

Physiological implications of altitude training for endurance performance at sea level: a review

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Summary

Acclimatisation to environmental hypoxia initiates a series of metabolic and musculoskeletal-respiratory adaptations that influence oxygen transport and utilisation. Whilst it is clear that adequate acclimatisation, or better still, being born and raised at altitude, is necessary to achieve optimal physical performance at altitude, scientific evidence to support the potentiating effects after return to sea level is at present equivocal. Despite this, elite athletes continue to spend considerable time and resources training at altitude, misled by subjective coaching opinion and the inconclusive findings of a large number of uncontrolled studies. Scientific investigation has focused on the optimisation of the theoretically beneficial aspects of altitude acclimatisation, which include increases in blood haemoglobin concentration, elevated buffering capacity, and improvements in the structural and biochemical properties of skeletal muscle. However, not all aspects of altitude acclimatisation are beneficial; cardiac output and blood flow to skeletal muscles decrease, and preliminary evidence has shown that hypoxia in itself is responsible for a depression of immune function and increased tissue damage mediated by oxidative stress. Future research needs to focus on these less beneficial aspects of altitude training, the implications of which pose a threat to both the fitness and the health of the elite competitor.

Paul Bert was the first investigator to show that acclimatisation to a chronically reduced inspiratory partial pressure of oxygen (P_{iO_2}) invoked a series of central and peripheral adaptations that served to maintain adequate tissue oxygenation in healthy skeletal muscle,¹ physiological adaptations that have been subsequently implicated in the improvement in exercise performance during altitude acclimatisation. However, it was not until half a century later that scientists suggested that the additive stimulus of environmental hypoxia could potentially compound the normal physiological adaptations to endurance training and accelerate performance improvements after return to sea level. This has stimulated an exponential increase in scientific research, and, since 1984, 22 major reviews have summarised the physiological implications of altitude training for both aerobic and anaerobic performance at altitude and after return to sea level. Of these reviews, only eight have specifically focused on physical performance changes after return to sea level,²⁻⁹ the most comprehensive of which was recently written by Wolski *et al.*⁹

Few reviews have considered the potentially less favourable physiological responses to moderate altitude exposure, which include

decreases in absolute training intensity,¹⁰ decreased plasma volume,¹¹ depression of haemopoiesis and increased haemolysis,¹² increases in sympathetically mediated glycogen depletion at altitude,¹³ and increased respiratory muscle work after return to sea level.¹⁴ In addition, there is a risk of developing more serious medical complications at altitude, which include acute mountain sickness, pulmonary oedema, cardiac arrhythmias, and cerebral hypoxia.¹⁵ The possible implications of changes in immune function at altitude have also been largely ignored, despite accumulating evidence of hypoxia mediated immunosuppression.¹⁶

In general, altitude training has been shown to improve performance at altitude, whereas no unequivocal evidence exists to support the claim that performance at sea level is improved. Table 1 summarises the theoretical advantages and disadvantages of altitude training for sea level performance.

This review summarises the physiological rationale for altitude training as a means of enhancing endurance performance after return to sea level. Factors that have been shown to affect the acclimatisation process and the subsequent implications for exercise performance at sea level will also be discussed.

Studies were located using five major database searches, which included Medline, Embase, Science Citation Index, Sports Discus, and Sport, in addition to extensive hand searching and cross referencing. All published English studies, dating back from the present day to 1956, that included physiological measurements during exercise before and after hypoxic training were incorporated in the overall analysis. Ninety one investigations were selected, which included 772 hypoxically trained experimental and 209 normoxically trained control subjects.

The investigations were subdivided according to whether a normoxically trained control group was incorporated into the experimental design. Other classifications were made depending on the characteristics of the hypoxic stimulus, which included type (normobaric or hypobaric hypoxia; continuous or intermittent), duration, and magnitude (calculated ambient P_{O_2}), and timing of physiological testing after the descent to sea level.

