altitude-trained top swimmers (five weeks at 2,000m — 6,560 ft) showed essentially:

a) higher resting levels of blood serum haptoglobin, transferrin, iron, copper, ceruloplasmin, and haemopexin 10 days after return to sea level compared with the levels before altitude training; and

b) a decreased response of these factors to the same exercise programme (120 minutes swimming training) done 10 days after return from altitude, compared with the response immediately before starting the altitude training (22).

Fig. 12. Content of lactic acid in the blood of well-trained athletes at rest, and during and after maximal exercise. It is clearly evident that the lactic acid levels during and 3 minutes after maximal exercise at Mexico City were markedly higher than those found under the same conditions in Freiburg. After a four week residence at Mexico City the differences were small. Also after preceding period of acclimatization at Font Romeu (1,800m – 25,900 ft), the lactic acid level on arrival at Mexico City was higher. There was a drop in the lactic acid level on sub-maximal exercise during the stay at Mexico City (34).

This latter finding lends support to the belief in a favourable effect of training at moderate altitude – after altitude training, the same exercise stimulus was unable to evoke the same response as before. We suggested that these aspects as well as related ones, should be given more attention when the various facets of altitude training are studied.

The Lungs

We should also point out here that the first four to five days at altitude may be critical as far as further adaptation is concerned and for determining the quantity and quality of training which will be carried out for the remaining period. During the initial 72 hours at altitudes above 3,000m (9,850 ft), the pulmonary system shows a “negative” adaptation; alveolar-arterial pO_2 differences increased from 3.1 to 11 mm Hg presumably due to a decrease in pulmonary capillary blood volume leading to a decreased diffusing capacity (11, 38). Dempsey et al (11) showed that there was no further decrement in pulmonary performance after the initial four days at 3,000m. There are indications, however, that longer residence (more than 1 year) may result in an increase of the alveolar surface area, thus

effectively enlarging the area available for gas exchange. In a study on 10 untrained sea-level residents Reddan et al (47) could find no effect on pulmonary gas exchange of training at 3,000m; but again, it does seem that longer residence at altitude may produce adaptations which give the athlete at altitude an oxygen transport system similar to that of the athlete at sea level (20).

Summary

Thus, the following main advantages derive from altitude training and persist for a period, after return to sea level:

1. Increase of haemoglobin and total blood volume.
2. Increased enzyme activity in the glycolytic and oxidative energy delivering system including myoglobin.
3. Shift to the right of the oxygen dissociation curve resulting from a higher 2-3-diphosphoglycerate level.

The disadvantages are an increase in the viscosity of the blood with a consequent addition to the work of the heart, and an increase in the work of breathing due to the higher ventilation rate.

From our understanding of the tests done at altitude, various physiological adaptations *can* promote a better physical performance. The question still remains, though, whether hard training at altitude effects a greater increase in performance than the same training carried out at sea level.

The problem has been studied, but with inconclusive results. On the one hand higher physical performance after altitude training has been reported (3, 17, 37), but on the other, an increased maximal oxygen uptake has not been confirmed (8, 18, 21). In these studies with one exception (21), there were no training groups at sea level to act as controls. The exception was the large study of Mellerowicz et al (43) on untrained persons (policemen). The following conditions were the same in both the sea-level group and the group training at an altitude of 2,000m (6,560 ft):

1. Type and duration of training. Intensity, however, was set at the same percent of maximal performance capacity. This meant that due to the decreased maximal performance capacity, intensity was always lower at altitude.
2. Training groups and environmental conditions; for instance, diet, sleeping time, and so forth.
3. Methods and times of measurement of the performance of physical work.

The running time of the altitude training group was significantly faster when they returned to sea level (Fig.

Fig. 13. Mean increase in maximal 3,000m running performance (sec) between the last measurement before starting the main training programme and after training measured in groups I Ma and II SMO. (I Malente = sea level; II St Moritz = 1,800 - 2,500m - 5,900 - 8,200 ft) (43).

Fig. 14. Mean increase in maximal $\dot{V}O_2$ measured before and 14 days after training in groups I Ma and II SMO. (I Malente = sea level; II St Moritz = 1,800 - 2,500m - 5,900 - 8,200 ft.) (43).

Fig. 15. Mean maximal $\dot{V}O_2$ ($ml \cdot min^{-1}$, STPD) during bicycle ergometer work in groups I Ma and II SMO. Points left to right: before, immediately after, and 14 days after training. Maximal $\dot{V}O_2$ were measured at 50m (164 ft) altitude. (I Malente = sea level; II St Moritz = 1,800 - 2,500m - 5,900 - 8,200 ft) (43).

Fig. 16. A comparison of 3,000m performance increase (sec) with the increase in maximal $\dot{V}O_2$. $\bullet$ = group Ma, $\circ$ = group SMO. (Malente = sea level; St Moritz = 1,800 - 2,500m - 5,900 - 8,200 ft) (43).

13), an effect which lasted more than three weeks. The oxygen uptake after altitude training was also significantly higher on return to sea level and also remained so for more than three weeks (Figs. 14, 15 and 16).

Conclusions

But what we do not know is whether we can transfer these data obtained on untrained persons to top athletes. The physiological regulation and adaptation processes of top athletes are already well extended by their training programmes at sea level and the limit to any increase in

individual performance has possibly been reached. It may also be that the necessary reduction of the intensity of training at altitude limits the positive effect of hypoxia.

If we were to advise on the strength of both the scientific and the practical observations we would recommend altitude training for endurance events — in spite of still unresolved problems. Although we cannot state that training at altitude (2,000 — 2,500m; 6,560 — 8,200 ft) has a *positive* effect on performance, we can say, with reasonable certainty, that no definite *negative* effects have been identified.

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BRITISH ASSOCIATION OF SPORTS MEDICINE

ADVANCE NOTICE

The British Association of Sport and Medicine is preparing to hold a one week residential course in "The Medical Aspects of Sport" in the autumn of 1975.

The subjects to be covered include the physiological and biomechanical aspects of sport and training; clinical aspects of the management of sportsmen and their medical and psychological problems; the uses of sport in rehabilitation; and the role of the doctor, the coach and the remedial therapist in sport.

The syllabus meets the requirements of, and the participants may become eligible for membership of, the International Federation of Sports Medicine (F.I.M.S.). Section 63 approval is expected for general practitioners.

Small group tutorials will be a part of the course and in order to plan the most satisfactory arrangements for participants the organisers invite those interested to communicate with the Secretary. **In the light of the recent change in the D.Phys.Med. diploma which allows Sports Medicine as a special subject in Part II in the new D.Med.Rehab. from 1976, this course may be of particular interest to Registrars in Rheumatology and Rehabilitation.**

For further information please communicate with the Honorary Secretary, British Association of Sport and Medicine,

DR. P. N. SPERRY, 63 ALRIC AVENUE, NEW MALDEN, SURREY.