The continued popularity of altitude training has been influenced by two factors. Firstly, hypoxia in itself increases blood haemoglobin (Hb) concentration, which has been shown to improve endurance performance. Secondly, several of the best endurance runners in the world have originated from East African countries that are based at altitude (1500-2000 m). Is it possible that either living and/or training at

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Table 1 Physiological changes during altitude acclimatisation in native lowlanders; time course and theoretical implications for exercise performance at sea level

| Physiological advantages | Response time | Physiological disadvantages | Response time |
|--|-------------------|--|---------------------|
| Increased free fatty acid mobilisation | Weeks | Increased ventilation | Immediate |
| Increased haemoglobin | Days | Decreased cardiac output | Days |
| Increased capillarity | Months/ years? | Decreased blood flow | Days |
| Increased oxidative enzyme activity | Weeks | Immunosuppression | Immediate?/ days |
| Increased mitochondrial volume | Weeks | Increased oxidative stress and tissue damage | Immediate |
| | | Increased dehydration | Immediate |
| | | Jet lag | Immediate |
| | | Decreased training intensity | Immediate |
| | | Acute mountain sickness | Days |
| | | Sunburn due to increased ultraviolet B (290-320nm) | Immediate |
| | | Catecholamine mediated glycogen depletion | Days-weeks |
| | | Increased haemolysis | Weeks |

altitude may contribute to their running success?

Physiological rationale for altitude training

AUTOLOGOUS BLOOD REINFUSION AND ENDURANCE PERFORMANCE

One of the most documented physiological adaptations to a reduced P_{iO_2} is the increased release of erythropoietin, which causes a transient increase in red blood cell mass.¹⁷ The implications of secondary polycythaemia to both submaximal and maximal indices of endurance performance have been clearly shown by studies that have artificially induced erythrocythaemia after either autologous blood reinfusion¹⁸ or subcutaneous injections of recombinant human erythropoietin.^{19, 20} Table 2 summarises the major research findings. It has been reported that absolute maximal oxygen uptake ($\dot{V}O_{2MAX}$) values are increased by about 200 ml/min per g/dl increase in Hb, irrespective of the methods by which polycythaemia is induced.²¹

However, the use of blood doping as an ergogenic aid is considered unethical and potentially dangerous and is banned by the International Olympic Committee.²²

PHYSIOLOGICAL ADAPTATIONS OF THE NATIVE HIGHLANDER: A SUPERIOR ATHLETE?

Figure 1 illustrates the apparently disproportionate running success of the native highlander. This figure represents data obtained

Table 2 Effects of autologous blood reinfusion on $\dot{V}O_{2MAX}$

| Author/reference | Volume of blood reinfused (ml) | Change in Hb after reinfusion (%) | Change in $\dot{V}O_{2MAX}$ after reinfusion (%) |
|-------------------------|--------------------------------|-----------------------------------|--|
| Ekblom ¹⁹ | 1350 | +9* | +8* |
| Celsing ²¹ | 2250 | +11 | +7** |
| Buick ²³ | 900 | +8** | +5** |
| Spriet ²⁴ | 1200 | NR | +7* |
| Williams ²⁵ | 920 | +7** | NR |
| Goforth ²⁶ | 760 | +4* | +11** |
| Robertson ²⁷ | 750 | +28* | +13* |
| Robertson ²⁸ | 475 | +16* | +10* |
| Thompson ²⁹ | 1000 | +12* | +11* |
| Sawka ³⁰ | 600 | +10* | +11* |
| Robertson ³¹ | 475 | +16* | +10** |

* Significantly different from before reinfusion ($P < 0.05$).

** Significantly different from before reinfusion ($P < 0.01$).

NR, not reported.

from athletes who were born and raised at a median altitude of 2000 m above sea level. This phenomenon has prompted several comparative investigations into what, if any, physiological adaptations mediated by hypoxia could contribute to their superiority in distance running events. Much interest has focused on the four steps of the oxygen transport system, namely alveolar ventilation, lung diffusion, circulatory oxygen transport, and tissue oxygen extraction. Studies have shown that the native highlander is characterised by a larger pulmonary diffusion capacity³² and adaptations in the structural and metabolic organisation of skeletal muscle that result in a tighter coupling between ATP hydrolysis and oxidative phosphorylation.³³ These are the major factors that facilitate oxygen transport and utilisation. The significance of these adaptations has been elucidated in a series of investigations that have reported higher values for $\dot{V}O_{2MAX}$,³⁴ power output,³⁵ arterial oxygen saturation,³⁶ and cerebral oxygen delivery³⁷ during maximal exercise and decreased blood lactate^{33, 35} and ammonia concentrations³⁸ for a given submaximal work rate.

To what extent these physiological adaptations are acquired as the result of inheritance or hypobaric hypoxia is not well defined. The influence of genetic factors on quantitative oxygen transport was recently investigated in a unique study by Beall *et al.*³⁹ They identified a major gene that enhances arterial oxygen saturation in sedentary Tibetan natives. The physiological significance of this was shown by Niermeyer *et al.*,⁴⁰ who concluded that genetic adaptations to hypobaric hypoxia resulted in improved oxygenation and conferred resistance to subacute infantile mountain sickness. These adaptations were more pronounced in a cohort of Tibetan newborns whose ancestors have resided at altitude for 50 000 to 100 000 years, in comparison with Han newborns whose ancestors had resided at altitude for only 45 years.⁴¹ In general, these findings would suggest that a lifetime or perhaps generations of altitude exposure are responsible for the biological distinctiveness of the high altitude population.

Altitude training and sea level endurance performance in native lowlanders

Table 3 summarises the effects of altitude training on sea level endurance performance. The weight of scientific evidence does not support the potentiating effects of altitude training. However, it is becoming clearer that a number of methodological deficiencies may preclude the potential synergistic effects of hypoxia and physical exercise, the physiological implications of which will be discussed in the following sections.

Intensity and duration of the hypoxic stimulus and associated haematological adaptation

There is still much controversy about the optimal altitude and duration required for athletes to train in an attempt to optimise endurance performance at sea level. Much attention has

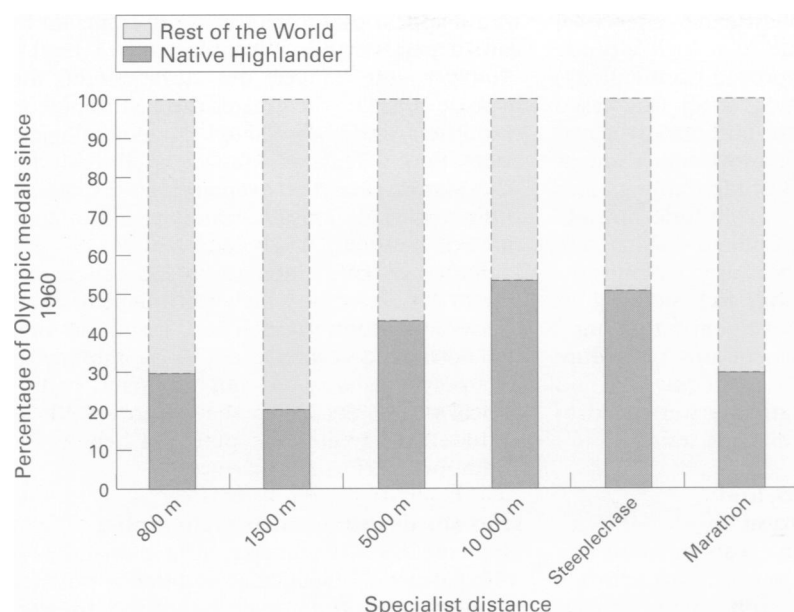


Figure 1 Percentage of Olympic medals for middle and long distance running events won by native highlanders since 1960.

Table 3 Effects of hypoxic training on sea level endurance performance

| Hypoxic stimulus | Altitude (m) | Exposure time (days) | Time tested after altitude (days) | Submaximal improvement | Change in $\dot{V}O_{2\text{MAX}}$ (%) | Control group |
|--------------------------------|--------------|----------------------|-----------------------------------|------------------------|--|---------------|
| <i>Potentiating effects</i> | | | | | | |
| CH ⁴² | 1300–2500 | 28 | 1 | Yes† | +4† | No |
| CH ⁴³ | 1900 | 21 | 1/14 | Yes† | NS/NS | No |
| CH ⁴⁴ | 2100–2700 | 14 | 2 | Yes† | NS | No |
| CH ⁴⁵ | 2300 | 23 | 3/21 | Yes† | +8†/+10† | No |
| CH ⁴⁶ | 2500 | 28 | 7 | ND | +6† | No |
| IH ⁴⁷ | 3049–4268 | 23 | 3–4 | Yes† | NS | No |
| CH ⁴⁸ | 3800 | 35 | 14 | ND | +14† | No |
| IH ⁴⁹ | 4020 | 21/28 | 1 | Yes† | +8†/+26‡ | No |
| CH ⁵⁰ | 1250–2500 | 28 | 7 | Yes† | +4† | Yes |
| IH ⁵¹ | 2300 | 21–28 | 1 | Yes† | NS | Yes |
| IH ⁵² | 2300 | 28 | 1–2 | Yes† | ND | Yes |
| IH ⁵³ | 4000 | 70 | 1 | Yes† | NS | Yes |
| <i>No potentiating effects</i> | | | | | | |
| CH ⁴⁵ | 2300 | 14 | 1 | No | NS | No |
| CH ⁵⁴ | 1695–2700 | 7 | 4 | ND | NS | No |
| CH ⁵⁵ | 2240 | 20 | 4/22 | ND | +6/+9* | No |
| CH ⁵⁶ | 2300 | 42 | 4–5 | No | NS | No |
| CH ⁵⁷ | 2300 | 70 | 5 | ND | NS | No |
| CH ⁵⁸ | 2800 | 10 | 2–4 | No | +7* | No |
| CH ⁵⁹ | 3090 | 17 | 1 | ND | NS | No |
| CH ⁶⁰ | 3110 | 21 | 7 | ND | -5* | No |
| CH ⁶¹ | 4000 | 48–63 | 2–15 | No | NS | No |
| IH ⁶² | 4000 | 21 | 1 | ND | NS | No |
| CH ³⁸ | 2000 | 14 | 6/12 | ND | NS/NS | Yes |
| CH ⁶³ | 1600–1800 | 18–28 | 7 | ND | NS | Yes |
| CH ⁶⁴ | 1640 | 28 | 20 | No | NS | Yes |
| CH ⁶⁵ | 1700–2000 | 28 | 7 | No | NS | Yes |
| CH ⁶⁶ | 2300 | 21 | 1 | No | NS | Yes |
| IH ⁶⁷ | 2250 | 28 | 1 | ND | +17.5* | Yes |
| IH ⁶⁷ | 3450 | 28 | 1 | ND | +10.0* | Yes |
| IH ⁶⁸ | 2500 | 28 | 1 | No | NS | Yes |
| IH ⁶⁹ | 2500 | 35 | 1 | ND | NS | Yes |
| CH ⁷⁰ | 2600 | 11 | 1 | ND | NS | Yes |
| IH ⁷¹ | 3100 | 19 | 6 | No | NS | Yes |
| IH ⁷² | 3345 | 42 | 1 | ND | NS | Yes |
| IH ⁷³ | 4020 | 15 | 1 | ND | NS | Yes |
| IH ⁷⁴ | 4100–5700 | 21 | 1 | ND | NS | Yes |
| CH ⁷⁵ | 4300 | 28 | 1–5 | ND | NS | Yes |

CH, Chronic hypobaric; IH, intermittent hypobaric; ND, no data.

* Level of significance not reported.

† Significantly different from pre-altitude value ($P < 0.05$).

‡ Significantly different from pre-altitude value ($P < 0.01$).

NS, not significantly different from pre-altitude value ($P > 0.05$).

can train the better. However, other factors that inhibit exercise performance are exacerbated with a reduction in PO_2 . Acute mountain sickness presents at altitudes above 2000 to 3000 m,⁷⁷ with the possibility of the elite athlete suffering physiological symptoms at even lower altitudes.¹⁵ Prolonged exposure to altitudes above 4500 m has been shown to result in a reduction in muscle mass, the underlying physiological mechanisms for which have been recently reviewed by Kayser.⁷⁸ Finally, the effects of training at a lower PO_2 may result in a reduction in work rate, so that detraining may override the potential benefits of altitude acclimatisation.⁷⁹

Hypoxia and detraining

A recent study has shown that $\dot{V}O_{2\text{MAX}}$ is significantly reduced at an altitude as low as 610 m above sea level in elite endurance athletes.⁸⁰ This is a phenomenon peculiar to about 50% of trained subjects, with $\dot{V}O_{2\text{MAX}}$ values of above 65 ml/kg per min or 4 litres/min.⁸¹ These elite athletes develop more severe levels of arterial hypoxaemia during maximal and submaximal exercise than sedentary controls both under normoxic and hypoxic conditions.^{82 83} Several mechanisms have been proposed to explain these findings, which include hypoventilation, venoarterial shunting, ventilation-perfusion inequality, and an alveolar-capillary diffusion limitation.^{84 85}

These observations led early investigators to hypothesise that altitude exposure may result in a detraining response.⁷⁹ Daniels and Oldridge⁵⁷ have shown the importance of training intensity at altitude and its effects on sea level performance. They suggested that intermittent exposures to altitudes of 2300 to 3300 m and sea level optimised the balance between hypoxic acclimatisation and training intensity. Despite the experimental limitations of a single group design, two world records and 12 personal best times were recorded by athletes on return to sea level, which presented a reasonable endorsement for such an approach. However, from our experience, it is equally possible to have expected similar improvements in a control group training at sea level.⁶⁴

The detraining effect induced during chronic exposure to hypobaric hypoxia has been quantified in a sequence of studies by Levine *et al.*^{42 50 68} In their most recent study,⁵⁰ 39 competitive runners were randomly assigned to four weeks of (a) living high (2500 m) and training low (1250 m), (b) living high (2500 m) and training high (2500 m), or (c) living low (150 m) and training low (150 m). They showed that, although $\dot{V}O_{2\text{MAX}}$ values significantly improved 5 km race performance times by 4% in the two altitude trained groups, the running velocity that corresponded to $\dot{V}O_{2\text{MAX}}$ and the ventilatory threshold at sea level were significantly improved only in the group that lived high and trained low. An unusual finding was that 5 km performance time was 31 seconds slower in the sea level control group, which would suggest that the training stimulus was not absolutely controlled during the experimental period. Nevertheless, it was

focused on the erythropoietic response to hypoxia and subsequent haematological adaptation. Considering the inverse relationship between PO_2 and resting Hb concentration,⁷⁶ it would seem logical that the higher the athlete

concluded that the potentiating effects of altitude training were due to a high altitude acclimatisation effect (improved haematology) and a low altitude training effect (increased training intensity). Thus the authors advocated the practice of living high and training low as the optimal approach to altitude training. This has popularised the use of "altitude houses" recently developed in Finland which are portable hypobaric chambers used by elite athletes, who alternate living and sleeping at simulated altitude with normobaric training.⁸⁶ However, the effectiveness of this procedure should at present be considered equivocal, and further scientific investigation is warranted to endorse this approach to altitude training.

Concept of a critical P_{O_2} and haematological adaptation

Few athletes can afford the costs inherent in a "live high, train low" approach to altitude training. Therefore is it possible that a "threshold" altitude exists that optimises the benefits of haematological acclimatisation and minimises the negative effects of detraining? Weil *et al.*⁸⁷ have presented the most comprehensive evidence indicating the existence of such a threshold, albeit in sedentary highland natives (B Levine, personal communication). They identified a biphasic relationship between the arterial partial pressure of oxygen (P_{aO_2}) and red blood cell mass, and shown a clear inflection point at a "critical" P_{aO_2} of 67 mm Hg, equivalent to an interpolated arterial oxygen saturation of 92%. This point corresponds to the steeper portion of the oxygen-Hb dissociation curve. The equivalent P_{O_2} would equate to about 135 mm Hg, which is comparable with an altitude of 2200–2500 m above sea level required to stimulate sufficient haemopoiesis at rest to influence endurance performance.⁴ However, it has been shown that the decrement in $\dot{V}O_{2MAX}$ measured in hypobaric hypoxia is directly proportional to $\dot{V}O_{2MAX}$ measured in normoxia.⁸⁸ This would suggest that elite athletes are more prone to developing arterial hypoxaemia and may gain more benefit haematologically by training at lower altitudes in comparison with sedentary controls. This contention was supported by Ingjer *et al.*,⁴³ who showed that three weeks of altitude training at 1900 m in elite cross country skiers was sufficient to elevate Hb by 5% ($P < 0.02$) and decrease blood lactate concentration during a standardised submaximal test, despite no changes in $\dot{V}O_{2MAX}$. However, it should be noted that these authors did not measure their subjects' plasma volumes, and their comments that the polycythaemia was independent of a haemoconcentration remains only speculative. The scarcity of training studies conducted at moderate altitudes of 1500 to 2000 m in elite athletes does not allow definitive conclusions to be made.

Optimal duration

Few data are available on the optimal time an athlete should spend training at altitude. On the basis of subjective coaching opinion as opposed to objective scientific evidence, it

would appear that three weeks are sufficient to gain a performance advantage at sea level.⁸⁹ However, the longer the duration of the hypoxic stimulus the greater the erythropoietic response and associated haematological adaptation.¹⁷ This was shown by Berglund,⁹⁰ who summarised the haematological changes during previous altitude training studies conducted between 1829 and 3048 m. He identified a "true" increase in Hb concentration of 1% per week, which was independent of a haemoconcentration. Thus, assuming that the detraining response could be minimised and polycythaemia did not approach pathological values, the longer the athlete spends at altitude, the greater the potential benefit for endurance performance.

Iron status during altitude training

Hypoxia in itself increases iron demand and mobilisation,^{91 92} such that endurance athletes training at altitude may be prone to iron deficiency. Lack of this critical erythropoietic factor has been shown to inhibit complete haematological adaptation.⁹³ Despite its importance, few studies have actually reported iron status of athletes during their hypoxic exposure. Suboptimal iron stores may account for the vast majority of training studies that have failed to show increases in Hb concentration and endurance performance on return to sea level after the hypoxic exposure. The differences in iron status may also characterise the highly individualised haematological responses observed during altitude training.⁴³

Interval between descent and event

There is some evidence to suggest that endurance performance is affected by the timing of the descent to sea level after a sojourn to altitude. The general consensus amongst top coaches would suggest that endurance performance is optimised after 14 days at sea level after a bout of altitude training,⁸⁹ yet there is no scientific evidence to support this claim. Suslov⁹⁴ characterised the undulating nature of endurance performance after altitude training. His research was based on over 1000 competitive track results obtained from middle and long distance runners after different periods of altitude training (1300–2500 m) and repeated sea level $\dot{V}O_{2MAX}$ tests conducted after training at 1800 m. He identified a decrease in competition performance during the first two days at sea level and the first phase of enhanced work capacity occurring between days 3 and 7, followed by a decrease between days 8 and 10. Performance was shown to continue to improve between days 12 and 13, with the best results achieved on days 18 to 20. He also identified an additional upsurge in performance between days 36 and 48 after altitude. He failed to identify the physiological mechanisms responsible for this phenomenon.

Few studies have tested subjects on more than one occasion after return to sea level. Asahina *et al.*⁹⁵ and Faulkner *et al.*⁹⁵ did not show any significant changes in $\dot{V}O_{2MAX}$ values after either 3 or 22 days at sea level. Ingjer *et al.*⁹³ showed that after a group of elite cross country

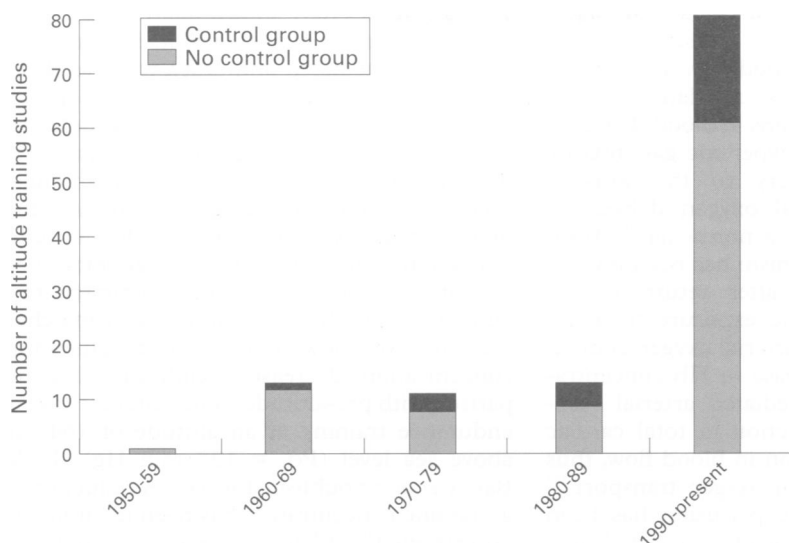


Figure 2 Number of hypoxic training studies conducted with or without a normoxically trained control group since 1950.

skiers had trained for three weeks at an altitude of 1900 m, submaximal blood lactate values were lower than pre-altitude values on day 1 but not day 14 at sea level. The authors concluded that a 0.8 g/dl increase in Hb concentration measured on day 1 was responsible for the observed improvement in submaximal exercise. However, their failure to quantify plasma volume and blood flow changes weakens the validity of their haematological findings. Svedenhag *et al.*⁸⁸ studied a group of Swedish middle distance runners who trained for a period of two weeks at altitude (2000 m) and were tested after 6 and 12 days on return to sea level. They did not identify any significant changes in $\dot{V}O_{2\text{MAX}}$, maximal oxygen deficit, and submaximal blood lactate values compared with pre-altitude values or between days 6 and 12 at sea level. However, they showed a significant reduction in heart rate, Borg rating of perceived exertion, and plasma ammonia concentration during a standardised submaximal treadmill test, which was more apparent after 12 days at sea level.

The physiological mechanisms responsible for these subtle changes in performance at sea level remain elusive. Intermittent altitude training has been shown to increase the hypoxic ventilatory response in a group of sedentary subjects, whereas an equivalent training programme at sea level had no effect.^{14 95} Acute exposure to altitude in the native lowlander may potentiate the hypoxic ventilatory response because of an increased peripheral chemoreceptor sensitivity, which would subsequently increase the work performed by the respiratory muscles. This has not been quantified in the elite athlete but may be implicated in the performance decrements shortly after return to sea level. Plasma volume has been shown to decrease by 25% during chronic exposure to hypobaric hypoxia¹¹ and may take as long as two months to normalise.⁹¹ After return to sea level, this may remain depressed for six days,⁹⁶ which may also negatively affect performance. Altitude training may also involve considerable travelling time, and the

negative impact of jet lag on exercise performance cannot be ignored.⁹⁷

Measurement of the altitude effect independent of training

Figure 2 shows that, since 1956, only 27 (30%) of the 91 hypoxic training studies reviewed have incorporated a normoxically trained control group. This makes it impossible to determine whether the physiological changes that occur after a bout of altitude training can be attributed to an improvement in physical conditioning or to the additive effects of hypoxia itself.

To our knowledge, the altitude training studies conducted by Asano *et al.*,⁵³ Terrados *et al.*,^{51 52} and Levine *et al.*⁶⁰ would appear to be the only investigations employing a control group that have reported statistically significant improvements in aerobic performance after return to normoxia. Asano *et al.*⁵³ studied ten elite middle to long distance male runners, who trained for a ten week period at the same relative exercise intensity at either sea level or a simulated altitude of 4000 m. After training, there were no improvements in $\dot{V}O_{2\text{MAX}}$ at sea level, yet 10 km personal best running times improved by about 6% ($P < 0.05$). Using a one legged training model, Terrados *et al.*^{51 52} attributed the potentiating effects of intermittent hypobaric training to increases in citrate synthase activity and myoglobin content. The findings of Levine *et al.*⁶⁰ have already been described in this review.

Whilst previous investigations have dealt primarily with aerobic responses to altitude training, there is some evidence to suggest that anaerobic performance is improved on return to sea level.^{44 98 99} Mizuno *et al.*⁴⁴ showed that exercise time to exhaustion after altitude training improved by 17% ($P < 0.05$) when compared with pre-altitude values, which they attributed to a 6% increase ($P < 0.05$) in muscle buffer capacity. However, the validity of these findings is questionable because of the lack of a normoxically trained control group. A well controlled investigation by Martino *et al.*,⁹⁸ which incorporated a performance matched control group based at sea level, investigated the effects of three weeks of altitude training at 2800 m on anaerobic measures of swimming performance. Sea level sprint performance time over 100 m was 2.4 seconds quicker in the altitude trained group than the control group ($P < 0.05$). The largest improvements in the altitude trained group were noted in an upper body Wingate test. Peak power output increased by 27.9 W more than the control group ($P < 0.05$). In a recent investigation, Nummela *et al.*⁹⁹ showed that ten days of living high (~2200 m) and training low (sea level) resulted in greater improvements in 400 m running time ($P < 0.05$) and running velocity at a fixed concentration of blood lactate ($P < 0.05$) when compared with an equivalent programme of sea level training.

However, the vast majority of altitude training studies have not identified performance improvements at sea level. Whilst a decrease in absolute training intensity may be implicated,¹⁰

a decrease in muscle perfusion may also play a contributory role; oxygen transport, determined as a product of blood flow and arterial oxygen concentration is regulated during changes in P_{aO_2} . Reductions in blood flow during the inhalation of a hyperoxic gas mixture regulates oxygen delivery to the working muscles, such that total oxygen delivery is similar to that observed in normoxia¹⁰⁰. Autoregulation of this mechanism has been investigated at altitude and after return to sea level.^{101 102} Whilst chronic exposure to hypobaric hypoxia increased arterial oxygen content as the result of an increase in Hb concentration, sympathetically mediated arterial vasoconstriction and a reduction in total cardiac output caused a reduction in blood flow, thus preventing an increase in oxygen transport.¹⁰¹ This decrease in muscle perfusion has been shown to persist after return to sea level. Using ¹³³Xe, blood flow to the vastus lateralis was shown to decrease by up to 39% ($P < 0.001$) during submaximal exercise after a three month expedition to 8398 m.¹⁰²

Favier *et al.*⁷² suggested that the negative findings reported in the literature could, in part, be attributed to the fact that subjects were not fully acclimatised to hypobaric hypoxia. In a unique experiment they used three groups of sedentary high altitude residents, who trained for 30 minutes a day at a constant work rate on a bicycle ergometer, during a six week period. Group 1 trained at a P_{O_2} that was equivalent to an interpolated altitude of 3345 m at 70% of $\dot{V}O_{2MAX}$ determined in hypoxia. The remaining two groups trained under normoxic conditions at either the same relative work rate (70% of the normoxic $\dot{V}O_{2MAX}$) or the same absolute work rate (70% of the hypoxic $\dot{V}O_{2MAX}$) as the hypoxically trained group. An incremental test to exhaustion was performed by all groups in normoxia and hypoxia immediately before and after training in an attempt to ascertain the physiological responses to submaximal and maximal exercise. The authors showed that $\dot{V}O_{2MAX}$ values improved similarly in all groups. However, they suggested that a lower reduction in base excess and bicarbonate stores observed in the hypoxically trained group could only potentially benefit anaerobic metabolism and, although time to exhaustion was not measured, facilitate exercise performance.

Hypoxia and immune function

Changes in total leucocyte, granulocyte, monocyte, lymphocyte, natural killer cell, and T cell count, helper/suppression cell ratio, cell proliferation in response to mitogens, and serum immunoglobulin levels have all been implicated in some form of immunosuppression, which may subsequently cause underperformance in the athlete at sea level.¹⁰³ The additive stress of a reduction in the inspiratory P_{O_2} , in conjunction with the extensive training loads employed by athletes at altitude, may explain why some investigators have reported physiological evidence for a less favourable modulation of immune function in vivo during acute and chronic exposure to hypobaric hypoxia.^{63 104-106}

Human studies have shown that chronic exposure to hypobaric hypoxia results in a suppression of cell mediated immunity, whereas B cell function remains unimpaired.¹⁶ Animal studies have further shown that murine host defences against bacterial pathogens are also impaired in hypoxia. The contributory immunomodulatory role of endogenous glucocorticoids and neuropeptides, which are increased at altitude, may contribute to the observed alterations in immune competence. In an experiment that employed elite distance runners and matched controls, we showed that plasma glutamine concentrations decreased significantly in comparison with pre-altitude values after 20 days of endurance training at an altitude of 1640 m above sea level ($P_{O_2} = 135$ mm Hg) (D M Bailey *et al.*, unpublished work). A reduction in glutamine concentration has been identified in "overtrained" athletes and may be a contributory factor leading to immunosuppression and underperformance.¹⁰⁷ It is difficult to comment on the physiological mechanisms responsible for these changes, but there is evidence that suggests that chronically elevated levels of circulating catecholamine levels decrease the rate of glutamine transport out of muscle incubated in vitro (Parry-Billings M, unpublished data). In addition to this, Wagenmakers¹⁰⁸ has proposed an alternative mechanism, again related to elevated catecholamine levels observed at altitude.¹¹ He suggested that hypoxia induced glycogen depletion would result in a reduction in the availability of tricarboxylic acid cycle intermediates, in particular 2-oxoglutarate. This is required for the activation of the branched chain amino acid aminotransferase reaction, which ultimately produces glutamine. The implications of the immunosuppressive influence of hypobaric hypoxia for endurance performance warrants further investigation in order to elucidate potential mechanisms that may modulate performance after return to sea level.

Reactive oxygen species at altitude

There is a limited body of evidence suggesting that oxidative injury mediated by free radicals is increased at altitude.¹⁰⁹⁻¹¹¹ Simon-Schnass¹⁰⁹ identified significant increases in indirect indices of free radical mediated lipid peroxidation at altitude, which included increased pentane excretion and thiobarbituric acid reactive substances, decreased erythrocyte filterability, and increased leucocyte and granulocyte counts. Daily supplementation with an antioxidant such as tocopherol (vitamin E) equivalent to 300-400 mg has been shown to improve endurance performance, by theoretically limiting tissue damage.^{109 110} An accelerated production of the highly toxic hydroxyl radical may occur as a consequence of an increased production of free iron derived from altitude induced and training induced destruction of red blood cells.¹¹¹ Thus it would appear that hypobaric hypoxia significantly increases oxidative stress, which has been shown to negatively influence energy metabolism and membrane integrity.

Summary and future research

Physiological acclimatisation to a chronically reduced P_{iO_2} is a prerequisite to achieve optimal physical performance in environmental hypoxia. However, scientific evidence to support the claim that either continuous or intermittent hypoxic training will enhance sea level performance remains at present equivocal. Future research should focus on methodological technicalities that optimise the balance between the favourable and less favourable responses to hypoxia and potential mediators of performance after return to sea level. Preliminary evidence showing that the additive stress of hypobaric hypoxia may provoke an adverse immune response and further potentiate free radical mediated oxidative injury has important implications which, if confirmed by scientific rigor, would present a threat to both the fitness and health of the elite competitor.

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